

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

AASTROM BIOSCIENCES, INC.

(Exact name of registrant as specified in its charter)

MICHIGAN	2834	94-3096597
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(IRS Employer Identification No.)

24 FRANK LLOYD WRIGHT DRIVE
P.O. BOX 376
ANN ARBOR, MICHIGAN 48106
(313) 930-5555

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

R. DOUGLAS ARMSTRONG, PH.D.
PRESIDENT, CHIEF EXECUTIVE OFFICER
AASTROM BIOSCIENCES, INC.
24 FRANK LLOYD WRIGHT DRIVE
P.O. BOX 376
ANN ARBOR, MICHIGAN 48106
(313) 930-5555

(Name, address, including zip code, and telephone number, including area code, of agent for service)

COPIES TO:

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SAN DIEGO, CALIFORNIA 92121	

Approximate date of commencement of proposed sale to the public: As soon as practicable after this Registration Statement becomes effective.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. ☐

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box. ☐

CALCULATION OF REGISTRATION FEE

TITLE OF EACH CLASS OF SECURITIES TO BE REGISTERED	PROPOSED MAXIMUM AGGREGATE OFFERING PRICE(1)	AMOUNT OF REGISTRATION FEE
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Common Stock, No Par Value.....	\$37,375,000	\$11,326
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(1) Estimated solely for the purpose of computing the registration fee.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission acting pursuant to said Section 8(a), may determine.

+-----+
 +INFORMATION CONTAINED HEREIN IS SUBJECT TO COMPLETION OR AMENDMENT. A +
 +REGISTRATION STATEMENT RELATING TO THESE SECURITIES HAS BEEN FILED WITH THE +
 +SECURITIES AND EXCHANGE COMMISSION. THESE SECURITIES MAY NOT BE SOLD NOR MAY +
 +OFFERS TO BUY BE ACCEPTED PRIOR TO THE TIME THE REGISTRATION STATEMENT +
 +BECOMES EFFECTIVE. THIS PROSPECTUS SHALL NOT CONSTITUTE AN OFFER TO SELL OR +
 +THE SOLICITATION OF AN OFFER TO BUY NOR SHALL THERE BE ANY SALE OF THESE +
 +SECURITIES IN ANY STATE IN WHICH SUCH OFFER, SOLICITATION OR SALE WOULD BE +
 +UNLAWFUL PRIOR TO REGISTRATION OR QUALIFICATION UNDER THE SECURITIES LAWS OF +
 +ANY SUCH STATE. +
 +-----+

PROSPECTUS (Subject to Completion)
 Dated November 1, 1996

3,250,000 Shares

[LOGO] AASTROM BIOSCIENCES INC

Common Stock

All of the shares of Common Stock, no par value per share (the "Common
 Stock"), offered are being sold by Aastrom Biosciences, Inc. ("Aastrom" or the
 "Company").

Prior to this offering, there has been no public market for the Common Stock
 of the Company. It is currently estimated that the initial public offering
 price will be between \$8.00 and \$10.00 per share. See "Underwriting" for a
 discussion of the factors considered in determining the initial public offering
 price. Application will be made for quotation of the Common Stock on the Nasdaq
 National Market under the symbol "ASTM."

THIS OFFERING INVOLVES A HIGH DEGREE OF RISK. SEE "RISK FACTORS" BEGINNING ON
 PAGE 5 OF THIS PROSPECTUS.

THESE SECURITIES HAVE NOT BEEN APPROVED OR
 DISAPPROVED BY THE SECURITIES AND EXCHANGE
 COMMISSION OR ANY STATE SECURITIES COMMISSION
 NOR HAS THE SECURITIES AND EXCHANGE
 COMMISSION OR ANY STATE SECURITIES
 COMMISSION PASSED UPON THE ACCURACY OR
 ADEQUACY OF THIS PROSPECTUS. ANY
 REPRESENTATION TO THE CONTRARY IS A
 CRIMINAL OFFENSE.

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	Price to Public	Underwriting Discounts and Commissions(1)	Proceeds to Company(2)
Per Share.....	\$	\$	\$
Total(3).....	\$	\$	\$

- (1) The Company has agreed to indemnify the Underwriters against certain
 liabilities, including liabilities under the Securities Act of 1933. See
 "Underwriting."
 (2) Before deducting expenses payable by the Company, estimated to be \$900,000.
 (3) The Company has granted to the Underwriters an option, exercisable within
 30 days of the date hereof, to purchase an aggregate of up to 487,500
 additional shares at the Price to Public less Underwriting Discounts and
 Commissions to cover over-allotments, if any. If all such additional shares
 are purchased, the total Price to Public, Underwriting Discounts and
 Commissions and Proceeds to Company will be \$, \$ and \$,
 respectively. See "Underwriting."

The Common Stock is offered by the several Underwriters named herein when, as
 and if received and accepted by them, subject to their right to reject orders
 in whole or in part and subject to certain other conditions. It is expected
 that delivery of the certificates for the shares will be made at the offices of
 Cowen & Company, New York, New York, on or about , 1996.

COWEN & COMPANY

J.P. MORGAN & CO.

, 1996

[COLOR FLOW CHART DEPICTING "STEM CELL THERAPY METHODS"
DESCRIBING STEM CELL THERAPY UTILIZING BONE MARROW HARVEST,
PROGENITOR BLOOD CELL MOBILIZATION AND THE AASTROM CPS]

[COLOR PHOTOGRAPH OF A PROTOTYPE OF THE AASTROM CPS WITH A
CLINICIAN INNOCULATING CELLS]

A prototype of the Aastrom CPS is currently being used in a clinical trial and ongoing development activities are directed at completing production level components of the Aastrom CPS. The Company may not market the Aastrom CPS unless and until FDA and other necessary regulatory approvals are received.

IN CONNECTION WITH THIS OFFERING, THE UNDERWRITERS MAY OVER-ALLOT OR EFFECT TRANSACTIONS WHICH STABILIZE OR MAINTAIN THE MARKET PRICE OF THE COMMON STOCK OFFERED HEREBY AT A LEVEL ABOVE THAT WHICH MIGHT OTHERWISE PREVAIL IN THE OPEN MARKET. SUCH TRANSACTIONS MAY BE EFFECTED ON THE NASDAQ NATIONAL MARKET, IN THE OVER-THE-COUNTER MARKET OR OTHERWISE. SUCH STABILIZING, IF COMMENCED, MAY BE DISCONTINUED AT ANY TIME.

PROSPECTUS SUMMARY

The following summary is qualified in its entirety by the more detailed information and financial statements, including the notes thereto, appearing elsewhere in this Prospectus. Prospective investors should carefully consider the information set forth under the heading "Risk Factors."

THE COMPANY

Aastrom Biosciences, Inc. is developing proprietary process technologies and devices for a range of cell therapy applications, including stem cell therapies and gene therapy. The Company's lead product under development, the Aastrom Cell Production System (the "Aastrom CPS") consists of a clinical cell culture system with disposable cassettes and reagents for use in the rapidly growing stem cell therapy market. The Company believes that the Aastrom CPS method will be less costly, less invasive and less time consuming than currently available stem cell collection methods. The Aastrom CPS is designed as a platform product which implements the Company's pioneering stem cell replication technology and which the Company believes can be modified to produce a wide variety of cell types for emerging therapies. The Aastrom CPS is currently in a pre-pivotal clinical trial under an Investigational Device Exemption for autologous stem cell therapy. The Company has entered into a strategic collaboration for the development of the Aastrom CPS in stem cell therapy with Cobe BCT, Inc., a subsidiary of Gambro AB and a world leader in blood cell processing products. In ex vivo gene therapy, the Company is developing a proprietary directed motion gene transfer process (the "Aastrom Gene Loader") and the Aastrom CPS to enable high efficiency genetic modification and production of cells.

Stem cell therapy is a rapidly growing form of cell therapy used to restore blood and immune system function to cancer patients following chemotherapy or radiation therapy. The Company estimates that over 35,000 stem cell therapy procedures were completed worldwide in 1995 and that the number of such procedures is growing at a compound annual rate of over 20%. Other novel cell therapies are under development by third parties, including stem cell therapy for the treatment of autoimmune diseases and for augmenting recipient acceptance of organ transplants. Current stem cell therapy methods, including bone marrow harvest and peripheral blood progenitor cell mobilization, are costly, invasive and time-consuming for both medical personnel and patients. Technologies which facilitate a more readily available source of cells may contribute to additional growth in cell therapy procedures. Umbilical cord blood ("UCB") is emerging as a new source of cells for stem cell therapy, offering additional market opportunity, although the more widespread use of UCB transplants has been restricted by cell quantity limitations.

The Company believes that the Aastrom CPS will offer significant advantages over traditional cell collection methods. Compared with current stem cell collection methods, the Aastrom CPS is expected to involve one patient visit rather than approximately five to seven visits, less than two hours of procedure time rather than in excess of twenty hours of procedure time and approximately four to ten patient needle sticks rather than twenty-five or more patient needle sticks. The Aastrom CPS may permit higher and more frequent doses of chemotherapy to be administered to cancer patients by enabling the production of multiple doses of therapeutic stem cells from patient samples taken at the initial collection.

Aastrom is currently conducting a pre-pivotal autologous stem cell therapy trial. The trial is designed to show that cells produced in the Aastrom CPS can by themselves safely enable recovery of bone marrow and cells of the blood and immune systems in accordance with trial endpoints in patients who have received ablative chemotherapy. Based on the outcome of this and other related trials, the Company intends to seek FDA approval to begin a multi-center pivotal trial for use of the Aastrom CPS in stem cell therapy. It is anticipated that the results of this pivotal trial will be used to support the Company's Pre-Market Approval ("PMA") submission to the FDA. In the near future, the Company plans to initiate a stem cell therapy clinical trial in France, the results of which are expected to be used for the CE Mark registration necessary to market the Aastrom CPS in Europe.

The Company's business strategy is to: (i) establish a consumable-based business model; (ii) focus initially on the currently-reimbursed stem cell therapy market; (iii) leverage Aastrom's cell production technology across multiple cell therapy market opportunities; and (iv) market through collaborative relationships.

Aastrom has entered into a strategic collaboration with Cobe BCT to support the development and marketing of the Aastrom CPS in the field of stem cell therapy. In 1993, the Company entered into a series of agreements in which Cobe BCT purchased \$15,000,000 of the Company's equity securities and acquired the worldwide distribution rights to the Aastrom CPS for stem cell therapy. Under the terms of the collaboration, Aastrom retains manufacturing rights as well as the majority share of all revenue generated by Cobe BCT's sale of the Aastrom CPS. Aastrom also retains all marketing and distribution rights to the Aastrom CPS for other cell types and ex vivo gene therapy applications, including stem cells.

The Company's patent portfolio includes patents relating to both stem and progenitor cell production, processes for the genetic modification of stem and other cell types, and cell culture devices for human cells. As of September 30, 1996, the Company had exclusive rights to five issued U.S. and three foreign patents, and a number of U.S. patent applications and certain corresponding foreign applications.

THE OFFERING

Common Stock offered..... 3,250,000 shares
Common Stock to be out- 13,235,734 shares(1)
standing after this of-
fering.....
Use of proceeds..... For clinical trials, the development and manufacture
of the Aastrom CPS, research and development of
other product candidates, working capital and other
general corporate purposes.
Proposed Nasdaq National
Market symbol..... ASTM

SUMMARY FINANCIAL DATA

	YEAR ENDED JUNE 30,					THREE MONTHS ENDED SEPTEMBER 30,	
	1992	1993	1994	1995	1996	1995	1996
STATEMENT OF OPERATIONS							
DATA:							
Total revenues.....	\$ --	\$ 784,000	\$ 872,000	\$ 517,000	\$ 1,609,000	\$ 211,000	\$ 224,000
Costs and expenses:							
Research and development.....	1,090,000	2,600,000	5,627,000	4,889,000	10,075,000	1,195,000	3,160,000
General and administrative.....	272,000	1,153,000	1,565,000	1,558,000	2,067,000	446,000	452,000
Total costs and expenses.....	1,362,000	3,753,000	7,192,000	6,447,000	12,142,000	1,641,000	3,612,000
Other income, net.....	94,000	122,000	180,000	213,000	616,000	131,000	115,000
Net loss.....	\$(1,268,000)	\$(2,847,000)	\$(6,140,000)	\$(5,717,000)	\$(9,917,000)	\$(1,299,000)	\$(3,273,000)
Pro forma net loss per share(2).....	\$ (.32)	\$ (.49)	\$ (.82)	\$ (.66)	\$ (.98)	\$ (.13)	\$ (.32)
Pro forma weighted average number of shares outstanding(2)...	3,919,000	5,840,000	7,461,000	8,644,000	10,103,000	10,094,000	10,107,000
						SEPTEMBER 30, 1996	
						ACTUAL	AS ADJUSTED(3)
BALANCE SHEET DATA:							
Cash, cash equivalents and short-term investments.....						\$ 7,108,000	\$33,410,500
Working capital.....						6,540,000	32,842,500
Total assets.....						8,931,000	35,233,500
Deficit accumulated during the development stage.....						(30,298,000)	(30,298,000)
Total stockholders' equity.....						7,618,000	33,920,500

- (1) Excludes options and warrants to purchase 1,132,361 shares of Common Stock at a weighted average exercise price of \$6.50 per share, assuming the closing of this offering at a price of \$9.00 per share. See "Management--Stock Option and Employee Benefit Plans" and Notes 4 and 9 of Notes to Financial Statements.
- (2) See Note 1 of Notes to Financial Statements for information concerning the computation of pro forma net loss per share and shares used in computing pro forma net loss per share.
- (3) Adjusted to reflect the sale by the Company of 3,250,000 shares of Common Stock offered hereby at an assumed initial public offering price of \$9.00 per share, after deduction of estimated underwriting discounts and commissions and estimated offering expenses. See "Use of Proceeds" and "Capitalization."

Unless otherwise indicated, all information contained in this Prospectus (i) gives effect to a two-for-three reverse stock split to be effected prior to the closing of this offering, (ii) gives effect to the conversion of all outstanding shares of the Company's Preferred Stock into 8,098,422 shares of Common Stock upon the closing of this offering, (iii) gives effect to the filing of an Amended and Restated Articles of Incorporation upon the closing of this offering to, among other things, create a new class of undesignated preferred stock and (iv) assumes no exercise of the Underwriters' over-allotment option. See "Description of Capital Stock" and "Underwriting." This Prospectus contains forward-looking statements which involve risks and uncertainties. The Company's actual results may differ significantly from the results discussed in the forward-looking statements. Factors that might cause such differences include, but are not limited to, those discussed in "Risk Factors."

RISK FACTORS

In addition to the other information in this Prospectus, prospective investors should consider the following risk factors in evaluating the Company and its business before purchasing any of the Common Stock offered hereby.

UNCERTAINTIES RELATED TO PRODUCT DEVELOPMENT AND MARKETABILITY

The Company has not completed the development or clinical trials of any of its cell culture technologies or product candidates and, accordingly, has not begun to market or generate revenue from their commercialization. Furthermore, the Company's technologies and product candidates are based on cell culture processes and methodologies which are not widely employed. Commercialization of the Company's lead product candidate, the Aastrom CPS, will require substantial additional research and development by the Company as well as substantial clinical trials. There can be no assurance that the Company will successfully complete development of the Aastrom CPS or its other product candidates, or successfully market its technologies or product candidates, which lack of success would have a material adverse effect on the Company's business, financial condition and results of operations.

The Company or its collaborators may encounter problems and delays relating to research and development, regulatory approval and intellectual property rights of the Company's technologies and product candidates. There can be no assurance that the Company's research and development programs will be successful, that its cell culture technologies and product candidates will facilitate the ex vivo production of cells with the expected biological activities in humans, that its technologies and product candidates, if successfully developed, will prove to be safe and efficacious in clinical trials, that the necessary regulatory approvals for any of the Company's technologies or product candidates and the cells produced in such products will be obtained or, if obtained, will be as broad as sought, that patents will issue on the Company's patent applications or that the Company's intellectual property protections will be adequate. The Company's product development efforts are primarily directed toward obtaining regulatory approval to market the Aastrom CPS as an alternative to the bone marrow harvest and peripheral blood progenitor cell ("PBPC") stem cell collection methods. These stem cell collection methods have been widely practiced for a number of years, and there can be no assurance that any of the Company's technologies or product candidates will be accepted by the marketplace as readily as these or other competing processes and methodologies, or at all. The failure by the Company to achieve any of the foregoing would have a material adverse effect on the Company's business, financial condition and results of operations.

UNCERTAINTIES RELATED TO CLINICAL TRIALS

The approval of the United States Food and Drug Administration (the "FDA") will be required before any commercial sales of the Company's product candidates may commence in the United States, and approvals from foreign regulatory authorities will be required before international sales may commence. Prior to obtaining necessary regulatory approvals, the Company will be required to demonstrate the safety and efficacy of its processes and product candidates and the cells produced by such processes and in such products for application in the treatment of humans through extensive preclinical studies and clinical trials. To date, the Company has only tested the safety of cells produced in the cell culture chamber predecessor of the Aastrom CPS, and only in a limited numbers of patients. The Company is currently conducting a pre-pivotal clinical trial to demonstrate the safety and biological activity of patient-derived cells produced in the Company's cell culture chamber in a limited number of patients with breast cancer and, if the results from this pre-pivotal trial are successful, the Company intends to seek clearance from the FDA to commence its pivotal clinical trial. The results of preclinical studies and clinical trials of the Company's product candidates, however, may not necessarily be predictive of results that will be obtained from subsequent or more extensive clinical trials. Further, there can be no assurance that pre-pivotal or pivotal clinical trials of any of the Company's product candidates will demonstrate the safety and efficacy of such products, or of the cells produced in such products, to the extent necessary to obtain required regulatory approvals or market acceptance.

The ability of the Company to complete its clinical trials in a timely manner is dependent upon many factors, including the rate of patient enrollment. Patient enrollment is a function of many factors, including the size of the patient population, the proximity of suitable patients to clinical sites and the eligibility criteria for the

study. The Company has experienced delays in patient accrual in its current pre-pivotal clinical trial. Further delays in patient accrual, in the Company's current pre-pivotal clinical trial or in future clinical trials, could result in increased costs associated with clinical trials or delays in receiving regulatory approvals and commercialization, if any. Furthermore, the progress of clinical investigations with the Aastrom CPS and the Company's other product candidates will be monitored by the FDA, which has the authority to cease clinical investigations, at any time, due to patient safety or other considerations. Any of the foregoing would have a material adverse effect on the Company's business, financial condition and results of operations. See "--Uncertainty of Regulatory Approval" and "--Extensive Government Regulation."

The Company's current pre-pivotal trial is designed to demonstrate specific biological safety and activity of cells produced in the Aastrom CPS, but is not designed to demonstrate long-term sustained engraftment of such cells. The patients enrolled in this pre-pivotal trial will have undergone extensive chemotherapy treatment prior to the infusion of cells produced in the Aastrom CPS. Such treatments will have substantially weakened these patients and may have irreparably damaged their hematopoietic systems. Due to these and other factors, there is risk that one or more of these patients may die or suffer severe complications during the course of the pre-pivotal trial. Further, there can be no assurance that patients receiving cells produced with the Company's technologies and product candidates will demonstrate long-term engraftment in a manner comparable to cells obtained from current stem cell therapy procedures, or at all. The failure to adequately demonstrate the safety or efficacy of the Company's technologies and product candidates, including long-term sustained engraftment, or the death of, or occurrence of severe complications in, one or more patients could substantially delay, or prevent, regulatory approval of such product candidates and have a material adverse effect on the Company's business, financial condition and results of operations.

MANUFACTURING AND SUPPLY UNCERTAINTIES; DEPENDENCE ON THIRD PARTIES

The Company does not operate and has no current intention to operate manufacturing facilities for the production of its product candidates. The Company currently arranges for the manufacturing of its product candidates and their components with third parties, and expects to continue to do so in the foreseeable future. The Company has entered into collaborative product development agreements with SeaMED Corporation ("SeaMED") and Ethox Corporation ("Ethox") for the collaborative development and manufacture of certain components of the Aastrom CPS. The Company is also dependent upon Immunex Corporation ("Immunex"), Life Technologies, Inc., Biowhittaker and Anchor Advanced Products for the supply of certain cytokines, serum, media and injection molded materials, respectively, to be used in conjunction with, or as components of, the Aastrom CPS. With regard to cytokines that are not commercially available from other sources, Immunex is currently the Company's sole supplier and few alternative supply sources exist. Apart from SeaMED, Ethox and Immunex, the Company currently does not have contractual commitments from any of these manufacturers or suppliers. There can be no assurance that the Company's supply of such key cytokines, components and other materials will not become limited, be interrupted or become restricted to certain geographic regions. Furthermore, the Company currently only has the right to distribute cytokines obtained from Immunex in the United States and there can be no assurance that the Company will be able to obtain the worldwide right to distribute such cytokines or manufacture such cytokines by or for itself in the event that the Company's agreement with Immunex is terminated. There can also be no assurance that the Company will be able to obtain alternative components and materials from other manufacturers on terms or in quantities acceptable to the Company or that the Company will not require additional cytokines, components and other materials to manufacture or use its product candidates. In the event that any of the Company's key manufacturers or suppliers fail to perform their respective obligations or the Company's supply of such cytokines, components or other materials become limited or interrupted, the Company would not be able to market its product candidates on a timely and cost-competitive basis, if at all which would have a material adverse effect on the Company's business, financial condition and results of operations.

Like SeaMED and Ethox, other suppliers would need to meet FDA manufacturing requirements and undergo rigorous facility and process validation tests required by federal and state regulatory authorities. Any significant delays in the completion and validation of such facilities could have a material adverse effect on the

ability of the Company to complete clinical trials and to market its products on a timely and profitable basis, which in turn would have a material adverse effect on the Company's business, financial condition and results of operations.

There can also be no assurance that the Company will be able to continue its present arrangements with its suppliers, supplement existing relationships or establish new relationships or that the Company will be able to identify and obtain the ancillary materials that are necessary to develop its product candidates in the future. The Company's dependence upon third parties for the supply and manufacture of such items could adversely affect the Company's ability to develop and deliver commercially feasible products on a timely and competitive basis.

HISTORY OF OPERATING LOSSES; ANTICIPATION OF FUTURE LOSSES

The Company is a development stage company and there can be no assurance that its product applications for cell therapy will be successful. The Company has not yet completed the development and clinical trials of any of its product candidates and, accordingly, has not yet begun to generate revenues from the commercialization of any of its product candidates. Aastrom was incorporated in 1989 and has experienced substantial operating losses since inception. As of September 30, 1996, the Company has incurred net operating losses totaling approximately \$30.3 million. Such losses have resulted principally from costs incurred in the research and development of the Company's cell culture technologies and the Aastrom CPS, general and administrative expenses, and the prosecution of patent applications. The Company expects to incur significant and increasing operating losses for at least the next several years, primarily owing to the expansion of its research and development programs, including preclinical studies and clinical trials. The amount of future losses and when, if ever, the Company achieves profitability are uncertain. The Company's ability to achieve profitability will depend, among other things, on successfully completing the development of its product candidates, obtaining regulatory approvals, establishing manufacturing, sales and marketing arrangements with third parties, and raising sufficient funds to finance its activities. No assurance can be given that the Company's product development efforts will be successful, that required regulatory approvals will be obtained, that any of the Company's product candidates will be manufactured at a competitive cost and will be of acceptable quality, or that the Company will be able to achieve profitability or that profitability, if achieved, can be sustained.

LIMITED SALES AND MARKETING CAPABILITIES; DEPENDENCE ON COLLABORATIVE RELATIONSHIPS

The Company has limited internal sales, marketing and distribution capabilities. If any of the Company's product candidates are successfully developed and the necessary regulatory approvals are obtained, the Company intends to market such products through collaborative relationships with companies that have established sales, marketing and distribution capabilities. The Company has established a strategic alliance with Cobe Laboratories, Inc. and Cobe BCT, Inc. (collectively, "Cobe") for the worldwide distribution of the Aastrom CPS for stem cell therapy and related uses. Cobe has the right to terminate its Distribution Agreement with the Company upon twelve month's notice upon a change of control of the Company, other than to Cobe, or at any time after December 31, 1997, if Cobe determines that commercialization of the Aastrom CPS for stem cell therapy on or prior to December 31, 1998 is unlikely. See "--Consequences of Cobe Relationship."

The amount and timing of resources that Cobe commits to its strategic alliance activities with the Company are, to a significant extent, outside of the control of the Company. There can be no assurance that Cobe will pursue the marketing and distribution of the Company's products, continue to perform its obligations under its agreements with the Company or that the Company's strategic alliance with Cobe will result in the successful commercialization and distribution of the Company's technologies and product candidates. There can also be no assurance that Cobe will be successful in its efforts to market and distribute the Company's products for stem cell therapy. The suspension or termination of the Company's strategic alliance with Cobe or the failure of the strategic alliance to be successful would have a material adverse effect on the Company's business, financial condition and results of operations.

Subject to the contractual requirements of the Cobe relationship, the Company will seek to enter into other agreements relating to the development and marketing of product candidates and in connection with such

agreements may rely upon corporate partners to conduct clinical trials, seek regulatory approvals for, manufacture and market its potential products. There can be no assurance that the Company will be able to establish collaborative relationships for the development or marketing of the Company's product candidates on acceptable terms, if at all. The inability of the Company to establish such collaborative relationships may require the Company to curtail its development or marketing activities with regard to its potential products which would have a material adverse effect on the Company's business, financial condition and results of operations.

FUTURE CAPITAL NEEDS; UNCERTAINTY OF ADDITIONAL FUNDING

To date, Aastrom has funded its operations primarily through the sale of equity securities and corporate collaborations. The Company anticipates that the net proceeds of this offering, together with the Company's available cash and expected interest income thereon, will be sufficient to finance its research and development and other working capital requirements for 18 months or less. This estimate is based on certain assumptions which could be negatively impacted by the matters discussed under this heading and elsewhere under the caption "Risk Factors." In order to grow and expand its business, and to introduce its product candidates into the marketplace, the Company will need, among other things, to raise additional funds.

The Company's future capital requirements will depend upon many factors, including, but not limited to, continued scientific progress in its research and development programs, costs and timing of conducting clinical trials and seeking regulatory approvals and patent prosecutions, competing technological and market developments, possible changes in existing collaborative relationships, the ability of the Company to establish additional collaborative relationships, and effective commercialization activities and facilities expansions if and as required. Because of the Company's potential long-term funding requirements, it may attempt to access the public or private equity markets if and whenever conditions are favorable, even if it does not have an immediate need for additional capital at that time. There can be no assurance that any such additional funding will be available to the Company on reasonable terms, or at all. If adequate funds are not available, the Company may be required to delay or terminate research and development programs, curtail capital expenditures, and reduce business development and other operating activities. If the Company is not successful in finding, entering into and maintaining arrangements with collaborative partners, its development efforts could be delayed. Furthermore, there can be no assurance that the Company will be able to implement collaborative development agreements under acceptable terms. Any of the foregoing capital constraints would have a material adverse effect on the Company's business, financial condition and results of operations. See "Management's Discussion and Analysis of Financial Condition and Results of Operations--Liquidity and Capital Resources."

UNCERTAINTY OF REGULATORY APPROVAL; EXTENSIVE GOVERNMENT REGULATION

The Company's research and development activities, preclinical studies, clinical trials, and the anticipated manufacturing and marketing of its product candidates are subject to extensive regulation by the FDA and other regulatory authorities in the United States. These activities are also regulated in other countries where the Company intends to test and market its product candidates. The approval of the FDA will be required before any commercial sales of the Company's product candidates may commence in the United States. Additionally, the Company will be required to obtain approvals from foreign regulatory authorities before international sales may commence.

The Company's products are potentially subject to regulation as medical devices under the Federal Food, Drug, and Cosmetic Act, or as biological products under the Public Health Service Act, or both. Different regulatory requirements may apply to the Company's products depending on how they are categorized by the FDA under these laws. To date, the FDA has indicated that it intends to regulate the Aastrom CPS for stem cell therapy as a Class III medical device through the Center for Biologics Evaluation and Research. However, there can be no assurance that the FDA will ultimately regulate the Aastrom CPS for stem cell therapy as a medical device or that regulatory approval for such product will be obtained in a timely fashion or at all.

Further, it is unclear whether the FDA will separately regulate the cell therapies derived from the Aastrom CPS. The FDA is in the process of developing its requirements with respect to somatic cell therapy and gene cell therapy products, and recently proposed a new type of license for autologous cells manipulated ex vivo and

intended for structural repair or reconstruction; autologous cells are cells obtained from, and administered to, the same patient. This proposal may indicate that the FDA will impose a similar approval requirement on other types of autologous cellular therapies, such as autologous cells for stem cell therapy. Any such additional regulatory or approval requirement could significantly delay the introduction of the Company's product candidates to the market, and have a material adverse effect on the Company's business, financial condition and results of operations. Until the FDA issues definitive regulations covering the Company's product candidates, the regulatory requirements for approval of such product candidates will continue to be subject to significant uncertainty.

Before marketing, the Aastrom CPS or other product candidates developed by the Company must undergo an extensive regulatory approval process. The regulatory process, which includes preclinical studies and clinical trials to establish safety and efficacy, takes many years and requires the expenditure of substantial resources. Data obtained from preclinical and clinical activities are susceptible to varying interpretations which could delay, limit or prevent FDA approval. In addition, delays or rejections may be encountered based upon changes in FDA policy for medical product approvals during the period of product development and FDA regulatory review of applications submitted by the Company for product approval. Similar delays may also be encountered in foreign countries. There can be no assurance that, even after the expenditures of substantial time and financial resources, regulatory approval will be obtained for any products developed by the Company. Moreover, if regulatory approval of a product is obtained, such approval may be subject to limitations on the indicated uses for which it may be marketed. Further, even if such regulatory approval is obtained, a marketed product, its manufacturer and its manufacturing facilities are subject to continual review and periodic inspections by the FDA, and later discovery of previously unknown problems with a product, manufacturer or facility may result in restrictions on such product or manufacturer, including a withdrawal of the product from the market. Failure to comply with the applicable regulatory requirements can, among other things, result in fines, suspensions of regulatory approvals, product recalls, operating restrictions and criminal prosecution. Further, additional government regulation may be established which could prevent or delay regulatory approval of the Company's products. See "Business--Government Regulation."

CONSEQUENCES OF COBE RELATIONSHIP

Following the completion of this offering, Cobe will be the largest single shareholder of the Company, beneficially owning approximately 19% of the outstanding Common Stock. In addition, Cobe has certain preemptive rights to maintain its relative percentage ownership and voting interest in the Company following this offering, and has the right, for a period of three years following this offering, to purchase from the Company an amount of Common Stock equal to 30% of the Company's fully diluted shares after the exercise of such option, at a purchase price equal to 120% of the public market trading price of the Company's Common Stock. If such option is exercised, Cobe would significantly increase its ownership interest in the Company and, as a consequence of such share ownership, obtain effective control of the Company. Such effective control would include the ability to influence the outcome of shareholder votes, including votes concerning the election of directors, the amendment of provisions of the Company's Restated Articles of Incorporation or Bylaws, and the approval of mergers and other significant transactions. Cobe also has been granted a "right of first negotiation" in the event that the Company determines to sell all, or any material portion, of its assets to another company or to merge with another company. Furthermore, the Company has agreed to use reasonable and good faith efforts to cause a nominee designated by Cobe to be elected to the Board of Directors for as long as Cobe owns at least 15% of the outstanding Common Stock. In addition, Edward C. Wood, Jr., the President of Cobe BCT, is a director of the Company. The existence of the foregoing rights or the exercise of such control by Cobe could have the effect of delaying, deterring or preventing certain takeovers or changes in control of the management of the Company, including transactions in which shareholders might otherwise receive a premium for their shares over then-current market prices. See "Description of Capital Stock--Rights of Cobe."

UNCERTAINTY REGARDING PATENTS AND PROPRIETARY RIGHTS

Aastrom's success depends in part on its ability, and the ability of its licensors, to obtain patent protection for its products and processes, preserve its trade secrets, defend and enforce its rights against infringement and

operate without infringing the proprietary rights of third parties, both in the United States and in other countries. The validity and breadth of claims in medical technology patents involve complex legal and factual questions and, therefore, may be highly uncertain. No assurance can be given that any patents based on pending patent applications or any future patent applications of the Company or its licensors will be issued, that the scope of any patent protection will exclude competitors or provide competitive advantages to the Company, that any of the patents that have been or may be issued to the Company or its licensors will be held valid if subsequently challenged or that others will not claim rights in or ownership of the patents and other proprietary rights held or licensed by the Company. Furthermore, there can be no assurance that others have not developed or will not develop similar products, duplicate any of the Company's products or design around any patents that have been or may be issued to the Company or its licensors. Since patent applications in the United States are maintained in secrecy until patents issue, the Company also cannot be certain that others did not first file applications for inventions covered by the Company's and its licensors' pending patent applications, nor can the Company be certain that it will not infringe any patents that may issue to others on such applications. The Company relies on certain licenses granted by the University of Michigan and Dr. Cremonese for the majority of its patent rights. If the Company breaches such agreements or otherwise fails to comply with such agreements, or if such agreements expire or are otherwise terminated, the Company may lose its rights under the patents held by the University of Michigan and Dr. Cremonese, which would have a material adverse effect on the Company's business, financial condition and results of operation. See "Business--Patents and Proprietary Rights--University of Michigan Research Agreement and License Agreement" and "Business--Patents and Proprietary Rights--License Agreement with J.G. Cremonese." The Company also relies on trade secrets and unpatentable know-how which it seeks to protect, in part, by confidentiality agreements with its employees, consultants, suppliers and licensees. There can be no assurance that these agreements will not be breached, that the Company would have adequate remedies for any breach, or that the Company's trade secrets or unpatentable know-how will not otherwise become known or be independently developed by competitors.

The Company's success will also depend in part on its ability to develop commercially viable products without infringing the proprietary rights of others. The Company has not conducted freedom of use patent searches and no assurance can be given that patents do not exist or could not be filed which would have an adverse effect on the Company's ability to market its products or maintain its competitive position with respect to its products. If the Company's technology components, devices, designs, products, processes or other subject matter are claimed under other existing United States or foreign patents or are otherwise protected by third party proprietary rights, the Company may be subject to infringement actions. In such event, the Company may challenge the validity of such patents or other proprietary rights or be required to obtain licenses from such companies in order to develop, manufacture or market its products. There can be no assurance that the Company would be able to obtain such licenses or that such licenses, if available, could be obtained on commercially reasonable terms. Furthermore, the failure to either develop a commercially viable alternative or obtain such licenses could result in delays in marketing the Company's proposed products or the inability to proceed with the development, manufacture or sale of products requiring such licenses, which could have a material adverse effect on the Company's business, financial condition and results of operations. If the Company is required to defend itself against charges of patent infringement or to protect its own proprietary rights against third parties, substantial costs will be incurred regardless of whether the Company is successful. Such proceedings are typically protracted with no certainty of success. An adverse outcome could subject the Company to significant liabilities to third parties, and force the Company to curtail or cease its development and sale of its products and processes. See "Business--Patents and Proprietary Rights."

NO ASSURANCE OF THIRD PARTY REIMBURSEMENT

The Company's ability to successfully commercialize its product candidates will depend in part on the extent to which payment for the Company's products and related treatments will be available from government healthcare programs, such as Medicare and Medicaid, as well as private health insurers, health maintenance organizations and other third party payors. Government and other third-party payors are increasingly attempting to contain health care costs, in part by challenging the price of medical products and services. Reimbursement by third-party payors depend on a number of factors, including the payor's determination that use of the product

is safe and effective, not experimental or investigational, medically necessary, appropriate for the specific patient and cost-effective. Since reimbursement approval is required from each payor individually, seeking such approvals is a time-consuming and costly process which will require the Company to provide scientific and clinical support for the use of each of the Company's products to each payor separately. Significant uncertainty exists as to the payment status of newly approved medical products, and there can be no assurance that adequate third-party payments will be available to enable the Company to establish or maintain price levels sufficient to realize an appropriate return on its investment in product development. If adequate payment levels are not provided by government and third-party payors for use of the Company's products, the market acceptance of those products will be adversely affected.

There can be no assurance that reimbursement in the United States or foreign countries will be available for any of the Company's product candidates, that any reimbursement granted will be maintained, or that limits on reimbursement available from third-party payors will not reduce the demand for, or negatively affect the price of, the Company's products. The unavailability or inadequacy of third-party reimbursement for the Company's product candidates would have a material adverse effect on the Company. Finally, the Company is unable to forecast what additional legislation or regulation relating to the healthcare industry or third-party coverage and reimbursement may be enacted in the future, or what effect such legislation or regulation would have on the Company's business.

COMPETITION AND TECHNOLOGICAL CHANGE

The Company is engaged in the development of medical products and processes which will face competition in a marketplace characterized by rapid technological change. Many of the Company's competitors have significantly greater resources than the Company, and have developed and may develop product candidates and processes that directly compete with the Company's products. Moreover, competitors that are able to achieve patent protection, obtain regulatory approvals and commence commercial sales of their products before the Company, and competitors that have already done so, may enjoy a significant competitive advantage. The Company's product development efforts are primarily directed toward obtaining regulatory approval to market the Aastrom CPS for stem cell therapy. That market is currently dominated by the bone marrow harvest and PBPC collection methods. The Company's clinical data, although early, is inconclusive as to whether or not cells expanded in the Aastrom CPS will enable hematopoietic recovery within the time frames currently achieved by the bone marrow harvest and PBPC collection methods. In addition, the bone marrow harvest and PBPC collection methods have been widely practiced for a number of years and, recently, the patient costs associated with these procedures have begun to decline. There can be no assurance that the Aastrom CPS method, if approved for marketing, will prove to be competitive with these established collection methods on the basis of hematopoietic recovery time, cost or otherwise. The Company also is aware of certain other products manufactured or under development by competitors that are used for the prevention or treatment of certain diseases and health conditions which the Company has targeted for product development. In particular, the Company is aware that competitors such as Amgen, Inc., CellPro, Incorporated, Systemix, Inc., Baxter Healthcare Corp. and Rhone-Poulenc Rorer Inc. ("RPR") are in advanced stages of development of technologies and products for use in stem cell therapy and other market applications currently being pursued by the Company. In addition, Cobe, a significant shareholder of the Company, is a market leader in the blood cell processing products industry and, accordingly, a potential competitor of the Company. There can be no assurance that developments by others will not render the Company's product candidates or technologies obsolete or noncompetitive, that the Company will be able to keep pace with new technological developments or that the Company's product candidates will be able to supplant established products and methodologies in the therapeutic areas that are targeted by the Company. The foregoing factors could have a material adverse effect on the Company's business, financial condition and results of operations.

HAZARDOUS MATERIALS

The Company's research and development activities involve the controlled use of hazardous materials, chemicals and various radioactive compounds. The Company is subject to federal, state and local laws and

regulations governing the use, manufacture, storage, handling and disposal of such materials and certain waste products. In the event of any contamination or injury from these materials, the Company could be held liable for any damages that result and any such liability could exceed the resources of the Company. Furthermore, the failure to comply with current or future regulations could result in the imposition of substantial fines against the Company, suspension of production, alteration of its manufacturing processes or cessation of operations. There can be no assurance that the Company will not be required to incur significant costs to comply with any such laws and regulations in the future, or that such laws or regulations will not have a material adverse effect on the Company's business, financial condition and results of operations. Any failure by the Company to control the use, disposal, removal or storage of, or to adequately restrict the discharge of, or assist in the cleanup of, hazardous chemicals or hazardous, infectious or toxic substances could subject the Company to significant liabilities, including joint and several liability under certain statutes. The imposition of such liabilities would have a material adverse effect on the Company's business, financial condition and results of operations.

POTENTIAL PRODUCT LIABILITY; AVAILABILITY OF INSURANCE

The Company is, and will continue to be, subject to the risk of product liability claims alleging that the use of its products has adverse effects on patients. This risk exists for product candidates tested in human clinical trials as well as products that are sold commercially, if any. Further, given the medical conditions for which the Aastrom CPS is expected to be utilized, any product liability claim could entail substantial compensatory and punitive damages. The assertion of product liability claims against the Company could result in a substantial cost to, and diversion of efforts by, the Company. There can be no assurance that the Company would prevail in any such litigation or that product liability claims, if made, would not result in a recall of the Company's products or a change in the indications for which they may be used. The Company maintains product liability insurance coverage in the aggregate of \$5,000,000 for claims arising from the use of its product candidates in clinical trials. There can be no assurance that the Company will be able to maintain such insurance or obtain product liability insurance in the future to cover any of its product candidates which are commercialized or that such existing or any future insurance and the resources of the Company would be sufficient to satisfy any liability resulting from product liability claims. Consequently, a product liability claim or other claim with respect to uninsured or underinsured liabilities could have a material adverse effect on the Company's business, financial condition and results of operations.

DEPENDENCE ON KEY PERSONNEL

The success of the Company depends in large part upon the Company's ability to attract and retain highly qualified scientific and management personnel. The Company faces competition for such personnel from other companies, research and academic institutions and other entities. There can be no assurance that the Company will be successful in hiring or retaining key personnel. See "Business--Employees" and "Management."

SHARES ELIGIBLE FOR FUTURE SALE

Sales of substantial amounts of Common Stock in the public market following this offering could adversely affect the prevailing market price of the Common Stock and the Company's ability to raise capital in the future. Upon completion of this offering, the Company will have a total of 13,235,734 shares of Common Stock outstanding, of which the 3,250,000 shares offered hereby will be freely tradeable without restriction under the Securities Act of 1933, as amended (the "Securities Act") by persons other than "affiliates" of the Company, as defined under the Securities Act. The remaining 9,985,734 shares of Common Stock outstanding are "restricted securities" as the term is defined by Rule 144 promulgated under the Securities Act (the "Restricted Shares"). Of the 9,985,734 Restricted Shares, 6,996,920 shares may be sold under Rule 144, subject in some cases to certain volume restrictions and other conditions imposed thereby. An additional 152,056 shares will become eligible for sale 90 days after completion of the offering pursuant to Rule 144 and 701. The remaining 2,836,758 shares will be eligible for sale upon the expiration of their respective holding periods as set forth in Rule 144. The Securities and Exchange Commission has proposed certain amendments to Rule 144 that would reduce by one year the holding periods required for shares subject to Rule 144 to become eligible for resale in

the public market. This proposal, if adopted, would permit earlier resale of shares of Common Stock currently subject to holding periods under Rule 144. No assurance can be given concerning whether or when the proposal will be adopted by the Securities and Exchange Commission. Furthermore, 9,810,503 of the Restricted Shares are subject to lock-up agreements expiring 180 days following the date of this Prospectus. Such agreements provide that Cowen & Company may, in its sole discretion and at any time without notice, release all or a portion of the shares subject to these lock-up agreements. Upon the expiration of the lock-up agreements, 7,148,976 of the 9,985,734 Restricted Shares may be sold pursuant to Rule 144 or 701, subject in some cases to certain volume restrictions imposed thereby. Certain existing stockholders have rights to include shares of Common Stock owned by them in future registration by the Company for the sale of Common Stock or to request that the Company register their shares under the Securities Act. See "Description of Capital Stock--Registration Rights." Following the date of this Prospectus, the Company intends to register on one or more registration statements on Form S-8 approximately 1,837,160 shares of Common Stock issuable under its stock option and stock purchase plans. Of the 1,837,160 shares issuable under its stock option and stock purchase plans, 336,254 shares are subject to outstanding options as of September 30, 1996, 318,920 of which shares are subject to lock-up agreements. Shares covered by such registration statements will immediately be eligible for sale in the public market upon the filing of such registration statements. In addition, the Company has issued warrants to purchase 69,444 shares of Common Stock which become exercisable 90 days after the closing of this offering and, upon the effective date of this offering, will grant an immediately exercisable option to purchase 333,333 shares of Common Stock, which shares are subject to a lock-up agreement. See "Management--Benefit Plans," "Certain Transactions" and "Shares Eligible for Future Sale."

CONTROL BY EXISTING MANAGEMENT AND SHAREHOLDERS

Upon completion of this offering, the Company's directors, executive officers, and certain principal shareholders, including Cobe, affiliated with members of the Board of Directors and their affiliates will beneficially own approximately 39% of the Common Stock (approximately 38% if the Underwriters' over-allotment option is exercised in full). Accordingly, such shareholders, acting together, may have the ability to exert significant influence over the election of the Company's Board of Directors and other matters submitted to the Company's shareholders for approval. The voting power of these holders may discourage or prevent certain takeovers or changes in control of the management of the Company unless the terms are approved by such holders. See "Principal Shareholders."

NO PRIOR PUBLIC MARKET; POSSIBLE STOCK PRICE VOLATILITY

Prior to this offering there has been no public market for the Common Stock, and an active public market for the Common Stock may not develop or be sustained. The initial public offering price will be determined through negotiation between the Company and the Representatives of the Underwriters based on several factors that may not be indicative of future market prices. See "Underwriting" for a discussion of the factors considered in determining the initial public offering price. The trading price of the Common Stock and the price at which the Company may sell securities in the future could be subject to wide fluctuations in response to announcements of clinical results, research activities, technological innovations or new products by the Company or competitors, changes in government regulation, developments concerning proprietary rights, variations in the Company's operating results, announcements by the Company of regulatory developments, litigation, disputes concerning patents or proprietary rights or public concern regarding the safety, efficacy or other implications of the products or methodologies to be developed by the Company or its collaborators or enabled by the Company's technology, general market conditions, the liquidity of the Company or its ability to raise additional funds, and other factors or events. In addition, the stock market has experienced extreme fluctuations in price and volume. This volatility has significantly affected the market prices for securities of emerging biotechnology companies for reasons frequently unrelated to or disproportionate to the operating performance of the specific companies. These market fluctuations as well as general fluctuations in the stock markets may adversely affect the market price of the Common Stock.

ANTI-TAKEOVER EFFECT OF CHARTER AND BY-LAW PROVISIONS AND MICHIGAN LAW

The Company's Restated Articles of Incorporation authorize the Board of Directors to issue, without shareholder approval, 5,000,000 shares of Preferred Stock with voting, conversion, and other rights and

preferences that could materially and adversely affect the voting power or other rights of the holders of Common Stock. The issuance of Preferred Stock or of rights to purchase Preferred Stock could be used to discourage an unsolicited acquisition proposal. The Company's Bylaws contain procedural restrictions on director nominations by shareholders and the submission of other proposals for consideration at shareholder meetings. The possible issuance of Preferred Stock and the procedures required for director nominations and shareholder proposals could discourage a proxy contest, make more difficult the acquisition of a substantial block of Common Stock, or limit the price that investors might be willing to pay in the future for shares of Common Stock. In addition, certain provisions of Michigan law applicable to the Company could also delay or make more difficult a merger, tender offer, or proxy contest involving the Company. See "Description of Capital Stock."

IMMEDIATE AND SUBSTANTIAL DILUTION; ABSENCE OF DIVIDENDS

Purchasers of the Common Stock in this offering will experience immediate and substantial dilution in the net tangible book value of the Common Stock. Additional dilution is likely to occur upon the exercise of outstanding options granted by the Company. The Company has never paid cash dividends and does not anticipate paying any cash dividends in the foreseeable future. See "Dilution" and "Dividend Policy."

THE COMPANY

Aastrom was incorporated in Michigan in March 1989 under the name Ann Arbor Stromal, Inc. In 1991, the Company changed its name to Aastrom Biosciences, Inc. The Company's principal executive offices are located at 24 Frank Lloyd Wright Drive, P.O. Box 376, Ann Arbor, Michigan 48106 and its telephone number is (313) 930-5555. Aastrom(TM) and the Company's stylized logo are trademarks of the Company. Leukine and Neupogen are registered trademarks of Immunex Corporation and Amgen, Inc., respectively.

USE OF PROCEEDS

The net proceeds to the Company from the sale of the 3,250,000 shares of Common Stock offered hereby are estimated to be \$26,302,500 (\$30,382,875 if the Underwriters exercise their over-allotment option in full), at an assumed initial public offering price of \$9.00 per share and after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company.

The net proceeds from this offering are expected to be used to fund product development of the Aastrom CPS, other research and development activities, including pre-pivotal and pivotal clinical trials of the Aastrom CPS, and for working capital and other general corporate purposes, including scheduled repayments of obligations under equipment leases. The Company has \$339,000 of outstanding equipment lease commitments as of September 30, 1996 with final payments due between November 1996 and May 1999 and bear interest ranging from 9.7% to 12.1%.

The Company anticipates that the net proceeds of this offering, together with the Company's available cash and expected interest income thereon, should be sufficient to finance the Company's research and development and other working capital requirements for approximately 18 months. This estimate is based on certain assumptions which could be negatively impacted by the matters discussed in "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations--Liquidity and Capital Resources." Pending such uses, the net proceeds will be invested in short-term, interest bearing investment grade securities.

DIVIDEND POLICY

The Company has never declared or paid any cash dividends on its Common Stock and does not anticipate paying such cash dividends in the foreseeable future. The Company currently anticipates that it will retain all future earnings, if any, for use in the development of its business.

CAPITALIZATION

The following table sets forth the capitalization of the Company (i) as of September 30, 1996, and (ii) on a pro forma as adjusted basis to reflect the conversion of all outstanding shares of Preferred Stock into Common Stock upon the closing of this offering and the receipt of the estimated net proceeds from the Company's sale of 3,250,000 shares of Common Stock pursuant to this offering. See "Use of Proceeds" and "Certain Transactions."

	SEPTEMBER 30, 1996	
	ACTUAL	PRO FORMA AS ADJUSTED
Long-term portion of capital lease obligations(1)....	\$ 147,000	\$ 147,000
Stockholders' equity(2):		
Preferred stock, no par value: 10,157,647 shares authorized, 9,657,648 shares issued and outstanding, actual; 5,000,000 shares authorized, no shares issued and outstanding, as adjusted.....	37,718,000	--
Common stock, no par value: 18,500,000 shares authorized, 1,887,312 shares issued and outstanding, actual; 40,000,000 shares authorized, 13,235,734 issued and outstanding, as adjusted, in each case net of stockholder notes receivable.....	198,000	64,218,500
Deficit accumulated during the development stage.....	(30,298,000)	(30,298,000)
Total stockholders' equity.....	7,618,000	33,920,500
Total capitalization.....	\$ 7,765,000	\$ 34,067,500

(1) See Note 7 of Notes to Financial Statements.

(2) Excludes options and warrants to purchase 1,132,361 shares of Common Stock at a weighted average exercise price of \$6.50 per share, assuming the closing of this offering at a price of \$9.00 per share. See "Management--Stock Option and Employee Benefit Plans" and Notes 4 and 9 of Notes to Financial Statements.

DILUTION

The Company's pro forma net tangible book value at September 30, 1996 was approximately \$7,618,000 or \$.76 per share. Pro forma net tangible book value per share represents the amount of the Company's shareholders' equity, less intangible assets, divided by 9,985,734, the number of shares of Common Stock outstanding as of September 30, 1996, after giving effect to the automatic conversion of all Preferred Stock into Common Stock upon the closing of this offering.

After giving effect to the sale of 3,250,000 shares of Common Stock in this offering at an assumed initial public offering price of \$9.00 per share and after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company, the pro forma net tangible book value of the Company as of September 30, 1996 would have been \$33,920,500, or \$2.56 per share. This represents an immediate increase in pro forma net tangible book value of \$1.80 per share to existing stockholders and an immediate dilution in pro forma net tangible book value of \$6.44 per share to purchasers of Common Stock in this offering, as illustrated in the following table:

Assumed initial public offering price per share.....	\$9.00
Pro forma net tangible book value per share as of September 30, 1996.....	\$.76
Increase per share attributable to new investors.....	1.80

Pro forma net tangible book value per share after this offering.....	2.56

Dilution per share to new investors.....	\$6.44
	=====

Utilizing the foregoing assumptions, the following table summarizes the total consideration paid to the Company and the average price per share paid by the existing stockholders and by purchasers of shares of Common Stock in this offering:

	SHARES PURCHASED		TOTAL CONSIDERATION		AVERAGE PRICE PER SHARE
	NUMBER	PERCENTAGE	AMOUNT	PERCENTAGE	
Existing stockholders...	9,985,734	75%	\$38,083,000	57%	\$3.81
New investors.....	3,250,000	25%	29,250,000	43%	9.00

Total.....	13,235,734	100%	\$67,333,000	100%	
	=====	===	=====	===	

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The foregoing excludes options and warrants to purchase 1,132,361 shares of Common Stock at a weighted average exercise price of \$6.50 per share, assuming the closing of this offering at a price of \$9.00 per share. In the event such options and warrants are exercised, investors may experience further dilution. See "Management--Stock Option and Employee Benefit Plans" and Notes 4 and 9 of Notes to Financial Statements.

SELECTED FINANCIAL DATA

The statement of operations data for the fiscal years ended June 1994, 1995 and 1996, and the balance sheet data at June 30, 1995 and 1996, are derived from, and are qualified by reference to, the audited financial statements included elsewhere in the Prospectus and should be read in conjunction with those financial statements and notes thereto. The statement of operations data for the fiscal years ended June 30, 1992 and 1993, and the balance sheet data at June 30, 1992, 1993 and 1994, are derived from audited financial statements not included herein. The information presented below for the three-month periods ended September 30, 1995 and 1996, and as of September 30, 1996, have been derived from the unaudited financial statements of the Company. In the opinion of the Company's management, the unaudited financial statements have been prepared by the Company on a basis consistent with the Company's audited financial statements and include all adjustments, consisting of only normal recurring accruals, necessary for a fair presentation of the financial position and the results of operations for those periods. Operating results for the three-month period ended September 30, 1996 are not necessarily indicative of the results that will be achieved for the entire year ended June 30, 1997. The data set forth below are qualified by reference to, and should be read in conjunction with, the financial statements and notes thereto, and Management's Discussion and Analysis of Financial Condition and Results of Operations.

	YEAR ENDED JUNE 30,					THREE MONTHS ENDED SEPTEMBER 30,	
	1992	1993	1994	1995	1996	1995	1996
STATEMENT OF OPERATIONS DATA:							
Revenues:							
Research and development agreements.....	\$ --	\$ --	\$ 49,000	\$ 396,000	\$ 1,342,000	\$ 172,000	\$ 195,000
Grants.....	--	784,000	823,000	121,000	267,000	39,000	29,000
Total revenues.....	--	784,000	872,000	517,000	1,609,000	211,000	224,000
Costs and expenses:							
Research and development....	1,090,000	2,600,000	5,627,000	4,889,000	10,075,000	1,195,000	3,160,000
General and administrative..	272,000	1,153,000	1,565,000	1,558,000	2,067,000	446,000	452,000
Total costs and expenses....	1,362,000	3,753,000	7,192,000	6,447,000	12,142,000	1,641,000	3,612,000
Loss before other income and expense.....	(1,362,000)	(2,969,000)	(6,320,000)	(5,930,000)	(10,533,000)	(1,430,000)	(3,388,000)
Other income (expense):							
Interest income.....	94,000	148,000	245,000	279,000	678,000	149,000	126,000
Interest expense.....	--	(26,000)	(65,000)	(66,000)	(62,000)	(18,000)	(11,000)
Net loss.....	\$(1,268,000)	\$(2,847,000)	\$(6,140,000)	\$(5,717,000)	\$(9,917,000)	\$(1,299,000)	\$(3,273,000)
Pro forma net loss per share(1).....	\$ (.32)	\$ (.49)	\$ (.82)	\$ (.66)	\$ (.98)	\$ (.13)	\$ (.32)
Pro forma weighted average number of shares outstanding(1).....							
	3,919,000	5,840,000	7,461,000	8,644,000	10,103,000	10,094,000	10,107,000

	JUNE 30,					SEPTEMBER 30,
	1992	1993	1994	1995	1996	1996
BALANCE SHEET DATA:						
Cash, cash equivalents and short-term investments.....	\$5,640,000	\$3,085,000	\$ 6,730,000	\$11,068,000	\$10,967,000	\$ 7,108,000
Working capital.....	5,399,000	2,744,000	6,187,000	10,319,000	9,851,000	6,540,000
Total assets.....	6,414,000	4,156,000	8,227,000	12,551,000	12,673,000	8,931,000
Deficit accumulated during the development stage....	(2,404,000)	(5,251,000)	(11,391,000)	(17,108,000)	(27,025,000)	(30,298,000)
Total stockholders' equity.....	6,104,000	3,268,000	6,985,000	11,186,000	10,850,000	7,618,000

(1) See Note 1 of Notes to Financial Statements for information concerning the computation of pro forma net loss per share and shares used in computing pro forma net loss per share.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF
FINANCIAL CONDITION AND RESULTS OF OPERATIONS

OVERVIEW

Since inception, the Company has been in the development stage and engaged in research and product development, conducted both on its own behalf and in connection with various collaborative research and development agreements with other entities. The Company expects that its revenue sources for at least the next several years will continue to be limited to grant revenues and research funding, milestone payments and licensing fees from potential future corporate collaborators. The timing and amount of such future revenues, if any, will be subject to significant fluctuations, based in part on the success of the Company's research activities and the timing of the achievement of certain milestones. Substantially all of the Company's revenues from product sales, if any, will be subject to royalty payments ranging from 2% to 5%. Further, under the Company's Distribution Agreement with Cobe, Cobe will perform marketing and distribution activities and in exchange will receive from 38% to 42% of the Company's product sales in the area of stem cell therapy, subject to negotiated discounts and volume-based adjustments. Research and development expenses may fluctuate due to the timing of expenditures for the varying stages of the Company's research and clinical development programs. Research and development expenses will increase as product development programs and applications of the Company's products progress through research and development stages. Under the Company's License Agreement with Immunex, annual renewal fees of \$1,000,000 are payable in each of the next four years. Under the Company's Distribution Agreement with Cobe, regulatory approval activities for the Company's products for stem cell therapies outside of the United States will be conducted, and paid for, by Cobe. As a result of these factors, the Company's results of operations have, and are expected to continue to, fluctuate significantly from year to year and from quarter to quarter and therefore may not be comparable to or indicative of the results of operations for other periods.

Over the past several years, the Company's net loss has primarily increased, consistent with the growth in the Company's scope and size of operations. In the near term, the Company plans additional moderate growth in employee headcount necessary to address increasing requirements in the areas of product development, research, clinical and regulatory affairs and administration. Assuming capital is available to finance such growth, the Company's operating expenses will continue to increase as a result. At least until such time as the Company enters into arrangements providing research and development funding, the net loss will continue to increase as well. The Company has been unprofitable since its inception and does not anticipate having net income for several years. Through September 30, 1996, the Company had an accumulated deficit of \$30,298,000. There can be no assurance that the Company will be able to achieve profitability on a sustained basis, if at all.

This Prospectus contains, in addition to historical information, forward-looking statements that involve risks and uncertainties. The Company's actual results could differ materially from the results discussed in the forward-looking statements. Factors that could cause or contribute to such differences include those discussed under this caption, as well as those discussed under the caption "Risk Factors" and elsewhere in this Prospectus.

RESULTS OF OPERATIONS

THREE MONTHS ENDED SEPTEMBER 30, 1996 AND 1995

Total revenues were \$224,000 for the three months ended September 30, 1996 compared to \$211,000 for the same period in 1995. These revenues consist primarily of research and development revenue under the Company's research collaboration with RPR, which was terminated in September 1996. See "Certain Transactions."

Total costs and expenses were \$3,612,000 for the three months ended September 30, 1996 compared to \$1,641,000 for the same period in 1995. The increase in costs and expenses in 1996 is primarily the result of an increase in research and development expenses to \$3,160,000 in 1996 from \$1,195,000 in 1995 and to a lesser extent by general and administrative expenses, which increased to \$452,000 for the three months ended September 30, 1996 from \$446,000 for the same period in 1995.

Interest income was \$126,000 for the three months ended September 30, 1996 compared to \$149,000 for the same period in 1995 and reflects a decrease in the levels of cash, cash equivalents and short-term investments in 1996.

The Company's net loss increased to \$3,273,000 for the three months ended September 30, 1996 from \$1,299,000 for the same period in 1995, primarily as a result of increased costs and expenses in 1996.

YEARS ENDED JUNE 30, 1996, 1995 AND 1994

Total revenues were \$1,609,000 in 1996, \$517,000 in 1995, and \$872,000 in 1994. Grant revenues increased to \$267,000 in 1996 from \$121,000 in 1995, which had decreased from \$823,000 in 1994, reflecting the timing of grant awards and related research activities and funding under the grants. Grant revenues accounted for 17%, 23% and 94% of total revenues for the years ended June 30, 1996, 1995 and 1994, respectively. Revenues from research and development agreements totaled \$1,342,000 in 1996, \$396,000 in 1995 and \$49,000 in 1994, reflecting research funding received by the Company under its collaboration with RPR which commenced in September 1995. Revenues from RPR accounted for 83% and 48% of such revenue in 1996 and 1995, respectively. In September 1996, the Company's research collaboration with RPR terminated.

Total costs and expenses were \$12,142,000 in 1996, \$6,447,000 in 1995, and \$7,192,000 in 1994. The increase in 1996 costs and expenses, compared with 1995, is primarily the result of an increase in research and development expense to \$10,075,000 in 1996 from \$4,889,000 in 1995. The increase in research and development expense reflects an increase in research, clinical development and product development activities. The decrease in costs and expenses in 1995, compared with 1994, is primarily the result of a decrease in research and development expense to \$4,889,000 in 1995 from \$5,627,000 in 1994. General and administrative expenses were \$2,067,000 in 1996, \$1,558,000 in 1995 and \$1,565,000 in 1994. The increase in general and administrative expenses in 1996 is the result of increasing finance, legal and other administrative and marketing expenses which are expected to continue to increase in support of the Company's increasing product development and research activities. The decrease in general and administrative expense in 1995 is reflective of generally lower spending in 1995 as compared to 1994.

Interest income was \$678,000 in 1996, \$279,000 in 1995, and \$245,000 in 1994. The increases in interest income in 1996 and 1995 are due primarily to corresponding increases in the levels of cash, cash equivalents and short-term investments for such periods. Interest expense was \$62,000 in 1996, \$66,000 in 1995, and \$65,000 in 1994, reflecting varying amounts outstanding under capital leases during the periods.

The Company's net loss was \$9,917,000 in 1996, \$5,717,000 in 1995, and \$6,140,000 in 1994. The Company expects to report substantial net losses for at least the next several years.

The Company has not generated any net income to date and therefore has not paid any federal income taxes since inception. At June 30, 1996, the Company had deferred tax assets totaling \$9,650,000 consisting primarily of net operating loss and research tax credits that begin to expire from 2004 through 2011, if not utilized. A full valuation allowance for deferred tax assets has been provided. Utilization of federal income tax carryforwards is subject to certain limitations under Section 382 of the Internal Revenue Code of 1986, as amended. The completion of this offering is likely to limit the Company's ability to utilize federal income tax carryforwards under Section 382. The annual limitation could result in expiration of net operating losses and research and development credits before their complete utilization.

LIQUIDITY AND CAPITAL RESOURCES

The Company has financed its operations since inception primarily through private placements of Preferred Stock and other equity investments, which from inception, have totaled approximately \$37,916,000, and to a lesser degree, through grant funding, payments received under research agreements and collaborations, interest

earned on cash, cash equivalents, and short-term investments, and funding under equipment leasing agreements. These financing sources have historically allowed the Company to maintain adequate levels of cash and other liquid investments.

The Company's combined cash, cash equivalents and short-term investments totaled \$10,967,000 at June 30, 1996, a decrease of \$101,000 from June 30, 1995. The primary uses of cash, cash equivalents and short-term investments during the year ended June 30, 1996 included \$8,967,000 to finance the Company's operations and working capital requirements, \$445,000 in capital equipment additions and \$270,000 in scheduled debt payments. During the year ended June 30, 1996, the Company received \$3,500,000 in equity payments from RPR and \$5,965,000 in net proceeds from the sale of Series E Convertible Preferred Stock. The Company plans to continue its policy of investing excess funds in short-term, investment-grade, interest-bearing instruments.

The Company's combined cash, cash equivalents and short-term investments totaled \$7,108,000 as of September 30, 1996 compared to \$10,967,000 at June 30, 1996. The decrease was primarily attributable to the use of \$3,614,000 to fund operations and working capital requirements during the period and to a lesser degree by \$173,000 in capital equipment purchases and \$73,000 in scheduled debt payments.

In October 1996, the Company executed a financing commitment to provide the Company with up to \$5,000,000 in additional equity funding from Cobe and \$5,000,000 under a convertible loan agreement with another current investor. In connection with the convertible loan agreement, the Company has issued warrants to purchase 69,444 shares of Common Stock for securing the commitment. The warrants expire on October 15, 2000 if not exercised, and may be exercised, in whole or in part, at a price equal to the lesser of (a) \$9.00 per share, which price increases by \$3.00 per share on each anniversary of the closing of the offering being made hereby; or (b) 85% of the fair market value of the Company's Common Stock at the time of exercise. As of the date of this Prospectus, the Company has not obtained any financing under these commitments. These funding commitments expire upon the closing of this offering.

The Company's future cash requirements will depend on many factors, including continued scientific progress in its research and development programs, the scope and results of clinical trials, the time and costs involved in obtaining regulatory approvals, the costs involved in filing, prosecuting and enforcing patents, competing technological and market developments and the cost of product commercialization. The Company does not expect to generate a positive cash flow from operations for several years, if at all, due to the expected increase in spending for research and development programs and the expected cost of commercializing its product candidates. The Company may seek additional funding through research and development agreements with suitable corporate collaborators and through public or private financing transactions. The Company anticipates that the net proceeds of this offering, together with the Company's available cash and expected interest income thereon, will be sufficient to finance its research and development and other working capital requirements for 18 months or less. This estimate is based on certain assumptions which could be negatively impacted by the matters discussed under this heading and elsewhere under the caption "Risk Factors." The Company expects that its primary sources of capital for the foreseeable future will be through collaborative arrangements and through the public or private sale of its equity securities. There can be no assurance that such collaboration arrangements, or any public or private financing transaction, will be available on acceptable terms, if at all, or can be sustained on a long-term basis. If adequate funds are not available, the Company may be required to delay, reduce the scope of, or eliminate one or more of its research and development programs, which may have a material adverse effect on the Company's business. See "Risk Factors--Future Capital Needs; Uncertainty of Additional Funding" and Notes to Financial Statements.

RECENT PRONOUNCEMENTS

During October 1995, the Financial Accounting Standards Board issued Statement No. 123, "Accounting for Stock-Based Compensation," which establishes a fair value based method of accounting for stock-based compensation and incentive plans and requires additional disclosures for those companies that elect not to adopt

the new method of accounting. Adoption of the new accounting pronouncement is required for the Company's fiscal year beginning July 1, 1996 and the Company intends to provide the additional disclosures required by the pronouncement in its financial statements for the year ended June 30, 1997.

During March 1995, the Financial Accounting Standards Board issued Statement No. 121, ("SFAS 121") "Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to Be Disposed Of," which requires the Company to review for impairment of long-lived assets, certain identifiable intangibles, and goodwill related to those assets whenever events or changes in circumstances indicate that the carrying amount of an asset might not be recoverable. In certain situations, an impairment loss would be recognized. SFAS 121 will become effective for the Company's fiscal year beginning July 1, 1996. Management has studied the effect of implementing SFAS 121 and, based upon its initial evaluation, does not expect it to have a significant impact on the Company's financial condition or results of operations.

OVERVIEW

Aastrom is developing proprietary process technologies and devices for a range of cell therapy applications, including stem cell therapies and gene therapy. The Company's lead product under development, the Aastrom Cell Production System (the "Aastrom CPS"), consists of a clinical cell culture system with disposable cassettes and reagents for use in the rapidly growing stem cell therapy market. The Company believes that the Aastrom CPS method will be less costly, less invasive and less time consuming than currently available stem cell collection methods. The Aastrom CPS is designed as a platform product which implements the Company's pioneering stem cell replication technology and which the Company believes can be modified to produce a wide variety of cell types for emerging therapies. The Aastrom CPS is currently in a pre-pivotal clinical trial under an IDE for autologous stem cell therapy. The Company has entered into a strategic collaboration for the development of the Aastrom CPS in stem cell therapy with Cobe BCT, Inc., a subsidiary of Gambro AB and a world leader in blood cell processing products. Additionally, Aastrom is developing products and processes for the delivery of ex vivo gene therapy that are designed to address the production of gene-modified cells.

CELL THERAPY

Cell therapy is the use of human cells to treat a medical disorder. The most common types of cell therapy, blood and platelet transfusions, have been widely used for many decades. More recently, bone marrow-derived cells have been used to restore the bone marrow and the blood and immune system cells which are damaged by chemotherapy and radiation therapy during the treatment of many cancers. Transplantation of these cells is known as stem cell therapy. Other cell therapies have recently been used for generating skin and cartilage tissue and additional cell therapies are being developed by various companies and researchers to restore immune system cells as well as bone, kidney, liver, vascular and neuronal tissues.

Cell therapies require the collection of cells, either from the patient or a suitably matched donor. These cells are typically processed and stored for administration to the patient. Although cell therapy is being developed for use in an increasing number of diseases, widespread application of new cell therapies remains limited by the difficulties and expense associated with current cell collection and processing procedures. The problems of current cell collection techniques are exemplified in the area of stem cell therapy where the patient or donor undergoes invasive, time-consuming and costly procedures to collect the large volume of cells currently required for effective treatment. The Company believes an alternative to collecting the required therapeutic dose of cells is to grow these cells ex vivo from a small starting volume. However, ex vivo cell expansion, when biologically possible, has typically required costly techniques, facilities and operations to comply with FDA good manufacturing practices ("GMP"), which are not generally available in hospitals. As a result, cells needed for such therapies often require specialized cell production facilities which use labor-intensive, manual cell culture techniques.

There are numerous forms of cell therapy at an early stage of development. One such example is ex vivo gene therapy, in which genes are introduced into target cells in order to selectively correct or modulate disease conditions, or to modify cells for production of a therapeutic protein. The Company believes that the successful practice of ex vivo gene therapy will require the development of processes and products for the reliable, high-efficiency transfer of genes into cells and a means to produce the necessary dose of the genetically modified cells under GMP conditions.

STEM CELL THERAPY

Stem cell therapy is used to treat cancer patients who undergo chemotherapy or radiation therapy at dose levels that are toxic to the hematopoietic system, which is comprised of the bone marrow and cells of the blood and immune systems. The objective of stem cell therapy is to restore the hematopoietic system via the infusion and subsequent engraftment of healthy cells to replace bone marrow and result in the rapid recovery of neutrophils and platelets that have been destroyed by chemotherapy and radiation therapy. Stem cell therapy

reduces the risk of life-threatening infections and bleeding episodes following cancer treatments. In order to treat many cancers, high intensity chemotherapy or radiation is often required, which may severely destroy ("myeloablation") or partially destroy ("myelosuppression") the patient's hematopoietic system.

Cells required for effective stem cell therapy include stem cells, to replenish depleted bone marrow and provide a long-term ongoing source of the multilineage progenitor cells of the blood and immune systems, and early and late stage hematopoietic progenitor cells, to provide for rapid neutrophil and platelet recoveries. Stromal accessory cells are believed to further augment the growth of bone marrow. In the adult, all of these cell types originate in the bone marrow. These cells are currently collected from the donor or patient directly through multiple syringe aspirations under anesthesia, known as bone marrow collection, or through blood apheresis following treatment with drugs which cause cells to be released or mobilized from the bone marrow into the blood. This latter technique is known as a peripheral blood progenitor cell ("PBPC") collection. See "--Current Stem Cell Collection Methods." Recently, it has been demonstrated that the blood cells found in the umbilical cord of newborn infants include cells effective for stem cell therapy. This source of cells is being explored by physicians as a major new direction in stem cell therapy, but is currently limited by difficulties in obtaining sufficient quantities of these cells.

Once collected, the stem cell mixture is infused intravenously and the stem and stromal accessory cells migrate into the bone cavity where they engraft to form a new marrow. The hematopoietic progenitor cell components of the cell mixture provide early restoration of circulating white blood cells and platelets. The replenished bone marrow will normally provide long-term hematopoietic function, but complete restoration of bone marrow may take years following myeloablative cancer therapy. When the patient's hematopoietic system is malignant, such as in the case of leukemia, cells from a suitable donor are generally required in order to avoid reintroducing the disease during cell infusion. Such donor derived transplants are termed "allogeneic" transplants. Procedures using cells derived from the patient are termed "autologous" transplants.

STEM CELL THERAPY MARKET OPPORTUNITY

The benefits of stem cell therapy in the treatment of cancer patients have been well established over the past two decades. Stem cell therapy, in the form of bone marrow transplantation, was originally used in patients who had received treatment for blood and bone marrow cancers such as leukemia, and genetic diseases of the blood. However, because stem cell therapy has been shown to promote the rapid recovery of hematopoietic function, it is now being increasingly used to enable patients with other forms of cancer to receive high dose or multicycle chemotherapy and radiation treatments. These high intensity therapies have a greater probability of eradicating dose sensitive cancers but, because of their hematopoietic toxicity, cannot generally be given without stem cell therapy. As a result, some patients are treated with lower and less effective doses, and fewer cycles, of therapy than might otherwise be used.

The Company estimates that over 35,000 stem cell therapy procedures were completed worldwide in 1995, and that the number of such procedures is growing at a compound annual rate of over 20%. This growth has been driven by encouraging clinical results in the treatment of dose-sensitive solid tumors, such as breast and ovarian cancers. The Company expects that stem cell therapy procedures will continue to grow due to increased incidence and prevalence of cancer, continued clinical demand for myelotoxic cancer treatment, and the increased cost effectiveness of stem cell therapy treatments.

Stem cell therapy may also enhance the effectiveness of blood cell growth factors. The timing and extent of additional cycles of chemotherapy is often limited by the recovery of a patient's white blood cells and platelets because a delayed recovery of these cells can leave the patient susceptible to life-threatening infection and bleeding episodes, and this limitation may allow for the regrowth of residual tumor cells. Many cancer patients are routinely treated with growth factors including G-CSF, such as Neupogen and GM-CSF, such as Leukine, which enhance the development of mature circulating white blood cells and platelets from the early progenitor bone-marrow derived cells, thereby decreasing the time between cycles of therapy and the probability of infection. However, during high dose or multi-cycle therapy, the stem and progenitor cells on which these growth

factors act are often depleted. Without these cells, growth factors have a limited or negligible effect. Stem cell therapy generally enhances the effectiveness of growth factors by introducing target stem and progenitor cells for growth factors to act upon such that patients generally exhibit a more rapid and consistent hematopoietic recovery.

CURRENT STEM CELL COLLECTION METHODS

Currently, the bone marrow-derived cells required for stem cell therapy are collected primarily either through the bone marrow harvest method or the PBPC collection method.

Bone Marrow Harvest

A traditional bone marrow harvest is a costly and invasive surgical procedure in which a physician removes approximately one liter of bone marrow from a patient or donor. This volume of bone marrow is removed using needles inserted into the cavity of the hip bone. The bone marrow harvest procedure typically requires between two to four hours of operating room time, with the physician often making more than 100 separate puncture sites in the hip bone to collect the necessary amount of bone marrow. Due to the length of the procedure and the trauma to the patient, general surgical anesthesia is administered and the patient is typically hospitalized for a day. Frequently, the patient suffers pain from the procedure for several days after being discharged from the hospital. Furthermore, complications resulting from the general anesthesia or invasive nature of the procedure occur in a small percentage of patients. Bone marrow harvest provides a reliable source of stem and stromal accessory cells and has been the preferred source of cells in allogeneic transplants.

PBPC Mobilization and Collection

PBPC mobilization is a newer technique in which bone marrow-derived cells are harvested from a patient's or donor's circulating blood, rather than from bone marrow. In a PBPC mobilization procedure, the patient receives multiple injections of growth factors or cytotoxic drugs, or both, over the course of a week or more, which cause stem and progenitor cells resident in the bone marrow to mobilize into the circulating blood. The mobilized cells are then collected by connecting the patient to a blood apheresis device, which draws and returns large volumes of the patient's or donor's blood in order to selectively remove the therapeutic volume of stem and progenitor cells. Each collection procedure typically lasts for two to six hours and is typically repeated on two to eight consecutive days. Specialized laboratory testing over the period of mobilization and cell harvesting is necessary to determine that a sufficient quantity of desired cells has been collected, adding to the cost of the procedure. The PBPC process has become the predominant procedure in autologous stem cell therapy.

Procedure Considerations

Although stem cell therapy is being utilized to treat more patients for a broader range of diseases, its availability continues to be limited by the high costs of procuring cells, the invasive nature of traditional cell procurement techniques, and by the technical difficulties related to those collection procedures. The Company estimates that current costs for bone marrow harvest and processing are approximately \$10,000 to \$15,000 per procedure, with considerable variability between institutions. The Company estimates that current costs for PBPC collection, including mobilization with growth factors, are approximately \$12,000 to \$20,000 for a two to three cycle procedure, with considerable variability between institutions depending on the total volume, time and number of aphereses required.

Overall costs of stem cell therapy include the costs of the cell collection procedure, and the costs associated with supporting the patient during post-transplant recovery. Post-transplant costs include hospitalization time, antibiotic support, management of adverse reactions to the large volume cell infusions, and infusions of platelets and red blood cells. Any new stem cell therapy process will generally need to provide similar recovery endpoints to be competitive with the current procedures. In this regard, PBPC procedures have gained popularity compared with bone marrow harvests because the number of platelet transfusions is reduced for some patients.

Recently, products to implement a cell isolation method known as CD34 selection have been developed by other companies in conjunction with bone marrow harvest and PBPC collections. CD34 selection is a process designed to isolate specific types of cells in order to decrease storage and infusion problems associated with the large volume of fluids collected in bone marrow or multiple apheresis procedures. CD34 selection is used after the initial collection of stem and progenitor cells and, therefore, does not address the difficulties or costs associated with the basic cell collection procedures. To date, the CD34 selection procedure has demonstrated limited therapeutic benefit to the patient, but substantially increases the costs of the procedure. A future objective of CD34 selection is to assist in depleting tumor cells from the transplant cells collected, thereby expanding the availability of stem cell therapy to new patient populations.

UMBILICAL CORD BLOOD

Umbilical cord blood ("UCB"), which is collected directly from the umbilical cord after delivery, without pain or risk to the infant or the mother, is emerging as a new source of cells for stem cell therapy. UCB has been reported to have stem cell concentrations that are much higher than that typically obtained from traditional bone marrow and PBPC collection methods. After collection, UCB is typically frozen for later use in a stem cell therapy procedure. Storage of UCB samples involves small volumes of cells, compared to typical bone marrow or PBPC storage. Accordingly, the costs of collection and storage of UCB cells are comparatively low. This source of cells is also "tumor-free," such that UCB would be preferred for many current stem cell therapy procedures in metastatic cancer patients. Before UCB can become a major supply source for stem cell therapy, a coordinated UCB banking system must emerge. In this regard, several organized UCB banking institutions have been established to date, and the group is growing in both number and size.

One current disadvantage of UCB is the relatively low number of available cells. Unlike bone marrow or PBPC harvest, where the collection of more cells to meet a particular treatment is typically achievable, the number of cells available from a UCB donor is limited. This problem is exacerbated by the required cryopreservation of the cells, which causes a significant cell loss. The resultant low cell number is believed to be responsible for the longer hematopoietic recovery times observed with UCB transplants, as compared with bone marrow or PBPC transplants. Further, because of the low cell number, UCB transplants are typically restricted to small patients. Therefore, increasing the number of therapeutic cells from a UCB sample would facilitate the more widespread use of UCB transplants. Aastrom believes that providing the transplant site with the capability to carry out the UCB cell expansion will be a major factor in the increased use of UCB for stem cell therapy and a significant business opportunity.

AASTROM TECHNOLOGY

Aastrom is developing proprietary process technologies that are pioneering the ex vivo production of human stem and progenitor cells. The Company has also developed a proprietary cell culture device that mimics the biological and physical environment necessary for the growth of certain human cells and tissues, including bone marrow. The Company's initial product candidate, the Aastrom CPS, utilizes the Company's process technology and is designed to enable the ex vivo production of human stem and progenitor cells as an alternative to the bone marrow harvest and PBPC mobilization methods and as an enhancement to the UCB collection method. The Company believes that the Aastrom CPS may be used for other cell production processes which are being developed by third parties and, in combination with the Company's proprietary gene transfer process, may have application in the developing field of ex vivo gene therapy.

CORE TECHNOLOGY

Stem Cell Growth Process

Aastrom has developed proprietary process technologies for ex vivo production of therapeutic stem and progenitor cells as well as other key cells found in human bone marrow. The Company's proprietary process entails the placement of a stem cell mixture in a culture environment that mimics the biology and physiology of

natural bone marrow. This process enables the stem and early and late-stage progenitor cells needed for an effective stem cell therapy procedure to be concurrently expanded. Growth factors can be added to stimulate specific cell lineages to grow or to increase cell growth to meet a particular therapeutic objective. The stem cell growth process can best be completed with little or no additional stem cell selection or purification procedures. This stem cell replication process can also enable or augment the genetic modification of cells by providing the cell division step needed for new genes to integrate into the stem cell DNA. Currently available cell culture methods tend to result in a loss of stem cells, either through death or through differentiation into mature cells. The Company has exclusive license to two U.S. patents and additional applications that cover these processes. See "--Additional Stem Cell and Other Cell Therapies."

Aastrom Cell Culture Chamber

Aastrom has developed a proprietary cell culture chamber to implement the Company's process technology. The culture chamber produces cells on a clinical scale, and allow for simple, sterile recovery of the cells for therapeutic use. The Company believes that the Aastrom cell culture chamber may also be used for growing other human therapeutic cells, such as T-Cells used for lymphocyte therapies, chondrocytes for cartilage replacement, and mesenchymal tissues for bone and cartilage replacement. The Company holds exclusive licenses to two U.S. patents and additional applications for its cell culture chamber device technology. See "--Additional Stem Cell and Other Cell Therapies."

Efficient Gene Transfer

Aastrom has developed proprietary processes and device technology that enables increased efficiency of vector-mediated gene transfer into cells as compared to conventional procedures. This directed-motion gene transfer or gene loading technology is intended to have applications for most cell and tissue types and most vector technologies. The Company intends to develop products based upon its gene loading technology that it believes will facilitate the advancement of numerous gene therapy protocols into the clinic and ultimately the market. The Company has received a U.S. Patent and has additional applications for this technology. See "Aastrom Product Candidates For Ex Vivo Gene Therapy."

THE AASTROM CPS

The Aastrom CPS is the Company's lead product under development for multiple cell therapy applications, including stem cell therapy. The Aastrom CPS is a proprietary system that the Company believes will enable the large scale ex vivo production of a variety of therapeutic cells at health care facilities, independent laboratories, transplant centers and blood banks, and has been designed to implement Aastrom's stem cell growth process as well as processes for the production of other cell types.

The Aastrom CPS is comprised of several components, including single-use disposable cassettes and reagents and microprocessor-controlled instruments, which are at various stages of development. The Cell Cassette is a single-use disposable cartridge which contains the Aastrom cell culture chamber and the related media supply waste reservoirs and harvest bag. The microprocessor-controlled instruments include the Incubator which controls the culture conditions for the operation of the Cell Cassette, and the Processor which automates the priming and harvesting of the cells from the cell cassette. The System Manager is a user interface computer that is being developed to simultaneously track and monitor the cell production process in over thirty CPS Incubators and record relevant process variables and operator actions. Prototype components of the Aastrom CPS are currently being used in a clinical trial and ongoing development activities are directed at completing other production level components of the Aastrom CPS.

The Aastrom CPS is designed to be operated with minimal operator activity by a medical or laboratory technician and can implement clinical scale cell production at the patient care site. The end product of the Aastrom process is a sterile bag of cells. The control and documentation features of the Aastrom CPS have been designed to meet GMP requirements for the therapeutic production of cells.

AASTROM CPS FOR STEM CELL THERAPY

The Company's initial application for the Aastrom CPS is expected to be in the growing field of stem cell therapy, where the Company believes that the Aastrom CPS may address many of the limitations of existing procedures. The Aastrom CPS is based on a comparatively simple process in which a small volume of bone marrow cells are collected from the patient or donor using a needle aspiration procedure under a local anesthetic or sedative. This cell mixture is quantified, and an appropriate volume of cells is then inoculated into one or more cell cassettes with the necessary growth media. Therapeutic growth-factor-stimulated cells are produced using the Aastrom CPS in approximately 12 to 13 days, with no further patient involvement. Depending upon the cell quantity necessary for a therapeutic application, single or multiple cell cassettes may be required, with a different volume requirement of starting cells. The Aastrom CPS has been designed to minimize operator involvement during the cell production process, and the steps required before and after the Aastrom CPS are standard laboratory procedures.

Advantages of Aastrom CPS

The Company believes that the Aastrom CPS, if approved for commercial sale by the FDA and foreign regulatory agencies, will provide improvements and efficiencies over traditional cell collection processes. The following table illustrates some potential advantages of the Aastrom CPS compared to approximated patient visits, procedure time and needle sticks in connection with currently established cell collection techniques:

CELL SOURCE	VISITS(1)	PROCEDURE TIME (HOURS)	NEEDLE STICKS(2)
Bone Marrow Harvest(3).....	6	22	100+
PBPC Mobilization and Collection(4).....	5-7	23-27	20-30
Aastrom CPS(5).....	1	1-2	4-10

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- (1) Includes all outpatient, inpatient, and home care episodes.
 - (2) Includes bone marrow aspirates, blood samples, catheter placements, and subcutaneous injections.
 - (3) Includes operating room procedure and all preparatory screening and testing.
 - (4) Based on two to three 4-hour rounds of PBPC mobilization and collection after sequential G-CSF blood mobilization injections.
 - (5) Based on data accumulated during the Company's clinical trials.

Reduced Cost. The Company believes the Aastrom CPS has the potential to replace more costly, labor intensive and invasive cell collection procedures currently employed for stem cell therapy and to reduce physician, staff and patient time requirements.

Reduced Patient and Physician Burden. Cell production with the Aastrom CPS is expected to require the collection of a small volume of starting material compared to current collection procedures, eliminating the requirement for general surgical anesthesia, multiple drug injections and blood apheresis. Patient benefits include fewer needle sticks than with current cell collection methods and a reduction in overall patient procedure time. Additionally, Aastrom's process for cell expansion is expected to minimize the time requirement for physicians compared with bone marrow harvest.

Enhanced Multicycle High-Dose Chemotherapy. The long restoration period for the hematopoietic system following myeloablative therapy effectively limits patients to one opportunity for cell collection prior to cancer therapy. The Aastrom CPS may enhance the practice of multi-cycle, high-dose chemotherapy by providing the ability to produce a therapeutic dose of cells from a small starting volume. The initial cell collection can be divided into multiple samples and stored frozen until expansion at a later time is required.

Reduced Quantity of Lymphocytes. The Company believes its approach to stem cell therapy may provide an additional benefit over current methods by depleting potentially harmful cells such as T-cells and B-cells. These cells are believed to be primarily responsible for graft-versus-host disease, a common manifestation of allogeneic transplants in which the grafted donor's cells attack the host's tissues and organs.

Tumor Cell Purging. Cancer patients with tumor metastases, in which the cancer has spread to the blood and bone marrow, have not traditionally been candidates for autologous stem cell transplants because transplant may reintroduce cancer cells into the patient. Additionally patients may have undetected tumor cells in their marrow or PBPC transplant, which can reestablish the cancer in the patient following transplant. The Aastrom CPS process may offer benefits for these groups of patients. The Company and other investigators have shown that some primary human tumor cells die or do not grow during hematopoietic cell culture. Further, the smaller volume of starting cells used for the Aastrom CPS compared with BMT or PBPC transplants shall provide approximately 10 to 70 fold less tumor cells in a transplant. This combination of passive depletion during culture with the lower starting volume of tumor cells may result in a tumor-free or tumor-reduced cell product for transplant. The benefit of such tumor depletion, if any, will vary depending upon the type of cancer and state of disease.

CLINICAL DEVELOPMENT

The Company's clinical development plan is initially to obtain regulatory approval in the United States to market the Aastrom CPS for autologous stem cell therapy and in Europe for more general cell therapy applications. The Company also intends to pursue approval of the Aastrom CPS for additional clinical indications.

The Company believes that the Aastrom CPS for stem cell therapy will be regulated as a medical device and that the Company will be required to submit a PMA application to, and obtain approval from, the FDA to allow it to market this product in the United States. In order to obtain PMA approval, the Company will be required to complete clinical trials under an IDE. See "-- Government Regulation--Devices."

In a dose-ranging study conducted by the University of Michigan (the "University") in 1993, ex vivo produced cells utilizing the Company's proprietary cell production technology were infused into seven patients with non-Hodgkin's lymphoma after they received myeloablative chemotherapy. These patients also received cells obtained from either an autologous bone marrow harvest or PBPC procedure. No safety issues attributable to the infused cells were observed in this trial and the patients exhibited recovery profiles consistent with traditional transplantation techniques.

Aastrom completed the first feasibility trial of its cell production system technology under an IDE at the MD Anderson Cancer Center in October 1995. In this trial, ten breast cancer patients, who were subjected to myeloablative chemotherapy, were treated with cells obtained from a bone marrow harvest and with cells produced from a sample of such cells with a predecessor of the Aastrom CPS. The patients exhibited standard clinical recoveries, providing evidence of the clinical safety of cells obtained from the Company's cell production process and of the feasibility of cell production with a predecessor of the Aastrom CPS by clinical personnel at an investigational site.

Aastrom is currently conducting a pre-pivotal stem cell therapy clinical trial under an IDE reviewed with the FDA. This clinical trial is designed to demonstrate that cells produced using the Aastrom CPS can provide hematopoietic recovery in accordance with trial endpoints in breast cancer patients who have received myeloablative chemotherapy. Bone marrow obtained from the patient by traditional methods will be available for precautionary reasons at defined clinical stages. The results from the five patients accrued at the first trial site have provided evidence of the clinical safety of the Aastrom CPS-produced cells in patients and that the hematopoietic recovery endpoints specified for the trial are achievable. The patients at this trial site were Stage IV breast cancer patients who had received significant prior cytotoxic therapies for their cancer. Four of these five patients received the precautionary back-up marrow pursuant to the trial protocol. Preliminary results from the first trial site were reviewed with the FDA, and the IDE was amended to expand the trial to a second site. The amended IDE provided for the enrollment of Stage II, III and IV patients, and a delayed use of the precautionary back-up bone marrow. As of the date of this Prospectus, patient accrual is ongoing and patient data from this site provides further evidence that the hematopoietic recovery endpoints specified for the trial are achievable.

The objective of the current and anticipated future trials is to establish the protocol for the pivotal trial of the Aastrom CPS in autologous stem cell therapy. Provided that these pre-pivotal trials provide evidence of feasibility and safety of the cells produced in the Aastrom CPS, the Company anticipates initiating a pivotal clinical trial at multiple sites, with the patient enrollment typical to support a PMA filing. See "Risk Factors--Uncertainties Related to Preclinical and Clinical Testing."

Aastrom, in partnership with Cobe, intends to initiate a clinical trial in France in early 1997 to evaluate the use of Aastrom CPS cells to promote hematopoietic recovery in breast cancer patients undergoing aggressive myelosuppressive chemotherapy. The Company intends to seek approval to market the Aastrom CPS in Europe through CE Mark Registration. See "--Government Regulation--Regulatory Process in Europe."

The preliminary results of the Company's pre-pivotal trial may not be predictive of results that will be obtained from subsequent patients in the trial or from more extensive trials. Further, there can be no assurance that the Company's pre-pivotal or pivotal trial will be successful, or that PMA approval or required foreign regulatory approvals for the Aastrom CPS will be obtained in a timely fashion, or at all.

BUSINESS STRATEGY

Aastrom's objective is to build a leadership position in cell therapy process technology. The primary elements of the Company's business strategy are as follows:

Establish Consumable Based Business Model. Aastrom's strategy is to sell the Aastrom CPS to institutions, hospitals, and other clinical care or commercial cell production facilities that are administering cell therapy. The Company plans to obtain ongoing revenue from the sale of single-use disposable Cell Cassettes and related cell culture media and reagents, which are utilized in individual cell therapy applications. After cells are cultured in the Cell Cassette, the cassette is discarded and a new cassette is utilized for a subsequent patient. Along with ongoing revenue from the sale of instruments and disposables for cell therapy applications, the Company believes it will be able to obtain license revenue from its stem cell therapy applications for its proprietary stem cell processes.

Focus Initially on Established and Reimbursed Therapies. Aastrom will seek to establish the use of the Aastrom CPS in the field of stem cell therapy for the treatment of toxicity resulting from many cancer therapies, including those for breast cancer, lymphoma, ovarian cancer, germ cell cancers, leukemias and aplastic anemias. Stem cell therapy is a well-established and growing treatment modality in cancer therapy, and current cell collection procedures are widely reimbursed by third party payors.

Leverage Platform Technology Across Multiple Market Opportunities. In addition to stem cell therapy applications, the Company believes that the Aastrom CPS may serve as a platform product that can be used to produce a variety of other cells for multiple therapeutic applications, such as T-cells for use in lymphocyte therapies, chondrocytes for cartilage replacement, and mesenchymal cells for use in certain solid tissue therapies. The Company believes that if the Aastrom CPS is well established as a method for cell production for use in stem cell therapy, the system will be positioned for commercialization of new cell and ex vivo gene therapies that are under development.

Market Through Collaborative Relationships. The Company plans to reach end user markets through collaborative relationships with companies that have established positions in those markets. In 1993, the Company formed a strategic partnership with Cobe, a world leader in the marketing and distribution of blood cell processing equipment and disposables. Cobe is the Company's exclusive, worldwide distributor of the Aastrom CPS for stem cell therapy applications, not including stem cell gene therapy. The Company will seek to establish additional collaborations for other cell therapies as those therapies and the Company's product lines develop. See "Business--Strategic Relationships."

ADDITIONAL STEM CELL AND OTHER CELL THERAPIES

The Company believes that the Aastrom CPS hardware and disposables may be developed to serve as platform products for application in a variety of other cell therapies in addition to stem cell therapy. The Company believes that the Aastrom CPS has the potential to supplant current manual cell culture methods to produce therapeutic quantities of cell types such as T-cells, chondrocytes, mesenchymal cells, keratinocytes, neuronal cells and dendritic cells. Currently such cells are often produced in specialized facilities generally using manual cell culture techniques which limit the effective commercialization of these cell types for therapy. Potential advantages of the Aastrom CPS in these therapies may include: (i) reducing labor and capital costs; (ii) enhancing process reliability; (iii) automating quality assurance; and (iv) reducing the need for environmentally controlled facilities.

Modification of such processes and application of the Company's products to the expansion of other cell types may require substantial additional development of specialized culture environments and which may need to be incorporated within the Company's existing cell cassettes. There can be no assurance that the Company will be able to successfully modify or develop existing or future products to enable such additional cell production processes. Furthermore, other than a limited application of chondrocyte therapy, novel cell therapies are still in early stages of development by third parties. The Company's business opportunity is dependent upon successful development and regulatory approval of these novel cell therapies. No assurance can be given that such novel therapies will be developed or approved or that the Company's processes or product candidates will find successful application in such therapies. See "--Business Strategy" and "--Clinical Development" and "Use of Proceeds."

Immunotherapies

Immunotherapy involves using cells of the immune system to eradicate a disease target. T-cell lymphocytes and dendritic cells are being actively investigated by other companies for this purpose, and these procedures require ex vivo cell production.

T-cells, a class of lymphocyte white blood cells, play a critical role in the human immune system and are responsible for the human immune response in a broad spectrum of diseases, including cancers and infectious diseases. Cytotoxic T-lymphocytes ("CTLs") is a new process that involves collecting T-cells from a patient and culturing them in an environment resulting in T-cells with specificity for a particular disease target. Clinical trials by third parties have been completed demonstrating CTL effectiveness for certain diseases. The ex vivo production of these cells under conditions for use in medical treatment represents a critical step in the advancement of this therapy.

Dendritic cells (the potent antigen presenting cells) are believed to play an important role in the function of the immune system. Researchers believe that cultured dendritic cells could augment the natural ability of a patient to present antigens from the infectious agents to the immune system and aid in the generation of a cytotoxic T-cell response to the infectious agent. The Company intends to explore application of its products and processes for the expansion of dendritic cells.

Solid Tissue Cell Therapies

One of the newest areas of cell therapy involves the production of chondrocytes for the restoration of cartilage. Chondrocyte therapy involves the surgical removal of a small amount of tissue from the patient's knee and a therapeutic quantity of chondrocytes is produced from this surgical biopsy. The cells are then implanted into the patient's knee. Published reports indicate that such cells then reestablish mature articular cartilage. Currently, this cell production process is completed in highly specialized laboratory facilities using trained scientists and manual laboratory procedures. The Aastrom CPS has the potential to reduce costs associated with the cell production procedure and may eventually facilitate the transfer of the cell production capability away from specialized facilities directly to the clinical care sites.

Other Stem Cell Therapies

Autoimmune Diseases. Stem cell therapy is under clinical investigation for the treatment of other diseases. Clinical studies have suggested a potential role for stem cell therapy in treatment of autoimmune diseases such as rheumatoid arthritis, multiple sclerosis and lupus erythematosus. The generic cause of these diseases is a malfunctioning immune system, including T-lymphocytes. Clinical trials in which the patient receives treatment resulting in immune ablation (usually involving myelotoxic cancer drugs or radiation), followed by stem cell therapy to restore the bone marrow and cells of the blood and immune system, have demonstrated remission of the autoimmune disease in some patients.

Organ Transplantation. Recently, a number of academic and corporate researchers and companies have identified the potential use of stem cell therapy to facilitate successful solid organ and tissue transplants between human donors and recipients, as well as using organs from non-human species for transplantation into humans. These proposed applications are based on the observation that donor-specific bone marrow, infused concurrent with or prior to the organ transplant, can provide for reduction of the normal immune rejection response by the transplant recipient (e.g. heart, lung, liver or kidney transplants).

A major limitation to the use of stem cell therapy in solid organ transplant is the limited availability of sufficient amounts of bone marrow to obtain a desired therapeutic response of immune tolerization. This limitation is particularly problematic when cadaveric donor organs are available, which has traditionally been the source of cells for these procedures. Bone marrow is also often available from the cadaveric donor, but only in a limited amount. Normally this amount may be sufficient for one transplant, but a donor might provide multiple organs for transplant into multiple recipients. Aastrom believes that the ability to expand the available bone marrow ex vivo will enhance the use of stem cell therapy for such transplant procedures.

AASTROM PRODUCT CANDIDATES FOR EX VIVO GENE THERAPY

A novel form of cell therapy is ex vivo gene therapy. For this type of cell therapy, cells procured from the patient or a donor are genetically modified prior to their infusion into the patient. Analogous to other cell therapies, the ability to produce a therapeutic dose of these gene-modified cells is a major limitation to the commercialization of these cell therapies. This limitation is further exacerbated by the additional requirement that the cells be genetically modified under conditions that are sterile and comply with GMP.

Gene therapy is a therapeutic modality that holds the potential to significantly impact the delivery of healthcare and the delivery of therapeutically useful protein-based drugs within the body. Gene therapies are generally targeted at the introduction of a missing normal gene into otherwise defective human tissue, or the introduction of novel biologic capability into the body via the introduction of a gene not ordinarily present (for example, genes providing for the enhanced recognition and destruction or inhibition of the HIV-1 virus). The major developmental focus of the ex vivo gene therapy industry has been to identify the therapeutic gene of interest, insert it into a suitable vector that can be used to transport and integrate the gene into the DNA of the target cell, and then cause the gene to become expressed. For gene therapy to progress to clinical applications, a process to produce a sufficient quantity of therapeutic cells is required as is an efficient means to insert the gene vector into target cells. Gene therapy is still in an early stage of development by third parties. The Company's business opportunity is dependent upon the successful development and regulatory approval of individual gene therapy applications. No assurance can be given that such applications will be developed or approved or that the Company's processes or product candidates will find successful applications in such therapies.

THE AASTROM CPS FOR GENE THERAPY (GT-CPS)

The Aastrom CPS has been developed to produce cells for therapy. Clinical cell production is a limiting requirement for gene therapy to effectively move into medical practice, and as such, the Company believes that the Aastrom CPS may be useful in many potential ex vivo gene therapy applications.

Further, the Company's proprietary stem cell production process technology implemented by the Aastrom CPS provides the conditions for clinical scale stem cell division, and enables or enhances the introduction of therapeutic genes into stem cell DNA. The Company believes that its technology may also enable expansion of more mature progeny of these stem cells to create a gene therapy cell product with potential short and long term therapeutic effect.

The Company has two principal objectives for the development of Aastrom GT-CPS: (i) the enablement of stem cell gene therapies for a variety of hematologic and other disorders, based on the GT-CPS's ability to enable large scale stem cell division ex vivo; and (ii) the enablement of gene transfer and therapeutic cell production by local and regional primary patient care facilities and ancillary service laboratories.

THE AASTROM GENE LOADER

The Aastrom Gene Loader product technology, which is under development, is being designed to transfer new therapeutic genes, which are carried by vectors into the target cell. This process, which is typically inefficient in many human cells, has represented a major hurdle preventing many ex vivo gene therapies from moving forward in the clinic. The Aastrom Gene Loader will incorporate the Company's proprietary directed motion gene transfer technology and is expected to incorporate single-use sterile disposables, operated by dedicated instrumentation.

A major product objective of the Aastrom Gene Loader is the enhancement of gene transfer efficiencies and reliability. Improving gene vector efficiencies may enable a wide spectrum of gene therapies currently unable to realize clinical application.

The Company believes that these issues represent a general bottleneck for other companies pursuing ex vivo gene therapy clinical applications. The Company's technology may favorably influence these gene therapy applications, the development of which are impeded due to low transduction efficiencies and the resultant need for use of extreme quantities of gene vectors and/or target "delivery" tissues.

STRATEGIC RELATIONSHIPS

On October 22, 1993, the Company entered into a Distribution Agreement (the "Distribution Agreement") with Cobe, a subsidiary of Gambro AB, for Cobe to be the Company's exclusive, worldwide distributor of the Aastrom CPS for stem cell therapy applications (the "Stem Cell Therapy Applications"). The Company has retained the right to market the Aastrom CPS for uses outside the Stem Cell Therapy Applications, such as for all gene therapy applications and for production of other cells and tissues. The initial term of the Distribution Agreement expires on October 22, 2003, and Cobe has the option to extend the term for an additional ten-year period. The Company is responsible for the expenses to obtain FDA and other regulatory approval in the United States, while Cobe is responsible for the expenses to obtain regulatory approval in foreign countries to allow for worldwide marketing of the Aastrom CPS for Stem Cell Therapy Applications. See "Risk Factors--Consequences of Cobe Relationship."

Under the terms of the Distribution Agreement, the Company will realize approximately 60% and 58% of the net sales price at which Cobe ultimately sells the Aastrom CPS in the United States and Europe, respectively, for Stem Cell Therapy Applications, subject to certain negotiated discounts and volume-based adjustments. The Company is also entitled to a premium on United States sales in any year in which worldwide sales exceed specified levels.

The Distribution Agreement may be terminated by Cobe upon twelve (12) months prior notice to the Company in the event that any person or entity other than Cobe beneficially owns more than 50% of the Company's outstanding Common Stock or voting securities. The Distribution Agreement may also be terminated by Cobe at any time after December 31, 1997 if Cobe determines that commercialization of the Aastrom CPS for stem cell therapy on or prior to December 31, 1998 is unlikely.

In conjunction with the Distribution Agreement, the Company also entered into a Stock Purchase Agreement with Cobe, whereby Cobe acquired certain option, registration, preemptive and other rights pertaining to shares of the Company's stock. See "Description of Capital Stock--Rights of Cobe."

MANUFACTURING

The Company has no current intention of internally manufacturing its product candidates and accordingly is developing relationships with third party manufacturers which are FDA registered as suppliers for the manufacture of medical products.

On May 10, 1994, the Company entered into a Collaborative Product Development Agreement with SeaMED Corporation, ("SeaMED"). Pursuant to this agreement, the Company and SeaMED will collaborate on the further design of certain instrument components in the Aastrom CPS, and enable SeaMED to manufacture pre-production units of the instrument components for laboratory and clinical evaluation. The Company is paying SeaMED for its design and pre-production work on a "time and materials" basis, utilizing SeaMED's customary hourly billing rates and actual costs for materials. Subject to certain conditions, the Company has committed to enter into a manufacturing agreement with SeaMED for commercial manufacture of the instrument components for three years after shipment by SeaMED of the first commercial unit pursuant to a pricing formula set forth in the agreement. The Company retains all proprietary rights to its intellectual property which is utilized by SeaMED pursuant to this agreement.

On November 8, 1994, the Company entered into a Collaborative Product Development Agreement with Ethox Corporation ("Ethox"). Pursuant to this Agreement, the Company and Ethox will collaborate on the further design of certain bioreactor assembly and custom tubing kit components of the Aastrom CPS, and enable Ethox to manufacture pre-production units of such components for laboratory and clinical evaluation. The Company is paying Ethox for its design and production work on a "time and materials" basis, utilizing Ethox's customary hourly billing rates and actual costs for materials. The Company retains all proprietary rights to its intellectual property which are utilized by Ethox pursuant to this Agreement.

In April 1996, the Company entered into a five-year License and Supply Agreement with Immunex to purchase and resell certain cytokines and ancillary materials for use in conjunction with the Aastrom CPS. The agreement required the Company to pay Immunex an initial up-front fee of \$1,500,000 to be followed by subsequent annual fee payments equal to \$1,000,000 per year during the term of the agreement in addition to payment for supplies purchased by the Company. The agreement may be terminated by the Company at any time subject to the payment to Immunex of a specified amount for liquidated damages. Immunex may terminate the agreement in the event that the Company fails to purchase a minimum amount of its forecasted annual needs.

There can be no assurance that the Company will be able to continue its present arrangements with its suppliers, supplement existing relationships or establish new relationships or that the Company will be able to identify and obtain the ancillary materials that are necessary to develop its product candidates in the future. The Company's dependence upon third parties for the supply and manufacture of such items could adversely affect the Company's ability to develop and deliver commercially feasible products on a timely and competitive basis. See "Risk Factors--Manufacturing and Supply Uncertainties; Dependence on Third Parties."

PATENTS AND PROPRIETARY RIGHTS

The Company's success depends in part on its ability, and the ability of its licensors, to obtain patent protection for its products and processes. The Company and its licensors are seeking patent protection for technologies related to (i) human stem and progenitor cell production processes; (ii) bioreactors and systems for stem and progenitor cell production and production of other cells; and (iii) gene transfer devices and processes. The Company has exclusive license rights to five issued United States patents that together claim (i) certain methods for ex vivo stem cell division and stable genetic transformation, optimization of hematopoietic progenitor cell cultures and increasing the metabolism or growth factor secretion of stromal cells, in a

continuously or periodically perfused liquid culture medium; (ii) certain devices for the simultaneous culture of stem cells and hematopoietic cells; and (iii) certain methods of infecting or transfecting target cells with genetic vectors. Patents equivalent to two of these United States patents have also been issued in other jurisdictions: one in Australia and another in Canada and under the European Patent Convention. These eight issued patents are due to expire beginning in 2006, through 2013. In addition, the Company and its exclusive licensors have filed applications for patents in the United States and equivalent applications in certain other countries claiming other aspects of the Company's products and processes, including five United States patent applications and corresponding applications in other countries related to various components of the Aastrom CPS. Of these pending patent applications, the Company has received notices of allowance for certain claims in a United States application relating to methods for obtaining ex vivo stem cell division, and claims in a European Patent Convention application and in a United States application relating to methods for efficient proliferation of hematopoietic cells in culture.

The validity and breadth of claims in medical technology patents involve complex legal and factual questions and, therefore, may be highly uncertain. No assurance can be given that any patents based on pending patent applications or any future patent applications of the Company or its licensors will be issued, that the scope of any patent protection will exclude competitors or provide competitive advantages to the Company, that any of the patents that have been or may be issued to the Company or its licensors will be held valid if subsequently challenged or that others will not claim rights in or ownership of the patents and other proprietary rights held or licensed by the Company. Furthermore, there can be no assurance that others have not developed or will not develop similar products, duplicate any of the Company's products or design around any patents that have been or may be issued to the Company or its licensors. Since patent applications in the United States are maintained in secrecy until patents issue, the Company also cannot be certain that others did not first file applications for inventions covered by the Company's and its licensors' pending patent applications, nor can the Company be certain that it will not infringe any patents that may issue to others on such applications.

The Company relies on certain licenses granted by the University of Michigan and Dr. Cremonese for the majority of its patent rights. If the Company breaches such agreements or otherwise fails to comply with such agreements, or if such agreements expire or are otherwise terminated, the Company may lose its rights under the patents held by the University of Michigan and Dr. Cremonese, which would have a material adverse effect on the Company's business, financial condition and results of operation. See "--University of Michigan Research Agreement and License Agreement" and "--License Agreement with J.G. Cremonese."

The Company also relies on trade secrets and unpatentable know-how which it seeks to protect, in part, by confidentiality agreements. It is the Company's policy to require its employees, consultants, contractors, manufacturers, outside scientific collaborators and sponsored researchers, and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with the Company. These agreements provide that all confidential information developed or made known to the individual during the course of the individual's relationship with the Company is to be kept confidential and not disclosed to third parties except in specific limited circumstances. The Company also requires signed confidentiality or material transfer agreements from any company that is to receive its confidential data. In the case of employees, consultants and contractors, the agreements generally provide that all inventions conceived by the individual while rendering services to the Company shall be assigned to the Company as the exclusive property of the Company. There can be no assurance, however, that these agreements will not be breached, that the Company would have adequate remedies for any breach, or that the Company's trade secrets or unpatentable know-how will not otherwise become known or be independently developed by competitors.

The Company's success will also depend in part on its ability to develop commercially viable products without infringing the proprietary rights of others. The Company has not conducted freedom of use patent searches and no assurance can be given that patents do not exist or could not be filed which would have an adverse effect on the Company's ability to market its products or maintain its competitive position with respect to its products. If the Company's technology components, devices, designs, products, processes or other subject matter are claimed under other existing United States or foreign patents or are otherwise protected by third party

proprietary rights, the Company may be subject to infringement actions. In such event, the Company may challenge the validity of such patents or other proprietary rights or be required to obtain licenses from such companies in order to develop, manufacture or market its products. There can be no assurances that the Company would be able to obtain such licenses or that such licenses, if available, could be obtained on commercially reasonable terms. Furthermore, the failure to either develop a commercially viable alternative or obtain such licenses could result in delays in marketing the Company's proposed products or the inability to proceed with the development, manufacture or sale of products requiring such licenses, which could have a material adverse effect on the Company's business, financial condition and results of operations. If the Company is required to defend itself against charges of patent infringement or to protect its own proprietary rights against third parties, substantial costs will be incurred regardless of whether the Company is successful. Such proceedings are typically protracted with no certainty of success. An adverse outcome could subject the Company to significant liabilities to third parties and force the Company to curtail or cease its development and sale of its products and processes.

Certain of the Company's and its licensors' research has been or is being funded in part by the Department of Commerce and by a Small Business Innovation Research Grant obtained from the Department of Health and Human Services. As a result of such funding, the United States Government has certain rights in the technology developed with the funding. These rights include a non-exclusive, paid-up, worldwide license under such inventions for any governmental purpose. In addition, the government has the right to require the Company to grant an exclusive license under any of such inventions to a third party if the government determines that (i) adequate steps have not been taken to commercialize such inventions, (ii) such action is necessary to meet public health or safety needs or (iii) such action is necessary to meet requirements for public use under federal regulations. Additionally, under the federal Bayh Dole Act, a party which acquires an exclusive license for an invention that was partially funded by a federal research grant is subject to the following government rights: (i) products using the invention which are sold in the U.S. are to be manufactured substantially in the U.S., unless a waiver is obtained; (ii) if the licensee does not pursue reasonable commercialization of a needed product using the invention, the government may force the granting of a license to a third party who will make and sell the needed product; and (iii) the U.S. government may use the invention for its own needs.

UNIVERSITY OF MICHIGAN RESEARCH AGREEMENT AND LICENSE AGREEMENT

In August 1989, the Company entered into a Research Agreement ("Research Agreement") with the University, pursuant to which the Company funded a research project at the University under the direction of Stephen G. Emerson, M.D., Ph.D., as the principal inventor, together with Michael F. Clarke, M.D., and Bernhard O. Palsson, Ph.D., as co-inventors. Pursuant to this Research Agreement, the Company was granted the right to acquire an exclusive, worldwide license to utilize all inventions, know-how and technology derived from the research project. By Extension Agreements, the Company and the University extended the scope and term of Research Agreement through December, 1994.

On March 13, 1992, the Company and the University entered into the License Agreement, as contemplated by the Research Agreement. There have been clarifying amendments to the License Agreement, dated March 13, 1992, October 8, 1993 and June 21, 1995. Pursuant to this License Agreement, (i) the Company acquired exclusive worldwide license rights to the patents and know-how for the production of blood cells and bone marrow cells as described in the University's research project or which resulted from certain further research conducted through December 31, 1994, and (ii) the Company is obligated to pay to the University a royalty equal to 2% of the net sales of products which are covered by the University's patents. Unless it is terminated earlier at the Company's option or due to a material breach by the Company, the License Agreement will continue in effect until the latest expiration date of the patents to which the License Agreement applies.

LICENSE AGREEMENT WITH J. G. CREMONESE

In July 1992, the Company entered into a License Agreement with Joseph G. Cremonese pursuant to which the Company obtained exclusive worldwide license rights for all fields of use, to utilize U.S. Patent No. 4,839,292, entitled "Cell Culture Flask Utilizing a Membrane Barrier," which patent was issued to

Dr. Cremonese on June 13, 1989, and to utilize any other related patents that might be issued to Dr. Cremonese. Pursuant to this License Agreement, the Company has reimbursed Dr. Cremonese for \$25,000 of his patent costs. Under the terms of the License Agreement, the Company is to pay to Dr. Cremonese a royalty of 3% of net sales of the products which are covered by said patent, subject to specified minimum royalty payments ranging from \$20,000 to \$50,000 per year, commencing in calendar year 1997. Unless it is terminated earlier at the Company's option or due to default by the Company, the License Agreement will continue in effect until the latest expiration date of the patents to which the License Agreement applies.

GOVERNMENT REGULATION

The Company's research and development activities and the manufacturing and marketing of the Company's products are subject to the laws and regulations of governmental authorities in the United States and other countries in which its products will be marketed. Specifically, in the United States the FDA, among other activities, regulates new product approvals to establish safety and efficacy of these products. Governments in other countries have similar requirements for testing and marketing. In the U.S., in addition to meeting FDA regulations, the Company is also subject to other federal laws, such as the Occupational Safety and Health Act and the Environmental Protection Act, as well as certain state laws.

REGULATORY PROCESS IN THE UNITED STATES

To the Company's knowledge, it is the first to develop a culture system for ex vivo human cell production to be sold for therapeutic applications. Therefore, to a certain degree, the manner in which the FDA will regulate the Company's products is uncertain.

The Company's products are potentially subject to regulation as medical devices under the Federal Food, Drug, and Cosmetic Act, and as biological products under the Public Health Service Act, or both. Different regulatory requirements may apply to the Company's products depending on how they are categorized by the FDA under these laws. To date, the FDA has indicated that it intends to regulate the Aastrom CPS product for stem cell therapy as a Class III medical device through the Center for Biologics Evaluation and Research. However, there can be no assurance that FDA will ultimately regulate the Aastrom CPS as a medical device.

Further, it is unclear whether the FDA will separately regulate the cell therapies derived from the Aastrom CPS. The FDA is still in the process of developing its requirements with respect to somatic cell therapy and gene cell therapy products and has recently issued a draft document concerning the regulation of umbilical cord blood stem cell products. If the FDA adopts the regulatory approach set forth in the draft document, the FDA may require separate regulatory approval for such cells in some cases. The FDA also recently proposed a new type of license, called a biologic license application ("BLA"), for autologous cells manipulated ex vivo and intended for structural repair or reconstruction. This proposal may indicate that the FDA will extend a similar approval requirement to other types of autologous cellular therapies, such as autologous cells for stem cell therapy. Any such additional regulatory or approval requirements could significantly delay the introduction of the Company's product candidates to the market, and have a material adverse impact on the Company.

Approval of new medical devices and biological products is a lengthy procedure leading from development of a new product through preclinical and clinical testing. This process takes a number of years and the expenditure of significant resources. There can be no assurance that the Company's product candidates will ultimately receive regulatory approval.

Regardless of how the Company's product candidates are regulated, the Federal Food, Drug, and Cosmetic Act and other Federal statutes and regulations govern or influence the research, testing, manufacture, safety, labeling, storage, recordkeeping, approval, distribution, use, reporting, advertising and promotion of such products. Noncompliance with applicable requirements can result in civil penalties, recall, injunction or seizure of products, refusal of the government to approve or clear product approval applications or to allow the Company to enter into government supply contracts, withdrawal of previously approved applications and criminal prosecution.

DEVICES

In order to obtain FDA approval of a new medical device sponsors must generally submit proof of safety and efficacy. In some cases, such proof entails extensive clinical and preclinical laboratory tests. The testing, preparation of necessary applications and processing of those applications by the FDA is expensive and may take several years to complete. There can be no assurance that the FDA will act favorably or in a timely manner in reviewing submitted applications, and the Company may encounter significant difficulties or costs in its efforts to obtain FDA approvals which could delay or preclude the Company from marketing any products it may develop. The FDA may also require postmarketing testing and surveillance of approved products, or place other conditions on the approvals. These requirements could cause it to be more difficult or expensive to sell the products, and could therefore restrict the commercial applications of such products. Product approvals may be withdrawn if compliance with regulatory standards is not maintained or if problems occur following initial marketing. For patented technologies, delays imposed by the governmental approval process may materially reduce the period during which the Company will have the exclusive right to exploit such technologies.

If human clinical trials of a proposed device are required and the device presents significant risk, the manufacturer or distributor of the device will have to file an IDE application with the FDA prior to commencing human clinical trials. The IDE application must be supported by data, typically including the results of pre-clinical and laboratory testing. If the IDE application is approved, human clinical trials may commence at a specified number of investigational sites with the number of patients approved by the FDA.

The FDA categorizes devices into three regulatory classifications subject to varying degrees of regulatory control. In general, Class I devices require compliance with labeling and recordkeeping regulations, GMPs, 510(k) pre-market notification, and are subject to other general controls. Class II devices may be subject to additional regulatory controls, including performance standards and other special controls, such as postmarket surveillance. Class III devices, which are either invasive or life-sustaining products, or new products never before marketed (for example, non-"substantially equivalent" devices), require clinical testing to demonstrate safety and effectiveness and FDA approval prior to marketing and distribution. The FDA also has the authority to require clinical testing of Class I and Class II devices.

If a manufacturer or distributor of medical devices cannot establish that a proposed device is substantially equivalent, the manufacturer or distributor must submit a PMA application to the FDA. A PMA application must be supported by extensive data, including preclinical and human clinical trial data, to prove the safety and efficacy of the device. Upon receipt, the FDA conducts a preliminary review of the PMA application. If sufficiently complete, the submission is declared filed by the FDA. By regulation, the FDA has 180 days to review a PMA application once it is filed, although PMA application reviews more often occur over a significantly protracted time period, and may take approximately one year or more from the date of filing to complete.

Some of the Company's products may be classified as Class II or Class III medical devices. The Company has submitted and obtained FDA approval for several IDEs for the Aastrom CPS, and is currently conducting clinical studies under these IDEs. The Company believes that the Aastrom CPS product will be regulated by the FDA as a Class III device, although there can be no assurance that the FDA will not choose to regulate this product in a different manner.

The Company and any contract manufacturer are required to be registered as a medical device manufacturer with the FDA. As such, they will be inspected on a routine basis by the FDA for compliance with the FDA's GMP regulations. These regulations will require that the Company and any contract manufacturer manufacture products and maintain documents in a prescribed manner with respect to manufacturing, testing, distribution, storage, design control and service activities, and that adequate design and service controls are implemented. The Medical Device Reporting regulation requires that the Company provide information to the FDA on deaths or serious injuries alleged to be associated with the use of its devices, as well as product malfunctions that are

likely to cause or contribute to death or serious injury if the malfunction were to recur. In addition, the FDA prohibits a company from promoting an approved device for unapproved applications and reviews company labeling for accuracy.

BIOLOGICAL PRODUCTS

For certain of the Company's new products which may be regulated as biologics, the FDA requires (i) preclinical laboratory and animal testing, (ii) submission to the FDA of an investigational new drug ("IND") application which must be effective prior to the initiation of human clinical studies, (iii) adequate and well-controlled clinical trials to establish safety and efficacy of the product for its intended use, (iv) submission to the FDA of a product license application ("PLA") and establishment license application ("ELA") and (v) review and approval of the PLA and ELA as well as inspections of the manufacturing facility by the FDA prior to commercial marketing of the product.

Preclinical testing covers laboratory evaluation of product chemistry and formulation as well as animal studies to assess the safety and efficacy of the product. The results of these tests are submitted to the FDA as part of the IND. Following the submission of an IND, the FDA has 30 days to review the application and raise safety and other clinical trial issues. If the Company is not notified of objections within that period, clinical trials may be initiated. Clinical trials are typically conducted in three sequential phases. Phase I represents the initial administration of the drug or biologic to a small group of humans, either healthy volunteers or patients, to test for safety and other relevant factors. Phase II involves studies in a small number of patients to assess the efficacy of the product, to ascertain dose tolerance and the optimal dose range and to gather additional data relating to safety and potential adverse effects. Once an investigational drug is found to have some efficacy and an acceptable safety profile in the targeted patient population, multi-center Phase III studies are initiated to establish safety and efficacy in an expanded patient population and multiple clinical study sites. The FDA reviews both the clinical plans and the results of the trials and may request the Company to discontinue the trials at any time if there are significant safety issues.

The results of the preclinical tests and clinical trials are submitted to the FDA in the form of a PLA for marketing approval. The testing and approval process is likely to require substantial time and effort and there can be no assurance that any approval will be granted on a timely basis, if at all. Additional animal studies or clinical trials may be requested during the FDA review period that may delay marketing approval. After FDA approval for the initial indications, further clinical trials may be necessary to gain approval for the use of the product for additional indications. The FDA requires that adverse effects be reported to the FDA and may also require post-marketing testing to monitor for adverse effects, which can involve significant expense.

Under current requirements, facilities manufacturing biological products must be licensed. To accomplish this, an ELA must be filed with the FDA. The ELA describes the facilities, equipment and personnel involved in the manufacturing process. An establishment license is granted on the basis of inspections of the applicant's facilities in which the primary focus is on compliance with GMP and the ability to consistently manufacture the product in the facility in accordance with the PLA. If the FDA finds the inspection unsatisfactory, it may decline to approve the ELA, resulting in a delay in production of products. Although reviewed separately, approval of both the PLA and ELA must be received prior to commercial marketing of a cellular biologic.

As part of the approval process for human biological products, each manufacturing facility must be registered and inspected by FDA prior to marketing approval. In addition, state agency inspections and approvals may also be required for a biological product to be shipped out of state.

REGULATORY PROCESS IN EUROPE

The Company believes that the Aastrom CPS will be regulated in Europe as a Class IIb medical device, under the authority of the new Medical Device Directives ("MDD") being implemented by European Union ("EU") member countries. This classification applies to medical laboratory equipment and supplies including,

among other products, many devices that are used for the collection and processing of blood for patient therapy. Certain ancillary products (e.g., biological reagents) used with the Aastrom CPS may be considered Class III medical devices.

The MDD regulations vest the authority to permit affixing of the "CE Mark" with various "Notified Bodies." These are private and state organizations which operate under license from the EU to certify that appropriate quality assurance standards and compliance procedures are followed by developers and manufacturers of medical device products or, alternatively, that a manufactured medical product meets a more limited set of requirements. Notified Bodies are also charged with responsibility for determination of the appropriate standards to apply to a medical product. Receipt of permission to affix the CE Mark enables a company to sell a medical device in all EU member countries. Other registration requirements may also need to be satisfied in certain countries, although there is a general trend among EU member countries not to impose additional requirements beyond those specified for CE Mark certification.

COMPETITION

The biotechnology and medical device industries are characterized by rapidly evolving technology and intense competition. The Company's competitors include major pharmaceutical, medical device, medical products, chemical and specialized biotechnology companies, many of which have financial, technical and marketing resources significantly greater than those of the Company. In addition, many biotechnology companies have formed collaborations with large, established companies to support research, development and commercialization of products that may be competitive with those of the Company. Academic institutions, governmental agencies and other public and private research organizations are also conducting research activities and seeking patent protection and may commercialize products on their own or through joint ventures. The Company's product development efforts are primarily directed toward obtaining regulatory approval to market the Aastrom CPS for stem cell therapy. That market is currently dominated by the bone marrow harvest and PBPC collection methods. The Company's clinical data, although early, is inconclusive as to whether or not cells expanded in the Aastrom CPS will enable hematopoietic recovery within the time frames currently achieved by the bone marrow harvest and PBPC collection methods. In addition, the bone marrow harvest and PBPC collection methods have been widely practiced for a number of years and, recently, the patient costs associated with these procedures have begun to decline. There can be no assurance that the Aastrom CPS method, if approved for marketing, will prove to be competitive with these established collection methods on the basis of hematopoietic recovery time, cost or otherwise. The Company is aware of certain other products manufactured or under development by competitors that are used for the prevention or treatment of certain diseases and health conditions which the Company has targeted for product development. In particular, the Company is aware that competitors such as Amgen, Inc., CellPro, Incorporated, Systemix, Inc., Baxter Healthcare Corp. and RPR are in advanced stages of development of technologies and products for use in stem cell therapy and other market applications currently being pursued by the Company. In addition, Cobe, a significant stockholder of the Company, is a market leader in the blood cell processing products industry and, accordingly, a potential competitor of the Company. There can be no assurance that developments by others will not render the Company's product candidates or technologies obsolete or noncompetitive, that the Company will be able to keep pace with new technological developments or that the Company's product candidates will be able to supplant established products and methodologies in the therapeutic areas that are targeted by the Company. The foregoing factors could have a material adverse effect on the Company's business, financial condition and results of operations.

The Company's products under development are expected to address a broad range of existing and new markets. The Company believes that its stem cell therapy products will, in large part, face competition by existing procedures rather than novel new products. The Company's competition will be determined in part by the potential indications for which the Company's products are developed and ultimately approved by regulatory authorities. In addition, the first product to reach the market in a therapeutic or preventive area is often at a significant competitive advantage relative to later entrants to the market. Accordingly, the relative speed with

which the Company or its corporate partners can develop products, complete the clinical trials and approval processes and supply commercial quantities of the products to the market are expected to be important competitive factors. The Company's competitive position will also depend on its ability to attract and retain qualified scientific and other personnel, develop effective proprietary products, develop and implement production and marketing plans, obtain and maintain patent protection and secure adequate capital resources. The Company expects its products, if approved for sale, to compete primarily on the basis of product efficacy, safety, patient convenience, reliability, value and patent position.

FACILITIES

The Company leases approximately 20,000 square feet of office and research and development space in Ann Arbor, Michigan under a lease agreement expiring in May 1998. The lease is renewable at the option of the Company for up to an additional five-year term. The Company believes that its facilities will be adequate for its currently anticipated needs. Contract manufacturing or additional facilities will be required in the future to support expansion of research and development and to manufacture products.

EMPLOYEES

As of September 30, 1996, the Company employed approximately 61 individuals full-time. A significant number of the Company's management and professional employees have had prior experience with pharmaceutical, biotechnology or medical product companies. None of the Company's employees are covered by collective bargaining agreements, and management considers relations with its employees to be good.

LEGAL PROCEEDINGS

The Company is not party to any material legal proceedings, although from time to time it may become involved in disputes in connection with the operation of its business.

MANAGEMENT

DIRECTORS AND EXECUTIVE OFFICERS

The following table provides information concerning directors and executive officers of the Company:

NAME ----	AGE ---	POSITION -----
Robert J. Kunze(2)(3).....	61	Chairman of the Board; Director
R. Douglas Armstrong, Ph.D.(3)...	43	President and Chief Executive Officer; Director
James Maluta.....	49	Vice President, Product Development
Todd E. Simpson.....	35	Vice President, Finance & Administration; Chief Financial Officer; Secretary; and Treasurer
Walter C. Ogier.....	39	Vice President, Marketing
Thomas E. Muller, Ph.D.....	61	Vice President, Regulatory Affairs
Alan K. Smith, Ph.D.....	41	Vice President, Research
Stephen G. Emerson, M.D., Ph.D...	42	Director; Scientific Advisor
Albert B. Deisseroth, M.D., Ph.D.(2).....	55	Director; Scientific Advisor
G. Bradford Jones(1)(3).....	41	Director
Horst R. Witzel, Dr.-Ing.....	69	Director
Edward C. Wood, Jr.(1)(3).....	51	Director

- - - - -
- (1) Member of Audit Committee.
(2) Member of Compensation Committee.
(3) Member of Executive Committee.

All directors hold office until the next annual meeting of stockholders and until their successors have been duly elected and qualified. The Company's Bylaws provide that the Board of Directors will consist of between five and nine members, and the number of directors is currently set at seven members. The Bylaws also provide that the Board of Directors will serve staggered three-year terms, or until their successors are elected and qualified. The terms of office of the Company's current directors expire as follows: Mr. Jones, Dr. Deisseroth and Mr. Wood, 1999; Mr. Kunze and Dr. Emerson, 1998; and Dr. Armstrong and Dr. Witzel, 1997. Officers are elected by and serve at the discretion of the Board of Directors. There are no family relationships among the directors or officers of the Company.

Robert J. Kunze a director of the Company since its inception in 1989, is a founder of the Company and served as its President and Chief Executive Officer through May 1991. Since 1987, he has been a General Partner of H&Q Life Science Venture Partners, a venture capital fund specializing in medical products and biotechnology investments. Previous to that, Mr. Kunze was Managing Partner of Hambrecht & Quist Venture Partners. Prior to that he served as a senior executive with W.R. Grace & Co. and General Electric. Mr. Kunze also serves on the Board of Directors of Escalon Medical Corporation.

R. Douglas Armstrong, Ph.D. joined the Company in June 1991 as a director and as its President and Chief Executive Officer. From 1987 to 1991, Dr. Armstrong served in different capacities, including as Executive Vice President and a Trustee of the La Jolla Cancer Research Foundation ("LJCRF"), a 250-employee scientific research institute located in San Diego, California. Dr. Armstrong received his doctorate in Pharmacology and Toxicology from the Medical College of Virginia, and has held faculty and staff positions at Yale University, University of California, San Francisco, LJCRF and University of Michigan. Dr. Armstrong also serves on the Board of Directors of Nephros Therapeutics, Inc.

James Maluta joined the Company in August 1992 as Vice President, Product Development. Mr. Maluta has a broad background in the development and manufacturing of medical devices, with 25 years of experience in the industry, principally with OHMEDA and with Cobe BCT, Inc. While with Cobe BCT, Inc., Mr. Maluta was Program Manager for the Cobe Spectra Apheresis System, a device for blood cell processing and apheresis. Mr. Maluta held other engineering management positions and also was director of Quality Assurance for Cobe BCT. Mr. Maluta received his degree in electrical engineering from the University of Wisconsin.

Todd E. Simpson joined the Company in January 1996 as Vice President, Finance and Administration and Chief Financial Officer and is also the Company's Secretary and Treasurer. Prior to that, Mr. Simpson was Treasurer of Integra LifeSciences Corporation ("Integra"), a biotechnology company, which acquired Telios Pharmaceuticals, Inc. ("Telios") in August 1995 in connection with the reorganization of Telios under Chapter 11 of the U.S. Bankruptcy Code. Mr. Simpson served as Vice President of Finance and Chief Financial Officer of Telios up until its acquisition by Integra and held various other financial positions at Telios after joining that company in February 1992. Telios was a publicly-held company engaged in the development of pharmaceutical products for the treatment of dermal and ophthalmic wounds, fibrotic disease, vascular disease, and osteoporosis. From August 1983 through February 1992, Mr. Simpson practiced public accounting with the firm of Ernst & Young, LLP. Mr. Simpson is a Certified Public Accountant and received his B.S. degree in Accounting and Computer Science from Oregon State University.

Walter C. Ogier joined the Company in March 1994 as Director of Marketing and was promoted to Vice President, Marketing during 1995. Prior to that, Mr. Ogier was at Baxter Healthcare Corporation's Immunotherapy Division, where he served as Director, Business Development from 1992 to 1994 and as Manager, Marketing and Business Development in charge of the company's cell therapy product lines from 1990 to 1992. Mr. Ogier previously held positions with Ibbottson Associates and with the Business Intelligence Center at SRI International (formerly Stanford Research Institute). Mr. Ogier received his B.A. degree in Chemistry from Williams College in 1979 and his Masters of Management degree from the Yale School of Management in 1987.

Thomas E. Muller, Ph.D. joined the Company in May 1994 as Vice President, Regulatory Affairs. Prior to that, Dr. Muller was Director, Biomedical Systems with W.R. Grace & Company in Lexington, Massachusetts. Prior to this, Dr. Muller was Vice President, Engineering and Director of Research and Development with the Renal Division of Baxter Healthcare in Deerfield, Illinois. Dr. Muller has also served as Adjunct Professor at Columbia University and as Visiting Professor at the University of Gent, Belgium. Dr. Muller graduated from the Technical University in Budapest, Hungary, in 1956 with a B.S. in Chemical Engineering. Dr. Muller received his M.S. degree in 1959 and was awarded a Ph.D. in 1964, both in Polymer Chemistry, from McGill University.

Alan K. Smith, Ph.D. joined the Company in November 1995 as Vice President, Research. Previously, Dr. Smith was Vice President of Research and Development at Genetic Sciences, Inc., a developmental stage bone marrow transplantation company. Prior to that, Dr. Smith held the position of Director, Cell Separations Research and Development of the Immunotherapy Division of Baxter Healthcare Corporation. In this capacity, he was responsible for the research and development activities for a stem cell concentration system approved for clinical use in Europe and currently in pivotal clinical trials in the United States. Dr. Smith has also held positions as Research and Development Manager at BioSpecific Technologies, as Director of Biochemistry at HyClone Laboratories and as a member of the Board of Directors of Dallas Biomedical. Dr. Smith received his B.S. degree in Chemistry from Southern Utah State College in 1976 and a Ph.D. in Biochemistry from Utah State University in 1983.

Stephen G. Emerson, M.D., Ph.D. a director since the inception of the Company in 1989, is a scientific founder of the Company and has been an active advisor of the Company since that time. Dr. Emerson has been a Professor of Medicine at the University of Pennsylvania since 1994 where he serves as head of Hematology and Oncology. From 1991 to 1994, Dr. Emerson was an Associate Professor of Medicine at the University of Michigan. Dr. Emerson received his doctorate degrees in Medicine and Cell Biology/Immunology from Yale University. He completed his internship and residency at Massachusetts General Hospital and his clinical and research fellowship in hematology at the Brigham and Women's Hospital, the Dana-Farber Cancer Institute and Children's Hospital Medical Center.

Albert B. Deisseroth, M.D., Ph.D. a director since August 1991, currently serves as an Ensign Professor of Medicine and the Chief, Section of Medical Oncology at Yale University and is a professor at both the University of Texas Graduate School of Biomedical Sciences and the University of Texas Health Science Center Medical

School in Houston, Texas. Prior to that, Dr. Deisseroth had been Chairman of the Department of Hematology and a Professor of Medicine and Cancer Treatment and Research at the University of Texas, M.D. Anderson Cancer Center in Houston, Texas. Previous to this, Dr. Deisseroth served as Professor of Medicine at the University of California, San Francisco, and Chief, Hematology/Oncology at the San Francisco Veteran's Administration Medical Center. Dr. Deisseroth received his doctorate degrees in Medicine and Biochemistry from the University of Rochester. Dr. Deisseroth is currently a member of the Scientific Advisory Boards of Ingenex, Inc., Genvec, Inc. and Incell.

G. Bradford Jones a director since April 1992, is a general partner of Brentwood V Ventures, L.P., the general partner of Brentwood Associates V, L.P. Brentwood Associates V, L.P. is a partnership organized by the firm Brentwood Venture Capital, which Mr. Jones joined in 1981. Mr. Jones was elected to the Board of Directors of the Company pursuant to the terms of the Series B Preferred Stock Purchase Agreement dated April 7, 1992 with the Company, of which Brentwood Associates V, L.P. is a party. Mr. Jones received a B.A. degree in Chemistry and an M.A. degree in Physics from Harvard University and M.B.A. and J.D. degrees from Stanford University. Mr. Jones also serves on the Board of Directors of Interpore International, ISOCOR, Onyx Acceptance Corporation, Plasma & Materials Technologies, and several privately-held companies.

Horst R. Witzel, Dr.-Ing. a director since June 1994, served as Chairman of the Board of Executive Directors of Schering AG in Berlin, Germany from 1986 until his retirement in 1989, whereupon he became a member of the Supervisory Board of Schering AG until 1994. Prior to that, Dr. Witzel held various leadership positions in research and development with Schering AG where he was responsible for worldwide production and technical services. Dr. Witzel received his doctorate in chemistry from the Technical University of West Berlin. Dr. Witzel also serves on the Board of Directors of The Liposome Company, Inc. and Cephalon, Inc. and is a member of the Supervisory Board of Brau and Brunnen AG.

Edward C. Wood, Jr. a director since August 1994, has served as president of Cobe BCT, Inc., a division of Cobe Laboratories, Inc., since 1991. Cobe is a subsidiary of Gambro AB, a Swedish company, a world leader in blood cell processing products. Prior to that, Mr. Wood held various positions in manufacturing, research and development, and marketing with Cobe. Mr. Wood received degrees in chemistry from Harvey Mudd College and in management from the University of Colorado.

LIMITATION OF LIABILITY AND INDEMNIFICATION MATTERS

The Company has adopted provisions in its Restated Articles of Incorporation that limit the liability of its directors for monetary damages arising from a breach of their fiduciary duty as directors, except under certain circumstances which include breach of the director's duty of loyalty to the Company or its shareholders, acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of the law.

The Company's Bylaws provide that the Company shall indemnify its directors to the fullest extent authorized or permitted by the Michigan Business Corporation Act. Additionally, the Company has entered into an Indemnification Agreement, originally dated as of December 14, 1993 (the "Indemnification Agreement"), with certain of its directors, officers and other key personnel, which may, in certain cases, be broader than the specific indemnification provisions contained under applicable law. The Indemnification Agreement may require the Company, among other things, to indemnify such officers, directors and key personnel against certain liabilities that may arise by reason of their status or service as directors, officers or employees of the Company, to advance the expenses incurred by such parties as a result of any threatened claims or proceedings brought against them as to which they could be indemnified, and to cover such officers, directors and key employees under the Company's directors' and officers' liability insurance policies to the maximum extent that insurance coverage is maintained.

At present, there is no pending litigation or proceeding involving a director, officer, employee or agent of the Company where indemnification by the Company will be required or permitted. The Company is not aware of any threatened litigation or proceeding which may result in a claim for such indemnification.

EXECUTIVE COMPENSATION

The following table summarizes the compensation paid to or earned by the Company's Chief Executive Officer and all other executive officers of the Company whose salary and bonus for services rendered in all capacities to the Company during the fiscal year ended June 30, 1996 exceeded \$100,000 (the "named executive officers"):

SUMMARY COMPENSATION TABLE

NAME AND 1996 PRINCIPAL POSITION	YEAR	ANNUAL COMPENSATION			ALL OTHER COMPENSATION (\$)
		SALARY (\$)	BONUS (\$)	OTHER ANNUAL COMPENSATION (\$)	
R. Douglas Armstrong, Ph.D. President and Chief Ex- ecutive Officer	1996	\$156,962	\$55,000	--	\$8,885(1)
James Maluta..... Vice President, Product Development	1996	\$118,942	\$10,000	--	--
Thomas E. Muller, Ph.D.. Vice President, Regula- tory Affairs	1996	\$118,560	--	--	--
Walter C. Ogier..... Vice President, Market- ing	1996	\$106,250	\$ 7,500	--	--

(1) Consists of vacation pay to Dr. Armstrong in 1996.

1996 Option Grants

The following table contains information about the stock option grants to the named executive officers in 1996:

OPTION GRANTS IN LAST FISCAL YEAR

NAME	INDIVIDUAL GRANTS				POTENTIAL REALIZED VALUE AT ASSUMED ANNUAL RATES OF STOCK PRICE APPRECIATION FOR OPTION TERM(1)	
	NUMBER OF SECURITIES UNDERLYING OPTIONS GRANTED (#)	% OF TOTAL OPTIONS GRANTED TO EMPLOYEES IN FISCAL YEAR	EXERCISE OR BASE PRICE (\$/SH)	EXPIRATION DATE	5% (\$)	10% (\$)
R. Douglas Armstrong, Ph.D.	--	--	--	--	--	--
James Maluta.....	--	--	--	--	--	--
Thomas E. Muller, Ph.D.. Walter C. Ogier.....	6,667 6,667	4.3% 4.3%	1.20 1.20	02/14/06 02/14/06	5,000 5,000	12,734 12,734

(1) The 5% and the 10% assumed rates of appreciation are established by the rules of the Securities and Exchange Commission and do not represent the Company's estimate or projection of the future Common Stock price. If the Common Stock price of \$1.20 on the date of grant for the options granted in 1996 were to appreciate at the rates indicated, it would be \$1.95 per share (at a 5% compounded appreciation) and \$3.11 per share (at a 10% compounded appreciation) on the date of expiration of those options.

Option Exercises and Year-End Values

The following table provides information about the number of shares issued upon option exercise by the named executive officers during 1996, and the value realized by the named executive officers. The table also provides information about the number and value of options held by the named executive officers at June 30, 1996:

AGGREGATED OPTION EXERCISES IN LAST FISCAL YEAR AND FY-END OPTION VALUES

NAME	SHARES ACQUIRED ON EXERCISE (#)	VALUE REALIZED(\$)	NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS AT FY-END (#)		VALUE OF UNEXERCISED IN-THE-MONEY OPTIONS AT FY-END (\$)(1)	
			EXERCISABLE	UNEXERCISABLE	EXERCISABLE	UNEXERCISABLE
R. Douglas Armstrong, Ph.D.....	--	--	--	--	--	--
James Maluta.....	29,999	86,847	16,668	--	\$48,254	--
Thomas E. Muller, Ph.D..	--	--	15,000	18,334	29,925	\$36,576
Walter C. Ogier.....	5,000	9,975	13,750	21,250	27,431	42,394

(1) The option value represents fair market value of the underlying securities on the exercise date minus the aggregate exercise price of such options, multiplied by the number of shares of Common Stock subject to the option. For purposes of this calculation, a fair market value of \$3.20 per share was used, the fair market value of the securities as determined by the Board of Directors on June 30, 1996.

No compensation intended to serve as incentive for performance to occur over a period longer than one fiscal year was paid pursuant to a long-term incentive plan during the last fiscal year to any of the persons named in the Summary Compensation Table. The Company does not have any defined benefit or actuarial plan with any of the persons named in the Summary Compensation Table under which benefits are determined primarily by final compensation or average final compensation and years of service.

EMPLOYMENT AGREEMENTS

The Company has a policy of entering into employment agreements with all of its employees, and has entered into such agreements with all of its executive officers other than Dr. Armstrong. Such employment agreements generally establish salary levels (which are subject to periodic review) and provide for customary fringe benefits such as vacation leave, sick leave and health insurance. The agreements also generally provide for the protection of confidential information and the assignment to the Company of inventions conceived by the employee during his or her employment and permit the termination of the employment relationship by either party upon fourteen days prior written notice. The following is a summary of the employment agreements between the Company and its executive officers.

The Company entered into employment agreements with no defined terms with James Maluta, Walter C. Ogier, Thomas E. Muller, Ph.D., Alan K. Smith, Ph.D. and Todd E. Simpson in June 1992, February 1994, April 1994, October 1995 and December 1995, respectively. Pursuant to these agreements, the Company agreed to pay Messrs. Maluta, Ogier, Muller, Smith and Simpson annual base salaries of \$90,000, \$87,500, \$110,000, \$122,500 and \$122,500, certain of which base salaries have been increased by the Board of Directors and are subject to annual review and adjustment. Pursuant to the terms of the foregoing employment agreements, either party may generally terminate the employment relationship without cause at any time upon 14 days prior written notice to the other party or immediately with cause upon notice.

STOCK OPTION AND EMPLOYEE BENEFIT PLANS

1989 STOCK OPTION PLAN

In 1989, the Company established the 1989 Stock Option Plan. As of September 30, 1996, options to purchase an aggregate of 932,266 shares of Common Stock have been exercised at \$0.15 per share. Options to purchase 13,127 shares of Common Stock at \$0.15 per share were cancelled unexercised. No additional shares remain available for grant under the 1989 Stock Option Plan.

ANCILLARY PLAN

In 1991, the Company established an Ancillary Plan to grant options to individuals who were not eligible to receive options under the 1989 Stock Option Plan. Options to purchase an aggregate of 7,498 shares of the Company's Common Stock were granted under the Ancillary Plan, of which options to purchase 4,328 shares have been exercised at \$0.15 per share and the remaining options to purchase 3,170 shares have been cancelled. No additional shares remain available for grant under the Ancillary Plan.

AMENDED AND RESTATED 1992 INCENTIVE AND NON-QUALIFIED STOCK OPTION PLAN

In 1992, the Company adopted the 1992 Incentive and Non-Qualified Stock Option Plan (the "1992 Plan"), providing for the grant of options to purchase 666,667 shares of Common Stock. The Company allocated an additional 100,000 shares of Common Stock during 1992, an additional 333,333 shares of Common Stock in 1994 and an additional 800,000 shares of Common Stock in 1996 to the 1992 Plan, resulting in a total share reserve of 1,900,000 shares. The 1992 Plan was amended and restated to its current form in 1996. Options under the 1992 Plan for a total of 462,840 shares have been exercised as of September 30, 1996. As of September 30, 1996, options to purchase 336,254 shares of Common Stock were outstanding with a weighted average exercise price of \$1.27 per share.

The 1992 Plan provides for grants to employees and officers of "incentive stock options" within the meaning of Section 422 of the Internal Revenue Code of 1986, as amended, provided that such employee or officer is an employee on the date of grant. The 1992 Plan also provides for grants to employees, officers, consultants or service providers of nonqualified stock options. The 1992 Plan previously has been administered by the Board of Directors, but is currently administered by the Compensation Committee of the Board of Directors (the "Committee"). Each option granted pursuant to the 1992 Plan is authorized by the Committee and evidenced by a notice in such form as the Committee may from time to time determine.

The exercise price of each incentive stock option granted under the 1992 Plan must be at least equal to the fair market value of a share of Common Stock on the date of grant, except for incentive stock options granted to individuals who, at the time of grant, own stock possessing more than 10% of the total combined voting power of the Company, which options must have an exercise price of at least 110% of the fair market value of a share of Common Stock on the date of grant and must expire five years from the date of grant. The exercise price of each nonqualified stock option granted under the 1992 Plan must be at least 85% of the fair market value of the shares on the date of grant. No option shall be treated as an incentive stock option to the extent that such option would cause the aggregate fair market value (determined as of the date of grant of such option) of the shares with respect to which incentive stock options are exercisable by such optionee for the first time during any calendar year to exceed \$100,000. The terms of all incentive stock options and nonqualified stock options granted under the 1992 Plan may not exceed ten years. The exercise price may be paid in cash or, at the Committee's discretion, by delivery of previously owned shares of the Company's Common Stock, by a combination of cash and shares, or any other form of legal consideration acceptable to the Committee. Options under the 1992 Plan generally may not be granted after April 2006.

The 1992 Plan provides that if the Company is a party to any merger in which the Company is not the surviving entity, any consolidation or dissolution (other than the merger or consolidation of the Company with one or more of its wholly-owned subsidiaries), the Company must cause any successor corporation to assume the options or substitute similar options for outstanding option or continue such options in effect. In the event that any successor to the Company in a merger, consolidation or dissolution will not assume the options or substitute similar options, then with respect to options held by optionees performing services for the Company, the time for exercising such options will be accelerated and such options will be terminated if not exercised prior to such merger, consolidation or dissolution.

1996 OUTSIDE DIRECTORS STOCK OPTION PLAN

A total of 150,000 shares of Common Stock have been reserved for issuance under the Company's 1996 Outside Directors Stock Option Plan (the "Directors Plan"). As of the effective date of this offering, no options have been granted under the Directors Plan. The Directors Plan provides for the automatic granting of non-qualified stock options to directors of the Company who are not employees of the Company ("Outside Directors"). Under the Directors Plan, each Outside Director serving on the effective date of this Offering or elected after the date of this offering will automatically be granted an option to purchase 5,000 shares of Common Stock on the effective date of this offering or on the date of his or her election or appointment. In addition, each serving Outside Director will thereafter automatically be granted an option to purchase 5,000 shares of Common Stock following each annual meeting of stockholders after their election, provided that the Outside Director continues to serve in such capacity and that the Outside Director has served continuously as a director for at least six months. The exercise price of the options in all cases will be equal to the fair market value of the Common Stock on the date of grant. Options granted under the Directors Plan generally vest over a one-year period in equal monthly installments and must be exercised within ten years from the date of grant.

1996 EMPLOYEE STOCK PURCHASE PLAN

A total of 250,000 shares of the Company's Common Stock have been reserved for issuance under the Company's 1996 Employee Stock Purchase Plan (the "Purchase Plan"), none of which have been issued. The Purchase Plan permits eligible employees to purchase Common Stock at a discount through payroll deductions, during sequential 24-month offering periods. Each offering period is divided into four consecutive six-month purchase periods. Unless otherwise provided by the Board of Directors prior to the commencement of an offering period, the price at which stock is purchased under the Purchase Plan for such offering period is equal to 85% of the lesser of the fair market value of the Common Stock on the first day of such offering period or the last day of the purchase period of such offering period. The initial offering period will commence on the effective date of this offering.

SECTION 401(K) PLAN

Effective January 1, 1994, the Company adopted the Aastrom Biosciences, Inc. 401(k) Plan (the "Plan"). The Plan is intended to be a qualified retirement plan under the Internal Revenue Code. Employees of the Company are eligible to participate in the Plan upon the completion of three consecutive months of employment. Participants may make salary deferral contributions to the Plan of up to 15% of compensation, subject to the limitations imposed under the Internal Revenue Code. The Company may, but is not required to, make matching contributions to the Plan based on the participants' salary-defined contributions. Employer contributions are subject to a graduated vesting schedule based upon an employee's years of service with the Company. It is not anticipated that the Company will make any contributions to the Plan for the 1997 Plan Year. All contributions to the Plan are held in a trust which is intended to be exempt from income tax under Section 501(a) of the Internal Revenue Code. The Plan's trustees are R. Douglas Armstrong and Todd E. Simpson. Participants may direct the investment of their contributions among specified Merrill Lynch investment funds. The Plan may be amended or terminated by the Company at any time, subject to certain restrictions imposed by the Internal Revenue Code and the Employee Retirement Income Security Act of 1974.

COMPENSATION OF DIRECTORS

Directors of the Company do not receive cash for services provided as a director, however, directors who are not employees of the Company will receive annual grants of options to purchase Common Stock in accordance with the Directors Plan. No stock options nor any other form of non-cash compensation was granted to directors of the Company during the Company's fiscal year ending June 30, 1996. See "Stock Option and Employee Benefit Plans--1996 Outside Directors Stock Option Plan."

COMPENSATION COMMITTEE INTERLOCKS AND INSIDER PARTICIPATION IN COMPENSATION DECISIONS

During the fiscal year ended June 30, 1996, Robert J. Kunze, formerly an officer of the Company until 1991, R. Douglas Armstrong, President and Chief Executive Officer of the Company, and G. Bradford Jones were the members of the Compensation Committee of the Board of Directors. Dr. Armstrong resigned from the Compensation Committee and was replaced by Albert B. Deisseroth, M.D., Ph.D. on April 30, 1996, however, Mr. Kunze continues to be a member of this committee.

CERTAIN TRANSACTIONS

During the last three fiscal years, the Company sold Preferred Stock to certain holders of more than 5% of the outstanding shares of the Company, or to their affiliates, as described below.

In April 1995, the Company sold 775,001 shares of Series D Preferred Stock at a price per share of \$4.00 to the following investors: (i) H&Q Life Science Technology Fund I purchased 167,001 shares for a purchase price of \$668,004, (ii) H&Q London Ventures purchased 100,000 shares for a purchase price of \$400,000, (iii) Brentwood Associates V, L.P. ("Brentwood") purchased 231,250 shares for a purchase price of \$925,000, (iv) Windpoint Partners II, L.P. purchased 89,250 shares for a purchase price of \$357,000, and (v) the State Treasurer of the State of Michigan ("Michigan") purchased 187,500 shares for a purchase price of \$750,000. In May 1995, Cobe purchased 1,250,000 shares of Series D Preferred Stock for a purchase price of \$5,000,000. Upon the closing of this offering, each outstanding share of Series D Preferred Stock will be converted into two-thirds of a share of Common Stock.

In April 1995, Dr. Armstrong and Dr. Emerson agreed to grant to Brentwood an option to purchase up to 28,000 shares and 14,667 shares of Common Stock, respectively, and, together with two other shareholders of the Company, an aggregate of up to 66,667 shares of Common Stock at a purchase price of \$100,000. Brentwood exercised this option in April, 1996 purchasing an aggregate of 66,667 shares of Common Stock at a purchase price of \$100,000 from such shareholders.

In September 1995, the Company and RPR entered into a collaborative relationship for use of the Aastrom CPS as a component of its lymphoid cell therapy program. On September 6, 1996, RPR notified the Company that it would not exercise its option to continue the collaboration. As a result, \$3,500,000 million of option payments previously paid to the Company by RPR were converted into 205,882 shares of the Company's Series E Preferred Stock.

In October 1995, the Company repurchased 62,500 shares of Series D Preferred Stock from Brentwood at the original purchase price of \$250,000 and in December 1995 resold these shares to Northwest Ohio Venture Fund, a shareholder of the Company, for a total purchase price of \$250,000.

In January 1996, the Company sold 1,411,765 shares of Series E Preferred Stock at a price per share of \$4.25 to the following investors: (i) Michigan purchased 470,588 shares for a total purchase price of \$1,999,999, and (ii) SBIC Partners, L.P. purchased 941,777 shares for a total purchase price of \$4,000,002. Upon the closing of this offering, each share of Series E Preferred Stock will be converted into two-thirds of a share of Common Stock.

On November 18, 1993, in connection with the purchase of Common Stock upon exercise of stock options granted to R. Douglas Armstrong under the 1989 Stock Option Plan, the Company loaned to Dr. Armstrong \$120,000 at an interest rate of 4% per annum pursuant to a full recourse promissory note. Interest on the note is payable on an annual basis and principal and accrued but unpaid interest is due on June 30, 1997. Dr. Armstrong is the President and Chief Executive Officer and is a director of the Company.

On October 20, 1993, in connection with the purchase of Common Stock upon exercise of stock options granted to Stephen G. Emerson under the 1989 Stock Option Plan, the Company loaned to Dr. Emerson \$47,303 at an interest rate of 6% per annum pursuant to a full recourse promissory note. Interest on the note is payable on an annual basis and principal and accrued but unpaid interest is due June 30, 1997. The loan is secured by 258,687 shares of Common Stock held by Dr. Emerson. Dr. Emerson is a director of the Company.

In October 1996, the Company executed a financing commitment with Cobe to provide the Company with up to \$5,000,000 (the "Equity Commitment") and up to \$5,000,000 in funding from Michigan under a convertible loan commitment agreement ("Convertible Loan Commitment"). As of the date of this Prospectus, the Company has not obtained any financing under these commitments. Both the Equity Commitment and the Convertible Loan Commitment will terminate upon the consummation of this offering.

Under the terms of the Equity Commitment, the Company has an option to sell up to \$5,000,000 of Series F Preferred Stock at a price of \$6.00 per share to Cobe upon at least ninety days notice, which notice may be given at any time until September 1, 1997. Cobe's obligation to purchase such shares will terminate upon the closing of this offering. Although no shares of Series F Preferred Stock are outstanding, any outstanding shares of Series F Preferred Stock would convert upon the closing of this offering into Common Stock based upon a conversion price of 80% of the price of two-thirds of a share of Common Stock sold in this offering. To the extent shares are sold to Cobe under the Equity Commitment, Cobe's preemptive right in the Company's next financing and the Company's Put Option to Cobe would be reduced.

Upon the sale of \$5,000,000 of Series F Preferred Stock under the Equity Commitment, the Company becomes entitled to borrow funds from Michigan under the Convertible Loan Commitment. The Company may borrow such funds upon at least 45 days notice, which notice may be given during a period commencing on October 15, 1996 and ending on November 1, 1997. Upon the completion by the Company of a Qualifying Financing (as defined in the Convertible Loan Commitment), the Company has the option to repay outstanding principal and interest under the Convertible Loan Commitment in cash or to convert such borrowings into convertible Preferred Stock at a conversion price equivalent to 90% of the price per share in such financing. Under certain circumstances, the Convertible Loan Commitment converts or is convertible into Series G Preferred Stock. Interest accrues at an annual rate of 10% under the Convertible Loan Commitment, and the Company may repay such principal and interest at any time without penalty.

The Company has issued warrants to Michigan to purchase 69,444 shares of Common Stock as consideration for securing the Convertible Loan Commitment and has agreed to issue additional warrants to purchase 8,333 shares of Common Stock for each \$1,000,000 borrowed under the Convertible Loan Commitment, as adjusted to the level of borrowing. The warrants become exercisable 90 days after the closing of this offering. The warrants expire on October 15, 2000 if not exercised, and may be exercised, in whole or in part, at a price equal to the lesser of (a) \$9.00 per share, which price increases by \$3.00 per share upon each anniversary of the closing of the offering made hereby; and (b) 85% of the fair market value of the Company's Common Stock at the time of exercise.

PRINCIPAL STOCKHOLDERS

The following table sets forth certain information regarding the beneficial ownership of the shares of the Company's Common Stock as of September 30, 1996, and as adjusted to give effect to the sale of 3,250,000 shares of Common Stock in this offering assuming (a) conversion of all of the Company's outstanding shares of Preferred Stock into Common Stock and (b) no exercise of the Underwriters' over-allotment option, and as adjusted to reflect the sale of shares offered in this offering, (i) by each person the Company knows to be the beneficial owner of 5% or more of the outstanding shares of Common Stock, (ii) each named executive officer listed in the Summary Compensation Table, (iii) each director of the Company, and (iv) all executive officers and directors of the Company as a group.

BENEFICIAL OWNER	SHARES BENEFICIALLY OWNED(1)	PERCENTAGE BENEFICIALLY OWNED(1)	
		BEFORE THE OFFERING	AFTER THE OFFERING
H&Q Life Science(2)..... Technology Fund I One Bush Street, 18th Floor San Francisco, CA 94104	1,061,334	10.6%	8.0%
H&Q London Ventures..... One Bush Street, 18th Floor San Francisco, CA 94104	816,666	8.2%	6.2%
State Treasurer of the State of Michigan,(3)..... Custodian of certain re- tirement systems c/o Venture Capital Divi- sion 430 West Allegan Lansing, MI 48992	1,338,724	13.4%	10.1%
SBIC Partners, L.P..... 201 Main Street, Suite 2302 Fort Worth, TX 76102	627,451	6.3%	4.7%
Brentwood Associates V, L.P.(4)..... 11150 Santa Monica Blvd., Suite 1200 Los Angeles, CA 90025	745,831	7.5%	5.6%
Wind Point Partners II, L.P..... 676 N. Michigan Ave., Suite 3300 Chicago, IL 60611	559,500	5.6%	4.2%
Cobe Laboratories, Inc.(5).. 1185 Oak Street Lakewood, CO 80215	2,499,999	25.0%	18.9%
R. Douglas Armstrong, Ph.D.(6).....	501,555	5.0%	3.8%
Albert B. Deisseroth, M.D., Ph.D.	25,000	*	*
Stephen G. Emerson, M.D., Ph.D.	256,789	2.6%	1.9%
G. Bradford Jones(7).....	745,831	7.5%	5.6%
Robert J. Kunze(8).....	1,061,334	10.6%	8.0%
James Maluta(9).....	83,333	*	*
Thomas E. Muller, Ph.D.(10).	15,000	*	*
Walter C. Ogier(11).....	20,833	*	*
Horst R. Witzel, Dr.- Ing.(12).....	8,237	*	*
Edward C. Wood, Jr.(13)....	2,499,999	25.0%	18.9%
All officers and directors as a group (12 per- sons)(14).....	5,237,911	52.1%	39.4%

* Represents less than 1% of outstanding Common Stock or voting power.

- (1) Shares beneficially owned and percentage of ownership are based on 9,985,734 shares of Common Stock outstanding before this offering and 13,235,734 shares of Common Stock outstanding after the closing. Beneficial ownership is determined in accordance with the rules of the SEC and generally includes voting or disposition power with respect to securities.
- (2) Robert J. Kunze, Chairman of the Board of the Company, is a general partner of H&Q Life Science Venture Partners. See footnote 8, below.
- (3) Does not include 69,444 shares issuable upon exercise of warrants held by Michigan that are exercisable 90 days after the closing of this offering.
- (4) G. Bradford Jones, a director of the Company, is a general partner of Brentwood Associates V Ventures, L.P., which is the general partner of Brentwood Associates V, L.P. See footnote 7, below.
- (5) In addition, pursuant to a Stock Purchase Agreement dated October 22, 1993 between Cobe and the Company, Cobe has an option to purchase from the Company an amount of Common Stock equal to 30% of the Company's fully diluted shares after the exercise of such option, at a purchase price equal to 120% of the public market trading price of the Company's Common Stock for a three-year period following the closing of this offering. Cobe also has a right of first negotiation in the event the Company receives any proposal concerning, or otherwise decides to pursue, a merger, consolidation or other transaction in which all or a majority of the Company's equity securities or all or substantially all of the Company's assets, or any material portion of the assets of the Company used by the Company in performing its obligations under the Distribution Agreement would be acquired by a third party outside of the ordinary course of business. Edward C. Wood, Jr., a director of the Company, is the President of Cobe BCT, Inc., an affiliate of Cobe. See footnote 13, below.
- (6) Does not include 333,333 shares issuable upon exercise of options held by Dr. Armstrong that are exercisable upon the effective date of this offering.
- (7) Consists of 745,831 shares held by Brentwood Associates V, L.P. See footnote 4, above. Mr. Jones, as a general partner of Brentwood Associates V Ventures, L.P., which is the general partner of Brentwood Associates V, L.P., may be deemed to beneficially own such shares, but Mr. Jones disclaims beneficial ownership of all such shares except to the extent of his pecuniary interest therein.
- (8) Consists of 1,061,334 shares held by H&Q Life Science Technology Fund I. See footnote 2, above. Mr. Kunze, as a general partner of H&Q Life Science Venture Partners, may be deemed to beneficially own such shares, but Mr. Kunze disclaims beneficial ownership of all such shares except to the extent of his pecuniary interest therein.
- (9) Includes 16,668 shares issuable upon exercise of options held by Mr. Maluta that are exercisable within the 60-day period following September 30, 1996. Also includes 66,665 shares held of record by James Maluta and Deborah Vincent, as Trustees, with shared voting and investment power, of the James Maluta and Deborah Vincent Living Trust dated October 26, 1993.
- (10) Consists of 15,000 shares issuable upon exercise of options held by Dr. Muller that are exercisable within the 60-day period following September 30, 1996.
- (11) Includes 15,833 shares issuable upon exercise of options held by Mr. Ogier that are exercisable within the 60-day period following September 30, 1996.
- (12) Includes 2,237 shares issuable upon exercise of options held by Dr. Witzel that are exercisable within the 60-day period following September 30, 1996.
- (13) Consists of 2,499,999 shares held by Cobe. See footnote 5, above. Mr. Wood, as the President of Cobe BCT, Inc., an affiliate of Cobe, may be deemed to beneficially own such shares, but Mr. Wood disclaims beneficial ownership of all such shares.
- (14) Includes 69,738 shares issuable upon exercise of options that are exercisable within the 60-day period following September 30, 1996. Does not include 333,333 shares issuable upon exercise of options that are exercisable upon the effective date of this offering.

DESCRIPTION OF CAPITAL STOCK

Upon the closing of this offering, the authorized capital stock of the Company will consist of 40,000,000 shares of Common Stock, no par value per share, and 5,000,000 shares of Preferred Stock, no par value per share.

COMMON STOCK

As of September 30, 1996, without giving effect to the conversion of each share of Preferred Stock into Common Stock upon the closing of this offering, there were 1,887,312 shares of Common Stock outstanding held of record by 32 shareholders.

The holders of Common Stock are entitled to one vote per share on all matters to be voted upon by the shareholders. Subject to preferences that may be applicable to outstanding shares of Preferred Stock, the holders of Common Stock are entitled to receive ratably such dividends, if any, as may be declared from time to time by the Board of Directors out of funds legally available therefor. See "Dividend Policy." In the event of liquidation, dissolution or winding up of the Company, the holders of Common Stock are entitled to share ratably in all assets remaining after payment of liabilities, subject to prior liquidation rights of holders of Preferred Stock then outstanding. The Common Stock has no preemptive or conversion rights or other subscription rights. There are no redemption or sinking fund provisions applicable to the Common Stock. All outstanding shares of Common Stock are fully paid and nonassessable. The rights, preferences and privileges of holders of Common Stock are subject to, and may be adversely affected by, the rights of the holders of any shares of any Preferred Stock which the Company may designate and issue in the future.

PREFERRED STOCK

As of the closing of the offering, no shares of Preferred Stock will be outstanding. Thereafter, the Board of Directors will be authorized, without further shareholder approval, to issue up to 5,000,000 shares of Preferred Stock in one or more series and to fix the rights, preferences, privileges and restrictions granted or imposed upon any unissued shares of Preferred Stock and to fix the number of shares constituting any series and the designations of such series.

The issuance of Preferred Stock may have the effect of delaying or preventing a change in control of the Company. The issuance of Preferred Stock could decrease the amount of earnings and assets available for distribution to the holders of Common Stock or could adversely affect the rights and powers, including voting rights, of the holders of the Common Stock. In certain circumstances, such issuance could have the effect of decreasing the market price of the Common Stock. The Company currently has no plans to issue any shares of Preferred Stock.

MICHIGAN LAW AND CERTAIN CHARTER PROVISIONS

The Company is a Michigan corporation and is subject to certain anti-takeover provisions of the Michigan Business Corporation Act (the "MBCA") which could delay or make more difficult a merger or tender offer involving the Company. Chapter 7A of the MBCA prevents, in general, an "interested shareholder" (defined generally as a person owning 10% or more of a corporation's outstanding voting shares) from engaging in a "business combination" (as defined therein) with a Michigan corporation unless: (a) the Board of Directors issues an advisory statement, holders of 90% of the shares of each class of stock entitled to vote approve the transaction, and holders of two-thirds of the "disinterested" shares of each class of stock approve the transaction; or (b) the interested shareholder has been an interested shareholder for at least five years and has not acquired beneficial ownership of any additional shares of the corporation subsequent to the transaction which resulted in such shareholder being classified as an interested shareholder, and meets certain requirements, including, but not limited to, provisions relating to the fairness of the price and the form of consideration paid; or (c) the Board of Directors, by resolution, exempts a particular interested shareholder from these provisions prior to the interested

shareholder becoming an interested shareholder. The MBCA also contains certain other provisions which could have anti-takeover effects, including, but not limited to, Section 368, which pertains to "greenmail."

The Company's Bylaws provide that the Board of Directors is divided into three classes of directors, with each class serving a staggered three-year term. The classification system of electing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of the Company and may maintain the incumbency of the Board of Directors, as it generally makes it more difficult for shareholders to replace a majority of the directors. The Company's Restated Articles of Incorporation eliminate the right of shareholders to act without a meeting and do not provide for cumulative voting in the election of directors. The amendment of any of these provisions would require approval by holders of at least two-thirds of the shares of outstanding Common Stock.

The foregoing and other statutory provisions and provisions of the Company's Restated Articles of Incorporation could have the effect of deterring certain takeovers or delaying or preventing certain changes in control or management of the Company, including transactions in which shareholders might otherwise receive a premium for their shares over then-current market prices.

REGISTRATION RIGHTS

Pursuant to the Amended and Restated Investors Rights Agreement, dated as of April 7, 1992, as amended (the "Investors Agreement"), certain holders of outstanding shares of Common Stock, including shares of Common Stock issuable upon conversion of the Preferred Stock (the "Registrable Securities"), are entitled to certain demand and incidental registration rights with respect to such shares, subject to certain customary limitations. Under the Investors Agreement, subject to certain exceptions, the holders of at least 50% of the Registrable Securities may require the Company to use its diligent best efforts to register Registrable Securities for public resale on one occasion (so long as such registration includes at least 20% of the Registrable Securities or a lesser percentage if the anticipated aggregate offering price net of underwriting discounts and commissions would exceed \$2 million). In addition, whenever the Company proposes to register any of its securities under the Act, holders of Registrable Securities are entitled, subject to certain restrictions (including customary underwriters "cut back" limitations), to include their Registrable Securities in such registration. Subject to certain limitations, the holders of Registrable Securities may also require the Company to register such shares on Form S-3 no more than once every twelve months, provided that the anticipated aggregate proceeds would exceed \$500,000. The Company is required to bear all registration and selling expenses (other than underwriter's discounts and commissions and more than a single special counsel to the selling shareholders) in connection with the registration of Registrable Securities in one demand registration and two piggy-back registrations. The participating investors are required to bear all expenses in connection with the registration of Registrable Securities on Form S-3.

Registration rights may be transferred to an assignee or transferee provided that such assignee or transferee acquires at least 66,667 shares of the Registrable Securities held by the transferring holder (13,333 shares in the case of a transfer from the holder of certain stock options). These registration rights may be amended or waived (either generally or in a particular instance) only with the written consent of the Company and the holders of a majority of the Registrable Securities then outstanding.

The registration rights granted under the Investors Agreement shall not be exercisable by a holder during the period in which the holder may sell all of the holder's shares under Rule 144 or Rule 144A during a single 90-day period.

Pursuant to the Stock Purchase Agreement between the Company and Cobe, dated October 22, 1993 (the "Cobe Stock Agreement"), the Company granted to Cobe certain stock registration rights for any and all of the Company's Common Stock which Cobe acquires by conversion or otherwise. Cobe's stock registration rights commence 30 months following an initial public offering, or earlier in the event of any termination of the Distribution Agreement. Pursuant to Cobe's registration rights, Cobe is entitled to two demand registration rights, and an unlimited number of piggyback registration rights. Cobe's stock registration rights are subject to

customary underwriter's "cut back" requirements. The registration rights granted to Cobe shall not be exercisable during the period in which Cobe has the ability to sell all of its shares pursuant to Rule 144 during a single ninety-day period. Subject to certain conditions, these registration rights may be transferred with the transfer of stock to certain affiliates of the transferor or to a transferee who acquires the greater of 66,667 shares or 20% of the transferor's registrable stock.

RIGHTS OF COBE

Pursuant to the Cobe Stock Agreement, Cobe purchased an aggregate of \$10,000,000 of shares of the Company's Series C Preferred Stock. Such shares of Series C Preferred Stock will automatically convert into 1,666,666 shares of Common Stock upon consummation of the offering.

Pursuant to the Cobe Stock Agreement, Cobe also has certain preemptive rights to purchase a portion of any new stock issued by the Company, subject to certain exceptions, so as to enable Cobe to maintain its relative percentage ownership and voting power interests in the Company. Under the terms of the Cobe Stock Agreement, the Company also has the right to require Cobe to purchase stock issued by the Company in certain qualifying offerings, under certain circumstances (the "Put Option"). The Put Option may generally require Cobe to purchase up to 25% of the stock issued by the Company in a qualifying offering upon the same terms and conditions as the underwriters or other purchasers participating in the offering provided that Cobe shall not be required to purchase stock having an aggregate purchase price of more than \$5 million. If the Company exercises its Put Option with respect to any such qualifying offering, Cobe has the option to purchase the greater of up to 40% of the number of shares to be offered in the qualifying offering or the number of shares necessary to maintain its percentage ownership interest in the Company.

Additionally, for a three-year period following the Company's completion of its initial public offering of stock, Cobe will have an option to purchase from the Company a quantity of new shares of the Company's Common Stock at a price equal to 120% of the public market trading price for the Company's Common Stock. The quantity of Common Stock to be purchased if Cobe exercises this option shall be equal to 30% of the Company's fully diluted shares after the exercise of this option.

In the Cobe Stock Agreement, the Company also granted to Cobe a "right of first negotiation" in the event the Company receives any proposal concerning, or otherwise decides to pursue, a merger, consolidation or other transaction in which all or a majority of the Company's equity securities or all or substantially all of the Company's assets, or any material portion of the assets of the Company used by the Company in performing its obligations under the Distribution Agreement would be acquired by a third party outside of the ordinary course of business.

Pursuant to the Stock Purchase Commitment Agreement with Cobe, dated October 29, 1996, the Company agreed to use reasonable and good faith efforts to cause a nominee of Cobe, who must be deemed by the Board of Directors to be qualified to be elected to the Board of Directors for as long as Cobe owns at least 15% of the outstanding Common Stock.

SHARES ELIGIBLE FOR FUTURE SALE

Upon completion of this offering, the Company will have 13,235,734 shares of Common Stock outstanding, assuming no exercise of any outstanding options under any of the Company's option plans after September 30, 1996. Of these shares, the 3,250,000 shares of Common Stock sold in this offering will be freely transferable without restriction under the Securities Act unless they are held by the Company's affiliates as that term is used in Rule 144 under the Securities Act.

The remaining 9,985,734 shares (the "Restricted Shares") were issued and sold by the Company in private transactions in reliance upon exemptions from registration contained in the Act. A total of 6,873 Restricted Shares held for more than three years by shareholders who are not affiliates of the Company and who are not subject to the lock-up agreements described below will be eligible for sale in the public market in reliance upon Rule 144(k) immediately following the commencement of this offering. A total of 8,735,744 additional outstanding shares will be eligible for sale in the public market commencing 180 days from the date of this Prospectus without restriction, other than volume limitations in certain instances, upon the expiration of certain lock-up agreements referred to below. As of the date 90 days after the date of this Prospectus, 31,014 additional shares will be available for sale pursuant to Rule 144 or 701 under the Act, and 1,212,103 Restricted Shares will have been held for less than two years and will not be eligible for sale in the market until they have met the two-year holding period requirements of Rule 144. The executive officers and directors of the Company, and certain other stockholders and optionholders of the Company, have executed 180-day lock-up agreements. Cowen & Company may release some or all of the shares subject to lock-up agreements at any time without notice.

In general, under Rule 144, a person (or persons whose shares are aggregated), stockholders, including an affiliate, who has beneficially owned shares for at least two years is entitled to sell in broker transactions, within any three-month period, commencing 90 days after this offering, a number of shares that does not exceed the greater of (i) 1% of the then outstanding Common Stock (approximately 132,357 shares immediately after this offering assuming no exercise of the Underwriters' over-allotment option) or (ii) the average weekly trading volume in the Common Stock during the four calendar weeks preceding the sale, subject to the filing of a Form 144 with respect to the sale and other limitations. In general, shares issued in compliance with Rule 701 may be sold by non-affiliates subject to the manner of sale requirements of Rule 144, but without compliance with the other requirements of Rule 144. Affiliates may sell shares they acquired under Rule 701 in compliance with the provisions of Rule 144, except that there is no required holding period. A person who is not an affiliate, has not been an affiliate within three months prior to sale and has beneficially owned the Restricted Shares for at least three years, is entitled to sell such shares under Rule 144 without regard to any of the limitations described above.

The Company intends to file a registration statement under the Securities Act to register Common Stock reserved for issuance under its 1992 Plan, Directors Plan and Purchase Plan. Such registration statement is expected to become effective approximately 90 days after the date of this Prospectus. Shares issued upon exercise of outstanding stock options under such plan after the effective date of such registration statement generally will be available for sale in the public market. As of September 30, 1996, options to purchase a total of 336,254 shares of Common Stock were outstanding and 1,100,906 options remained available for grant under the 1992 Plan. No options have been granted under the Directors Plan.

The Company has also agreed not to offer, sell, contract to sell or otherwise dispose of any shares of Common Stock or any securities convertible into or exercisable or exchangeable for Common Stock or any rights to acquire Common Stock for a period of 180 days after the date of this Prospectus, without the prior written consent of the Underwriters, subject to certain limited exceptions (including exercises of stock options).

Prior to this offering, there has been no public market for the Common Stock of the Company. No prediction can be made regarding the effect, if any, that the sale or availability for sale of shares of additional Common Stock will have on the market price of the Common Stock. Nevertheless, sales of substantial numbers of shares by existing stockholders or by stockholders purchasing in their offering could have a negative effect on the market price of the Common Stock.

UNDERWRITING

Subject to the terms and conditions of the Underwriting Agreement, the Underwriters named below (the "Underwriters"), through their Representatives, Cowen & Company and J.P. Morgan Securities Inc., have severally agreed to purchase from the Company the following respective number of shares of Common Stock at the initial public offering price less the underwriting discounts and commissions set forth on the cover page of this Prospectus:

UNDERWRITER -----	NUMBER OF SHARES OF COMMON STOCK -----
Cowen & Company.....	
J.P. Morgan Securities Inc.....	

Total.....	3,250,000 =====

The Underwriting Agreement provides that the obligations of the Underwriters are subject to certain conditions precedent and that the Underwriters will purchase all of the Common Stock offered hereby if any of such shares are purchased.

The Company has been advised by the Representatives of the Underwriters that the Underwriters propose to offer the shares of Common Stock to the public at the initial public offering price set forth on the cover page of this Prospectus and to certain dealers at such price less a concession not in excess of \$ per share. The Underwriters may allow, and such dealers may reallocate, a concession not in excess of \$ per share to certain other dealers. After the initial public offering, the offering price and other selling terms may be changed by the Representatives of the Underwriters.

The Company has granted to the Underwriters an option, exercisable not later than 30 days after the date of this Prospectus, to purchase up to 487,500 additional shares of Common Stock at the initial public offering price less the underwriting discounts and commissions set forth on the cover page of this Prospectus. To the extent that the Underwriters exercise such option, each of the Underwriters will have a firm commitment to purchase approximately the same percentage thereof that the number of shares of Common Stock to be purchased by it shown in the above table bears to 3,250,000, and the Company will be obligated, pursuant to the option, to sell such shares to the Underwriters. The Underwriters may exercise such option only to cover over-allotments made in connection with the sale of the Common Stock offered hereby. If purchased, the Underwriters will offer such additional shares on the same terms as those on which the 3,250,000 shares are being offered.

The Company has agreed to indemnify the several Underwriters against certain liabilities, including liabilities under the Securities Act.

The Company and its directors and officers, and certain of its other stockholders and optionholders, have entered into agreements providing that, for a period of 180 days after the date of this Prospectus, they will not, without the prior written consent of Cowen & Company, offer, sell, contract to sell or otherwise dispose of any shares of Common Stock or any securities convertible into, or exchangeable for, or warrants to purchase, any shares of Common Stock, or grant any option to purchase or right to acquire or acquire any option to dispose of any shares of Common Stock, except in certain limited circumstances. See "Shares Eligible for Future Sale."

The Representatives of the Underwriters have advised the Company that the Underwriters do not intend to confirm sales to any account over which they exercise discretionary authority.

Prior to this offering, there has been no public market for the Common Stock of the Company. Consequently, the initial public offering price for the Common Stock has been determined by negotiations between the Company and the Representatives of the Underwriters. Among the factors considered in such negotiations were prevailing market conditions, the results of operations of the Company in recent periods, the market capitalizations and stages of development of other companies that the Company and the Representatives of the Underwriters believe to be comparable to the Company, estimates of the business potential of the Company, the present state of the Company's development, and other factors deemed relevant.

TRANSFER AGENT AND REGISTRAR

The Transfer Agent and Registrar for the Common Stock is . Its telephone number in , is .

LEGAL MATTERS

The validity of the Common Stock offered hereby will be passed upon for the Company by Pepper, Hamilton & Scheetz, Detroit, Michigan. Michael B. Staebler, a partner at Pepper, Hamilton & Scheetz, is the beneficial owner of 3,333 shares of Common Stock. Gray Cary Ware & Freidenrich, A Professional Corporation, San Diego, California, has acted as special counsel to the Company in connection with the offering. Certain legal matters in connection with this offering will be passed upon for the Underwriters by Brobeck Phleger & Harrison LLP, New York, New York.

EXPERTS

The balance sheets of the Company as of June 30, 1995 and 1996, and the statements of operations, stockholders' equity, and cash flows for the years ended June 30, 1994, 1995 and 1996 and the cumulative period from March 24, 1989 (inception) to June 30, 1996 included in this Prospectus, have been included herein in reliance on the report of Coopers & Lybrand L.L.P., independent accountants, given upon the authority of that firm as experts in accounting and auditing.

ADDITIONAL INFORMATION

The Company has filed with the Securities and Exchange Commission, Washington, D.C. 20549, a Registration Statement on Form S-1 under the Securities Act of 1933, as amended, with respect to the Common Stock offered hereby. This Prospectus does not contain all of the information set forth in the Registration Statement and the exhibits and schedules thereto. For further information with respect to the Company and the Common Stock, reference is made to the Registration Statement and the exhibits and schedules filed as a part thereof. Statements contained in this Prospectus as to the contents of any contract or any other document referred to are not necessarily complete, and, in each instance, if such contract or document is filed as an exhibit, reference is made to the copy of such contract or document filed as an exhibit to the Registration Statement, each such statement being qualified in all respects by such reference to such exhibit. The Registration Statement, including exhibits and schedules thereto, may be inspected without charge at the Commission's principal office in Washington, D.C., and copies of all or any part thereof may be obtained from such office after payment of fees prescribed by the Commission.

The Company intends to furnish to its shareholders annual reports containing financial statements audited by its independent certified public accountants and make available to its stockholders quarterly reports containing unaudited financial data for the first three quarters of each fiscal year.

AASTROM BIOSCIENCES, INC.
(A DEVELOPMENT STAGE COMPANY)

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REPORT OF INDEPENDENT ACCOUNTANTS

To the Board of Directors of
Aastrom Biosciences, Inc.:

We have audited the accompanying balance sheets of Aastrom Biosciences, Inc. (a Michigan corporation in the development stage) as of June 30, 1995 and 1996, and the related statements of operations, stockholders' equity, and cash flows for the years ended June 30, 1994, 1995 and 1996, and the cumulative period from March 24, 1989 (inception) to June 30, 1996. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with generally accepted auditing standards. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Aastrom Biosciences, Inc. as of June 30, 1995 and 1996, and the results of its operations and its cash flows for the years ended June 30, 1994, 1995 and 1996, and the cumulative period from March 24, 1989 (inception) to June 30, 1996, in conformity with generally accepted accounting principles.

Detroit, Michigan
August 9, 1996

To the Board of Directors of
Aastrom Biosciences, Inc.:

The financial statements herein have been adjusted to give effect to the 2 for 3 reverse stock split of the Company's outstanding Common Shares as described more fully in Note 1 to the financial statements. The above report is in the form that will be signed by Coopers & Lybrand L.L.P. upon the effectiveness of such split assuming that, from October 31, 1996 to the effective date of such split, no other events shall have occurred that would affect the accompanying financial statements or notes thereto.

Coopers & Lybrand L.L.P.

Detroit, Michigan
October 31, 1996

AASTROM BIOSCIENCES, INC.
(A DEVELOPMENT STAGE COMPANY)

BALANCE SHEETS

	JUNE 30,		SEPTEMBER 30,	PRO FORMA STOCKHOLDERS' EQUITY AT SEPTEMBER 30,
	1995	1996	1996	1996
	-----	-----	-----	-----
			(UNAUDITED)	(UNAUDITED)
ASSETS				
CURRENT ASSETS:				
Cash and cash equivalents.....	\$ 2,680,000	\$10,967,000	\$ 5,908,000	
Short-term investments.....	8,388,000	--	1,200,000	
Receivables.....	99,000	81,000	220,000	
Prepaid expenses.....	105,000	437,000	378,000	
	-----	-----	-----	
Total current assets.....	11,272,000	11,485,000	7,706,000	
PROPERTY, NET.....	1,279,000	1,188,000	1,225,000	
	-----	-----	-----	
Total assets.....	\$ 12,551,000	\$12,673,000	\$ 8,931,000	
	=====	=====	=====	
LIABILITIES AND STOCKHOLDER'S EQUITY				
CURRENT LIABILITIES:				
Accounts payable and accrued expenses.....	\$ 328,000	\$ 1,192,000	\$ 841,000	
Accrued employee expenses.....	130,000	97,000	80,000	
Current portion of capital lease obligations.....	270,000	223,000	192,000	
Deferred revenue.....	225,000	122,000	53,000	
	-----	-----	-----	
Total current liabilities.....	953,000	1,634,000	1,166,000	
CAPITAL LEASE OBLIGATIONS.....	412,000	189,000	147,000	
COMMITMENTS (Note 7)				
STOCKHOLDERS' EQUITY:				
Preferred Stock, no par value, shares authorized--8,540,000, 9,951,765 and 10,157,647, respectively, issued and outstanding--8,040,001, 9,451,766 and 9,657,648, respectively (none--pro forma), (liquidation preference of \$34,560,000 and \$35,375,000 at June 30, 1996 and September 30, 1996, respectively).....	28,253,000	34,218,000	37,718,000	\$ --
Common Stock, no par value, shares authorized--17,000,000, 18,500,000 and 18,500,000, respectively, issued and outstanding--1,731,463, 1,886,479 and 1,887,312, respectively (9,985,734--pro forma)..<	241,000	324,000	365,000	38,083,000
Deficit accumulated during the development stage.....	(17,108,000)	(27,025,000)	(30,298,000)	(30,298,000)
Stockholder notes receivable.....	(198,000)	(167,000)	(167,000)	(167,000)
Stock purchase rights....	--	3,500,000	--	--
Unrealized losses on investments.....	(2,000)	--	--	--
	-----	-----	-----	-----
Total stockholders' equity.....	11,186,000	10,850,000	7,618,000	\$ 7,618,000
	-----	-----	-----	=====
Total liabilities and stockholders' equity.....	\$ 12,551,000	\$12,673,000	\$ 8,931,000	
	=====	=====	=====	

The accompanying notes are an integral part of these financial statements.

AASTROM BIOSCIENCES, INC.
(A DEVELOPMENT STAGE COMPANY)

STATEMENTS OF OPERATIONS

	YEAR ENDED JUNE 30,			MARCH 24, 1989 (INCEPTION) TO JUNE 30, 1996	THREE MONTHS ENDED SEPTEMBER 30,		MARCH 24, 1989 (INCEPTION) TO SEPTEMBER 30, 1996
	1994	1995	1996		1995	1996	
					(UNAUDITED)		(UNAUDITED)
REVENUES:							
Research and development agreements.....	\$ 49,000	\$ 396,000	\$ 1,342,000	\$ 1,787,000	\$ 172,000	\$ 195,000	\$ 1,982,000
Grants.....	823,000	121,000	267,000	1,995,000	39,000	29,000	2,024,000
Total revenues.....	872,000	517,000	1,609,000	3,782,000	211,000	224,000	4,006,000
COSTS AND EXPENSES:							
Research and development.....	5,627,000	4,889,000	10,075,000	25,075,000	1,195,000	3,160,000	28,235,000
General and administrative.....	1,565,000	1,558,000	2,067,000	7,089,000	446,000	452,000	7,541,000
Total costs and expenses.....	7,192,000	6,447,000	12,142,000	32,164,000	1,641,000	3,612,000	35,776,000
LOSS BEFORE OTHER INCOME AND EXPENSE.....	(6,320,000)	(5,930,000)	(10,533,000)	(28,382,000)	(1,430,000)	(3,388,000)	(31,770,000)
OTHER INCOME (EXPENSE):							
Interest income.....	245,000	279,000	678,000	1,576,000	149,000	126,000	1,702,000
Interest expense.....	(65,000)	(66,000)	(62,000)	(219,000)	(18,000)	(11,000)	(230,000)
Other income.....	180,000	213,000	616,000	1,357,000	131,000	115,000	1,472,000
NET LOSS.....	\$(6,140,000)	\$(5,717,000)	\$ (9,917,000)	\$(27,025,000)	\$(1,299,000)	\$(3,273,000)	\$(30,298,000)
PRO FORMA NET LOSS PER SHARE.....	\$ (.82)	\$ (.66)	\$ (.98)		\$ (.13)	\$ (.32)	
Pro forma weighted average number of common and common equivalent shares outstanding.....							
	7,461,000	8,644,000	10,103,000		10,094,000	10,107,000	

The accompanying notes are an integral part of these financial statements.

AASTROM BIOSCIENCES, INC.
(A DEVELOPMENT STAGE COMPANY)

STATEMENTS OF STOCKHOLDERS' EQUITY

	PREFERRED STOCK		COMMON STOCK		DEFICIT ACCUMULATED DURING THE DEVELOPMENT STAGE	STOCKHOLDER NOTES RECEIVABLE	STOCK PURCHASE RIGHTS	UNREALIZED GAINS (LOSSES) ON INVESTMENTS
	SHARES	AMOUNT	SHARES	AMOUNT				
Balance, March 24, 1989 (Inception)....	--	\$ --	--	\$ --	\$ --	\$ --	\$ --	\$ --
Non-cash issuance of Common Stock...			454,545	--				
Issuance of Series A Preferred Stock at \$1.00 per share in August 1989.....	1,500,000	1,500,000						
Net loss.....					(500,000)			
Balance, June 30, 1990.....	1,500,000	1,500,000	454,545	--	(500,000)	--	--	--
Issuance of Series A Preferred Stock in March 1991 at \$1.00 per share, net of issuance costs of \$5,000.....	1,000,000	995,000						
Net loss.....					(636,000)			
Balance, June 30, 1991.....	2,500,000	2,495,000	454,545	--	(1,136,000)	--	--	--
Issuance of Series B Preferred Stock in April 1992 at \$2.00 per share, net of issuance costs of \$46,000.....	3,030,000	6,014,000						
Net loss.....					(1,268,000)			
Balance, June 30, 1992.....	5,530,000	8,509,000	454,545	--	(2,404,000)	--	--	--
Issuance of Common Stock for services...			33,333	10,000				
Exercise of stock option...			6,873	1,000				
Net loss.....					(2,847,000)			
Balance, June 30, 1993.....	5,530,000	8,509,000	494,751	11,000	(5,251,000)	--	--	--
Issuance of Series C Preferred Stock in October 1993 at \$1,000 per share, net of issuance costs of \$175,000....	10,000	9,825,000						
Exercise of stock options..			1,222,609	229,000		(198,000)		
Net loss.....					(6,140,000)			
Balance, June 30, 1994.....	5,540,000	18,334,000	1,717,360	240,000	(11,391,000)	(198,000)	--	--
Issuance of Series D Preferred Stock in April and May 1995 at \$4.00 per share, net of issuance costs of \$81,000.....	2,500,001	9,919,000						
Exercise of stock options..			39,103	8,000				
Retirement of Common Shares outstanding....			(25,000)	(7,000)				
Unrealized loss on investments.								(2,000)
Net loss.....					(5,717,000)			
Balance, June 30, 1995.....	8,040,001	28,253,000	1,731,463	241,000	(17,108,000)	(198,000)	--	(2,000)

Issuance of Series E Preferred Stock in January 1996 at \$4.25 per share, net of issuance costs of \$35,000.....	1,411,765	5,965,000						
Exercise of stock options..			130,016	53,000				
Issuance of Common Stock at \$1.20 per share.....			25,000	30,000				
Issuance of Stock Purchase Rights for cash in September 1995 and March 1996.....						3,500,000		
Repurchase of Series D Preferred Stock at \$4.00 per share.....	(62,500)	(250,000)						
Sale of Series D Preferred Stock at \$4.00 per share.....	62,500	250,000						
Principal payment received under stockholder note receivable.....						31,000		
Unrealized gain on investments.								2,000
Net loss.....					(9,917,000)			
Balance, June 30, 1996.....	9,451,766	34,218,000	1,886,479	324,000	(27,025,000)	(167,000)	3,500,000	--
Unaudited:								
Exercise of stock options..			833	1,000				
Issuance of Series E Preferred Stock to RPR at \$17.00 per share.....	205,882	3,500,000					(3,500,000)	
Compensation expense related to stock options granted.....				40,000				
Net loss.....					(3,273,000)			
Balance, September 30, 1996 (Unaudited)....	9,657,648	\$37,718,000	1,887,312	\$365,000	\$(30,298,000)	\$(167,000)	\$ --	\$ --
	=====	=====	=====	=====	=====	=====	=====	=====

TOTAL
STOCKHOLDERS'
EQUITY

Balance, March 24, 1989 (Inception)....	\$ --
Non-cash issuance of Common Stock...	--
Issuance of Series A Preferred Stock at \$1.00 per share in August 1989.....	1,500,000
Net loss.....	(500,000)
Balance, June 30, 1990.....	1,000,000
Issuance of Series A Preferred Stock in March 1991 at \$1.00 per share, net of issuance costs of \$5,000.....	995,000
Net loss.....	(636,000)
Balance, June 30, 1991.....	1,359,000
Issuance of Series B Preferred Stock in April 1992	

at \$2.00 per share, net of issuance costs of \$46,000.....	6,014,000
Net loss.....	(1,268,000)

Balance, June 30, 1992.....	6,105,000
Issuance of Common Stock for services...	10,000
Exercise of stock option...	1,000
Net loss.....	(2,847,000)

Balance, June 30, 1993.....	3,269,000
Issuance of Series C Preferred Stock in October 1993 at \$1,000 per share, net of issuance costs of \$175,000....	9,825,000
Exercise of stock options..	31,000
Net loss.....	(6,140,000)

Balance, June 30, 1994.....	6,985,000
Issuance of Series D Preferred Stock in April and May 1995 at \$4.00 per share, net of issuance costs of \$81,000.....	9,919,000
Exercise of stock options..	8,000
Retirement of Common Shares outstanding....	(7,000)
Unrealized loss on investments.	(2,000)
Net loss.....	(5,717,000)

Balance, June 30, 1995.....	11,186,000
Issuance of Series E Preferred Stock in January 1996 at \$4.25 per share, net of issuance costs of \$35,000.....	5,965,000
Exercise of stock options..	53,000
Issuance of Common Stock at \$1.20 per share.....	30,000
Issuance of Stock Purchase Rights for cash in September 1995 and March 1996.....	3,500,000
Repurchase of Series D Preferred Stock at \$4.00 per share.....	(250,000)
Sale of Series D Preferred Stock at \$4.00 per share.....	250,000
Principal payment received under stockholder note receivable.....	31,000
Unrealized gain on investments.	2,000
Net loss.....	(9,917,000)

Balance, June 30, 1996.....	10,850,000
Unaudited: Exercise of stock options..	1,000
Issuance of Series E Preferred Stock to RPR at \$17.00 per	

share.....	--
Compensation	
expense related	
to stock	
options	
granted.....	40,000
Net loss.....	(3,273,000)

Balance,	
September 30,	
1996	
(Unaudited)....	\$7,618,000
	=====

The accompanying notes are an integral part of these financial statements.

AASTROM BIOSCIENCES, INC.
(A DEVELOPMENT STAGE COMPANY)

STATEMENTS OF CASH FLOWS

	YEAR ENDED JUNE 30,			MARCH 24, 1989 (INCEPTION) TO JUNE 30, 1996	THREE MONTHS ENDED SEPTEMBER 30,		MARCH 24, 1989 (INCEPTION) TO SEPTEMBER 30, 1996
	1994	1995	1996		1995	1996	
					(UNAUDITED)		(UNAUDITED)
OPERATING ACTIVITIES:							
Net loss.....	\$ (6,140,000)	\$ (5,717,000)	\$ (9,917,000)	\$ (27,025,000)	\$ (1,299,000)	\$ (3,273,000)	\$ (30,298,000)
Adjustments to reconcile net loss to net cash used for operating activities:							
Depreciation and amortization.....	248,000	329,000	536,000	1,267,000	91,000	136,000	1,403,000
Loss on property held for resale.....	--	--	--	110,000	--	--	110,000
Amortization of discounts and premiums on investments.....	--	(9,000)	(110,000)	(119,000)	(48,000)	--	(119,000)
Expense related to stock and stock options granted....	--	--	--	10,000	--	40,000	50,000
Changes in assets and liabilities:							
Receivables.....	11,000	132,000	18,000	(81,000)	4,000	(139,000)	(220,000)
Prepaid expenses...	(17,000)	(59,000)	(332,000)	(437,000)	27,000	59,000	(378,000)
Accounts payable and accrued expenses.....	(45,000)	(40,000)	864,000	1,192,000	(35,000)	(351,000)	841,000
Accrued employee expenses.....	53,000	28,000	(33,000)	97,000	(58,000)	(17,000)	80,000
Deferred revenue...	146,000	79,000	(103,000)	122,000	(172,000)	(69,000)	53,000
Net cash used for operating activities..	(5,744,000)	(5,257,000)	(9,077,000)	(24,864,000)	(1,490,000)	(3,614,000)	(28,478,000)
INVESTING ACTIVITIES:							
Organizational costs...	--	--	--	(73,000)	--	--	(73,000)
Purchase of short-term investments.....	(967,000)	(10,981,000)	--	(11,948,000)	--	(1,200,000)	(13,148,000)
Maturities of short- term investments.....	--	3,567,000	8,500,000	12,067,000	2,500,000	--	12,067,000
Capital purchases.....	(320,000)	(118,000)	(445,000)	(1,718,000)	(15,000)	(173,000)	(1,891,000)
Proceeds from sale of property held for resale.....	--	--	--	400,000	--	--	400,000
Net cash provided by (used for) investing activities.....	(1,287,000)	(7,532,000)	8,055,000	(1,272,000)	2,485,000	(1,373,000)	(2,645,000)
FINANCING ACTIVITIES:							
Issuance of Preferred Stock.....	9,825,000	9,919,000	5,965,000	34,218,000	--	--	34,218,000
Issuance of Common Stock.....	31,000	1,000	83,000	116,000	3,000	1,000	117,000
Payments received for stock purchase rights.	--	--	3,500,000	3,500,000	1,500,000	--	3,500,000
Payments received under stockholder notes....	--	--	31,000	31,000	--	--	31,000
Principal payments under capital lease obligations.....	(147,000)	(214,000)	(270,000)	(762,000)	(65,000)	(73,000)	(835,000)
Net cash provided by (used for) financing activities.....	9,709,000	9,706,000	9,309,000	37,103,000	1,438,000	(72,000)	37,031,000
NET INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS.....	2,678,000	(3,083,000)	8,287,000	10,967,000	2,433,000	(5,059,000)	5,908,000
CASH AND CASH EQUIVALENTS AT BEGINNING OF PERIOD....	3,085,000	5,763,000	2,680,000	--	2,680,000	10,967,000	--
CASH AND CASH EQUIVALENTS AT END OF PERIOD.....	\$ 5,763,000	\$ 2,680,000	\$10,967,000	\$ 10,967,000	\$ 5,113,000	\$ 5,908,000	\$ 5,908,000
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:							
Interest paid.....	\$ 65,000	\$ 66,000	\$ 62,000	\$ 219,000	\$ 18,000	\$ 11,000	\$ 230,000
SUPPLEMENTAL DISCLOSURES OF NON-CASH INVESTING AND FINANCING ACTIVITIES:							

Additions to capital								
lease obligations.....	\$ 348,000	\$ 270,000	\$ --	\$ 1,174,000	\$ --	\$ --	\$ 1,174,000	
	=====	=====	=====	=====	=====	=====	=====	

The accompanying notes are an integral part of these financial statements.

AASTROM BIOSCIENCES, INC.
(A DEVELOPMENT STAGE COMPANY)

NOTES TO FINANCIAL STATEMENTS

(INFORMATION AS OF SEPTEMBER 30, 1996 AND FOR THE THREE-MONTH PERIODS ENDED SEPTEMBER 30, 1995 AND 1996 IS UNAUDITED)

1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Overview--Aastrom Biosciences, Inc. (the "Company") was incorporated in March 1989 ("Inception") under the name Ann Arbor Stromal, Inc. The Company changed its name in 1991 concurrent with the commencement of employee-based operations. The Company is in the development stage with its principal business activities being research and product development, conducted both on its own behalf and in connection with various collaborative research and development agreements with other companies, involving the development of processes and instrumentation for the ex-vivo production of human stem cells and their progeny, and hematopoietic and other tissues. Successful future operations are subject to several technical and business risks, including satisfactory product development and obtaining regulatory approval and market acceptance for its products.

Significant Revenue Relationships--Two companies accounted for 77% of total revenues for the year ended June 30, 1995 and one company accounted for 83% of total revenues for the year ended June 30, 1996. These two companies have accounted for 47% of total revenues for the period from Inception to June 30, 1996. One company accounted for 82% and 87% of total revenues for the three months ended September 30, 1995 and 1996, respectively, and two companies accounted for 49% of total revenues for the period from Inception to September 30, 1996. Grant revenues consist of grants sponsored by the U.S. government.

Cash and Cash Equivalents--Cash and cash equivalents include cash and short-term investments with original maturities of three months or less.

Short-Term Investments--Short-term investments consist of U.S. government securities and commercial paper with original maturities of over three months but less than one year. Short-term investments are classified as available-for-sale, and are carried at market value, in accordance with Financial Accounting Standards Board Statement No. 115, "Accounting for Certain Investments in Debt and Equity Securities," which was adopted July 1, 1994. Application of this pronouncement results in the inclusion of unrealized gains and losses on investments in stockholders' equity. Application of this accounting treatment in prior periods would not have materially changed the amounts as presented.

Diversity of Credit Risk--The Company invests its excess cash in U.S. government securities and commercial paper, maintained in U.S. financial institutions, and has established guidelines relative to diversification and maturities in an effort to maintain safety and liquidity. The Company plans to continue to invest its excess funds in short-term, investment grade, interest-bearing instruments. These guidelines are periodically reviewed and modified to take advantage of trends in yields and interest rates. The Company has not experienced any significant losses on its cash equivalents or short-term investments.

Property--Property is recorded at cost and depreciated or amortized using the straight-line method over the estimated useful life of the asset (primarily five years) or the remaining lease term, if shorter, with respect to leasehold improvements and certain capital lease assets.

Revenue Recognition--Revenue from grants and research agreements is recognized on a cost reimbursement basis consistent with the performance requirements of the related agreement. Funding received in advance of costs incurred is presented as deferred revenue in the accompanying financial statements.

Research and Development Costs--Research and development costs are expensed as incurred. Such costs and expenses related to programs under collaborative agreements with other companies totaled \$49,000, \$146,000 and \$1,294,000 for the years ended June 30, 1994, 1995 and 1996, respectively, and \$1,489,000 for the period from Inception to June 30, 1996 and \$158,000, \$117,000 and \$1,606,000 for the three months ended September 30, 1995 and 1996 and for the period from Inception to September 30, 1996, respectively.

AASTROM BIOSCIENCES, INC.
(A DEVELOPMENT STAGE COMPANY)

NOTES TO FINANCIAL STATEMENTS--(CONTINUED)

(INFORMATION AS OF SEPTEMBER 30, 1996 AND FOR THE THREE-MONTH PERIODS ENDED SEPTEMBER 30, 1995 AND 1996 IS UNAUDITED)

Restatement of Common Stock Information--The Company's Board of Directors authorized a two-for-three reverse stock split of the Company's Common Stock ("Reverse Stock Split") to be effected prior to the closing of the proposed IPO. Accordingly, all references in the accompanying financial statements to common share or per common share information have been restated to reflect the Reverse Stock Split.

Pro Forma Information (Unaudited)--Pro forma net loss per share is computed using the weighted average number of common and common equivalent shares outstanding during the period. Common equivalent shares are not included in the per-share calculation where the effect of their inclusion would be anti-dilutive, except that common and common equivalent shares issued during the 12 month period preceding the filing of the registration statement for the proposed initial public offering ("IPO"), contemplated in the Prospectus in which these financial statements are included, at a price below \$8.00 per share (the lowest expected selling price in the proposed IPO) are considered to be cheap stock and have been included in the calculation as if they were outstanding for all periods using the treasury stock method, if applicable, even though their inclusion is anti-dilutive. Upon the completion of the Company's proposed IPO, all 9,657,648 shares of the Company's outstanding Preferred Stock will automatically convert into 8,098,422 shares of Common Stock. As a result, all outstanding shares of Preferred Stock are assumed to have been converted to Common Stock at the time of issuance, except for those shares considered to be cheap stock which are treated as outstanding for all periods presented. The pro forma effect of these conversions has been reflected in the accompanying balance sheet assuming the conversion had occurred on September 30, 1996.

Historical net loss per share information is not considered meaningful due to the significant changes in the Company's capital structure which will occur upon the closing of the proposed IPO; accordingly, such per-share data information is not presented.

Use of Estimates--The preparation of financial statements in accordance with generally accepted accounting principles requires management to make estimates that affect the amounts reported in the financial statements and disclosures made in the accompanying notes to financial statements. Actual results could differ from those estimates.

Financial Instruments--Management evaluates the fair value of those assets and liabilities identified as financial instruments under Statement of Financial Accounting Standards No. 107 and estimates that the fair value of such financial instruments generally approximates the carrying value in the accompanying financial statements. Fair values have been determined through information obtained from market sources and management estimates.

Recent Pronouncements--During October 1995, the Financial Accounting Standards Board issued Statement No. 123, "Accounting for Stock-Based Compensation," which establishes a fair value based method of accounting for stock-based compensation and incentive plans and requires additional disclosures for those companies that elect not to adopt the new method of accounting. Adoption of this pronouncement is required for the Company's fiscal year beginning July 1, 1996 and the Company intends to provide the additional disclosures required by the pronouncement in its financial statements for the year ended June 30, 1997.

During March 1995, the Financial Accounting Standards Board issued Statement No. 121 (SFAS 121), "Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to Be Disposed Of," which requires the Company to review for impairment of long-lived assets, certain identifiable intangibles, and goodwill related to those assets whenever events or changes in circumstances indicate that the carrying amount of an asset

AASTROM BIOSCIENCES, INC.
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NOTES TO FINANCIAL STATEMENTS--(CONTINUED)

(INFORMATION AS OF SEPTEMBER 30, 1996 AND FOR THE THREE-MONTH PERIODS ENDED SEPTEMBER 30, 1995 AND 1996 IS UNAUDITED)

might not be recoverable. In certain situations, an impairment loss would be recognized. SFAS 121 will become effective for the Company's fiscal year beginning July 1, 1996. Management has studied the effect of implementing SFAS 121 and, based upon its initial evaluation, does not expect it to have a significant impact on the Company's financial condition or results of operations.

Unaudited Financial Information--The financial information as of September 30, 1996, and for the three-month periods ended September 30, 1995 and 1996, and for the period from Inception to September 30, 1996, is unaudited. In the opinion of management, such information contains all adjustments, consisting only of normal recurring accruals, necessary for a fair statement of the results of operations for the interim periods. The results of operations for the three months ended September 30, 1996, are not necessarily indicative of the results to be expected for the full year.

2. SHORT-TERM INVESTMENTS

All short-term investments are available-for-sale, and have maturities of one year or less and are summarized as follows:

	COST	GROSS UNREALIZED GAINS	GROSS UNREALIZED LOSSES	ESTIMATED FAIR VALUE
June 30, 1995:				
U.S. Government Securities....	\$4,890,000	\$ --	\$ (2,000)	\$4,888,000
Commercial Paper.....	3,500,000	--	--	3,500,000
	<u>\$8,390,000</u>	<u>\$ --</u>	<u>\$ (2,000)</u>	<u>\$8,388,000</u>
	=====	=====	=====	=====

	COST	GROSS UNREALIZED GAINS	GROSS UNREALIZED LOSSES	ESTIMATED FAIR VALUE
September 30, 1996 (Unaudited):				
U.S. Government Securities....	\$1,200,000	\$ --	\$ --	\$1,200,000
	<u>=====</u>	<u>=====</u>	<u>=====</u>	<u>=====</u>

3. PROPERTY

Property consists of the following:

	JUNE 30,		SEPTEMBER 30,
	1995	1996	1996
			(UNAUDITED)
Machinery and equipment.....	\$1,140,000	\$1,337,000	\$1,341,000
Office equipment.....	405,000	482,000	604,000
Leasehold improvements.....	380,000	520,000	567,000
	<u>1,925,000</u>	<u>2,339,000</u>	<u>2,512,000</u>
Less accumulated depreciation and amortization.....	(646,000)	(1,151,000)	(1,287,000)
	<u>\$1,279,000</u>	<u>\$1,188,000</u>	<u>\$1,225,000</u>
	=====	=====	=====

Equipment under capital leases totaled \$1,162,000, \$1,131,000 and \$1,131,000 at June 30, 1995 and 1996 and September 30, 1996, respectively, with related accumulated amortization of \$407,000, \$622,000 and \$679,000, respectively (Note 7).

AASTROM BIOSCIENCES, INC.
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NOTES TO FINANCIAL STATEMENTS--(CONTINUED)

(INFORMATION AS OF SEPTEMBER 30, 1996 AND FOR THE THREE-MONTH PERIODS ENDED SEPTEMBER 30, 1995 AND 1996 IS UNAUDITED)

4. STOCKHOLDERS' EQUITY:

Preferred Stock--The Company has the following outstanding Convertible Preferred Stock:

	SHARES AUTHORIZED	SHARES ISSUED AND OUTSTANDING			LIQUIDATION PREFERENCE AT	
	SEPTEMBER 30, 1996	JUNE 30, 1995	JUNE 30, 1996	SEPTEMBER 30, 1996	JUNE 30, 1996	SEPTEMBER 30, 1996
	(Unaudited)			(Unaudited)		(Unaudited)
Series A.....	2,500,000	2,500,000	2,500,000	2,500,000	\$ 2,500,000	\$ 2,500,000
Series B.....	3,030,000	3,030,000	3,030,000	3,030,000	6,060,000	6,000,000
Series C.....	10,000	10,000	10,000	10,000	10,000,000	10,000,000
Series D.....	3,000,000	2,500,001	2,500,001	2,500,001	10,000,000	10,000,000
Series E.....	1,617,647	--	1,411,765	1,617,647	6,000,000	6,875,000
	10,157,647	8,040,001	9,451,766	9,657,648	\$34,560,000	\$35,375,000
	=====	=====	=====	=====	=====	=====

All preferred shares have voting rights equal to the equivalent number of common shares into which they are convertible. Conversion rights on all outstanding classes of preferred stock are on a two-for-three basis to give effect for the Reverse Stock Split, except for the Series C Preferred Stock, each share of which is convertible into approximately 250 shares of Common Stock. Conversion rights on certain classes of preferred stock are subject to anti-dilution adjustments. Dividends accrue annually at 8% on all series of Preferred Stock, but do not accumulate. No cash dividends have been declared or paid through September 30, 1996. Dividends and liquidation preferences on the Series B, Series C and Series D Preferred Stock are senior to those of the Series A Preferred Stock. Dividends and liquidation preferences on the Series E Preferred Stock are senior to those of all other outstanding series of preferred stock. Conversion of preferred stock is automatic in the event of the closing of an underwritten public stock offering meeting certain minimum requirements such as the offering contemplated by the Prospectus in which these financial statements are included.

Cobe Laboratories, Inc. Stock Purchase Rights--In connection with the purchase of the Series C Preferred Stock by Cobe Laboratories, Inc. ("Cobe") in October 1993, Cobe received a preemptive right to purchase a pro-rata portion of any newly issued shares of stock by the Company in order to maintain its then current percentage ownership interest. Any such purchase of newly issued shares shall be at the net price to the Company after deducting underwriters' discounts and commissions, if any. Cobe has waived its right to such discount on its intended purchase of shares in the proposed IPO. The Company has an option ("Put Option") to require Cobe to purchase the lesser of 20%, or \$5,000,000, in an offering of equity securities meeting certain minimum requirements. In the event that the Company exercises the Put Option, Cobe then has the option to purchase up to 40% of that offering.

During the three-year period following the completion of an initial public offering of Common Stock by the Company, Cobe has an option to purchase additional shares from the Company equal to 30% of the total number of shares outstanding assuming exercise of the option. Such option, if exercised, must be exercised in full with the purchase price of the shares being established at 120% of the public market trading price as determined by the 30-day average market price preceding the date of exercise of the option.

The Company has granted Cobe a right of first negotiation in the event the Company receives any proposal concerning, or otherwise decides to pursue, a merger, consolidation or other transaction in which all or a majority

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NOTES TO FINANCIAL STATEMENTS--(CONTINUED)

(INFORMATION AS OF SEPTEMBER 30, 1996 AND FOR THE THREE-MONTH PERIODS ENDED SEPTEMBER 30, 1995 AND 1996 IS UNAUDITED)

of the Company's equity securities or all or substantially all of the Company's assets, or any material portion of the assets of the Company used by the Company in performing its obligations under the Distribution Agreement (Note 6) would be acquired by a third party outside of the ordinary course of business.

Stock Option Plans--The Company has various stock option plans which provide for the issuance of nonqualified and incentive stock options to acquire up to 2,836,594 shares of Common Stock. Such options may be granted by the Company's Board of Directors to certain of the Company's founders, employees, directors and consultants. The exercise price of incentive stock options shall not be less than the fair market value of the shares on the date of grant. In the case of individuals who are also holders of 10% or more of the outstanding shares of Common Stock, the exercise price of incentive stock options shall not be less than 110% of the fair market value of the shares on the date of grant. The exercise price of non-qualified stock options shall not be less than 85% of the fair market value on the date of grant. Options granted under these plans expire no later than ten years from the date of grant and generally become exercisable ratably over a four-year period following the date of grant.

For certain options granted, the Company recognizes compensation expense for the difference between the deemed value for accounting purposes and the option exercise price on the date of grant. During the three-month period ended September 30, 1996, compensation expense totaling approximately \$40,000 has been charged with respect to these options. Additional future compensation expense with respect to the issuance of such options totals approximately \$130,000 and will be recognized through October 2000.

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NOTES TO FINANCIAL STATEMENTS--(CONTINUED)

(INFORMATION AS OF SEPTEMBER 30, 1996 AND FOR THE THREE-MONTH PERIODS ENDED SEPTEMBER 30, 1995 AND 1996 IS UNAUDITED)

The following table summarizes option activity under the Company's stock option plans:

	OPTIONS OUTSTANDING	OPTIONS AVAILABLE FOR GRANT	EXERCISE PRICE PER SHARE
	-----	-----	-----
March 24, 1989(Inception)			
Options authorized.....	--	1,703,261	
Options granted.....	1,528,778	(1,528,778)	\$.15 - \$.30
Options exercised.....	(6,873)	--	\$.15 - \$.15
Options canceled.....	(13,793)	13,793	\$.15 - \$.15
	-----	-----	
Balance, June 30, 1993.....	1,508,112	188,276	\$.15 - \$.30
Options granted.....	198,333	(198,333)	\$.30 - \$1.20
Options exercised.....	(1,222,609)	--	\$.15 - \$.30
Options canceled.....	(90,171)	90,171	\$.15 - \$1.20
	-----	-----	
Balance, June 30, 1994.....	393,665	80,114	\$.15 - \$1.20
Options authorized.....	--	333,333	
Options granted.....	55,333	(55,333)	\$ 1.20 - \$1.20
Options exercised.....	(39,103)	--	\$.30 - \$.30
Options canceled.....	(60,230)	60,230	\$.30 - \$1.20
	-----	-----	
Balance, June 30, 1995.....	349,665	418,344	\$.15 - \$1.20
Options authorized.....	--	800,000	
Options granted.....	155,337	(155,337)	\$ 1.20 - \$3.20
Options exercised.....	(130,016)	--	\$.15 - \$1.20
Options canceled.....	(44,690)	44,690	\$.30 - \$1.20
	-----	-----	
Balance, June 30, 1996.....	330,296	1,107,697	\$.30 - \$3.20
Unaudited:			
Options granted.....	13,334	(13,334)	\$ 3.20 - \$3.20
Options exercised.....	(833)	--	\$ 1.20 - \$1.20
Options canceled.....	(6,543)	6,543	\$ 1.20 - \$1.20
	-----	-----	
Balance, September 30, 1996 (Unaudited).....	336,254	1,100,906	\$.30 - \$3.20
	=====	=====	
Options Exercisable, June 30, 1996.....	101,021		\$.30 - \$1.20
September 30, 1996 (Unaudited).....	122,612		\$.30 - \$1.20
	=====		

Common Shares Reserved--The Company has reserved shares of Common Stock for future issuance as follows:

	JUNE 30, 1996	SEPTEMBER 30, 1996
	-----	-----
		(Unaudited)
Issuance under 1992 Stock Option Plan.....	1,437,993	1,437,160
Conversion of preferred stock.....	7,961,168	8,098,422
	-----	-----
	9,399,161	9,535,582
	=====	=====

AASTROM BIOSCIENCES, INC.
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NOTES TO FINANCIAL STATEMENTS--(CONTINUED)

(INFORMATION AS OF SEPTEMBER 30, 1996 AND FOR THE THREE-MONTH PERIODS ENDED SEPTEMBER 30, 1995 AND 1996 IS UNAUDITED)

5. FEDERAL INCOME TAXES

Deferred tax assets consist of the following:

	JUNE 30,	
	1995	1996
Net operating loss carryforwards.....	\$ 5,280,000	\$ 9,210,000
Tax credits and other.....	360,000	440,000
Gross deferred tax assets.....	5,640,000	9,650,000
Deferred tax assets valuation allowance.....	(5,640,000)	(9,650,000)
	\$ --	\$ --
	=====	=====

Due to the historical losses incurred by the Company, a full valuation allowance for deferred tax assets has been provided. If the Company achieves profitability, these deferred tax assets may be available to offset income taxes. The Company's net operating loss and tax credit carryforwards will expire from 2004 through 2011, if not utilized.

The Company's ability to utilize its net operating loss and tax credit carryforwards would be limited in the event of a future change in ownership for tax purposes. Such a change in ownership may likely occur upon the completion of an initial public offering of the Company's Common Stock.

6. LICENSES, ROYALTIES AND COLLABORATIVE AGREEMENTS

University of Michigan--In March 1989, the Company entered into a research agreement with the University of Michigan (the "University") for the development of an adaptable, high-efficiency blood cell factory and to conduct related research. Under the terms of this research agreement, as amended, the Company agreed to reimburse the University for research costs in this regard through the date of its expiration in December 1994. Payments made to the University under the aforementioned agreements totaled \$316,000, \$121,000 and \$2,521,000 for the years ended June 30, 1994, 1995, for the period from Inception to June 30, 1996. As part of this relationship, the Company issued to the University 454,545 shares of Common Stock in August 1989. No value has been assigned to these shares in the accompanying financial statements. In March 1992, the Company entered into a license agreement for the technology developed under the research agreement. The license agreement, as amended, provides for a royalty to be paid to the University equal to 2% of net sales of products containing the licensed technology sold by the Company.

Cobe BCT, Inc.--In connection with the issuance of the Series C Preferred Stock to Cobe in October 1993, the Company and Cobe BCT, Inc. ("Cobe BCT"), an affiliate of Cobe, entered into an agreement which grants to Cobe BCT exclusive worldwide distribution and marketing rights to the Company's Cell Production System ("CPS") for stem cell therapy applications ("Distribution Agreement"). The term of the Distribution Agreement is ten years, with an option, exercisable by Cobe BCT, to extend the term for an additional ten years. Pursuant to the Distribution Agreement, Cobe BCT will perform worldwide marketing and distribution activities of the CPS for use in stem cell therapy and will receive a share of the resulting net sales, as defined, ranging from 38% to 42%, subject to certain negotiated discounts and volume-based adjustments.

AASTROM BIOSCIENCES, INC.
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NOTES TO FINANCIAL STATEMENTS--(CONTINUED)

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The agreements establishing this collaboration provided for payments totaling \$5,000,000 to be made by Cobe BCT upon the Company meeting certain development milestones. In May 1995, the Company accepted, as part of the sale of the Series D Preferred Stock, an equity investment of \$5,000,000 from Cobe in lieu of those future milestone payments.

M.D. Anderson Cancer Center--In December 1992, the Company entered into a research agreement with the University of Texas, M.D. Anderson Cancer Center ("M.D. Anderson"). Under this agreement, the Company funded certain research being conducted at M.D. Anderson and issued to M.D. Anderson 33,333 shares of its Common Stock subject to vesting rights over the succeeding four year period. In November 1994, the Company and M.D. Anderson terminated the collaboration and 25,000 shares of Common Stock held by M.D. Anderson were returned to the Company.

License and Royalty Agreements--In July 1992, the Company licensed certain cell culture technology under which it obtained an exclusive worldwide license to the technology in exchange for a royalty of up to 3% of net sales on products utilizing the licensed technology.

In March 1996, the Company executed a license agreement which provides for the use of licensed products in the CPS. Pursuant to this license agreement, the Company recorded a charge to research and development expense of \$1,500,000 representing the license fee payable upon execution of the agreement. The license agreement provides for annual renewal fees of \$1,000,000 over the five year license term and can be extended at the Company's option for an additional five years.

Rhone-Poulenc Rorer Inc.--In September 1995, the Company entered into a research and development collaboration with Rhone-Poulenc Rorer Inc. ("RPR"), granting RPR a right to license the Company's CPS for Lymphoid cell applications. Prior to the establishment of this collaboration, the Company received a option fee of \$250,000 and a development deposit of \$225,000 to initiate the preliminary research and development plan. Pursuant to the agreements establishing this collaboration, RPR was obligated to fund certain costs associated with the development of the CPS for Lymphoid cell applications and was entitled to make equity purchases of up to \$12,500,000 subject to the Company's satisfaction of certain milestones and RPR's decision to exercise certain options. As of June 30, 1996, the Company has received \$3,500,000 in equity payments and recognized \$1,342,000 in research revenue through June 30, 1996 and \$1,537,000 through September 30, 1996. The remaining \$9,000,000 equity payment was to be paid by RPR by October 1996 pending RPR's evaluation of the research efforts for Lymphoid cell applications and its decision to proceed with the collaboration (Note 9).

7. COMMITMENTS

The Company leases certain machinery and equipment and office equipment under capital leases. Obligations under these leasing arrangements bear interest at rates ranging from 9.7% to 12.1% and mature at dates ranging from November 1996 to May 1999. Additionally, the Company leases its facilities under an operating lease which expires in May 1998, at which time the Company has the option to renew the lease for an additional period of up to five years.

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NOTES TO FINANCIAL STATEMENTS--(CONTINUED)

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Future minimum payments under capital leases and non-cancelable operating leases are as follows:

	CAPITAL LEASES	OPERATING LEASES
	-----	-----
Year Ended June 30,		
1997.....	\$255,000	\$453,000
1998.....	138,000	435,000
1999.....	69,000	--
	-----	-----
Total minimum lease payments.....	462,000	\$888,000
		=====
Less amount representing interest.....	(50,000)	

Obligations under capital lease.....	\$412,000	
	=====	

Certain of the Company's capital lease agreements contain restrictive provisions which require that the Company's total assets exceed its total liabilities by at least \$1,000,000. Should the Company fall out of compliance with this provision, and a waiver cannot be obtained from the lessor, remaining amounts due under the leases become immediately due and payable.

Rent expense for the years ended June 30, 1994, 1995 and 1996, was \$176,000, \$241,000 and \$338,000, respectively, and for the period from Inception to June 30, 1996 was \$822,000. Rent expense for the three months ended September 30, 1995 and 1996, was \$83,000 and \$107,000, respectively, and for the period from Inception to September 30, 1996 was \$929,000.

8. EMPLOYEE SAVINGS PLAN

The Company has a 401(k) plan that became effective in January 1994. The plan allows participating employees to contribute up to 15% of their salary, subject to annual limits and minimum qualifications. The Board may, at its sole discretion, approve Company contributions. Through June 30, 1996, the Company has made no contributions to the plan.

9. SUBSEQUENT EVENTS (UNAUDITED)

In September 1996, RPR notified the Company of its intent to terminate its collaboration with the Company. This notification was made after RPR had determined that for strategic reasons its support for the development of the technologies being pursued under the collaboration would be discontinued. As a result of this termination, no further equity payments or research funding is due from RPR and RPR's license rights to the Company's CPS for Lymphoid cell applications are terminated. Upon termination of the collaboration, RPR became entitled to receive shares of the Company's Series E Preferred Stock at \$17.00 per share for the \$3,500,000 in equity payments made by RPR under the collaboration. Accordingly, the accompanying financial statements as of September 30, 1996 reflect the issuance of 205,882 shares of Series E Preferred Stock issuable to RPR in this regard.

In October 1996, the Company executed a financing commitment for up to \$5,000,000 in additional equity funding from Cobe ("Equity Commitment") and \$5,000,000 in funding under a convertible loan agreement ("Convertible Loan Commitment") with another current investor. Under the terms of the Equity Commitment,

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the Company may sell up to \$5,000,000 of preferred stock at \$6.00 per share during a funding period that extends from January 1997 to December 1997. The conversion rights of such preferred stock will be adjusted to provide for a conversion at 80% of the per share price in the Company's next financing, as adjusted for the Reverse Stock Split, and provided that such financing meets certain minimum requirements ("Qualifying Financing"), such as the proposed IPO in which these financial statements appear. If such a financing is not completed by December 1997, then the conversion rights of this class of preferred stock into Common Stock will be set at \$6.98 per share of Common Stock. To the extent shares are sold to Cobe under the Equity Commitment, its preemptive right in the Company's next Qualifying Financing and the Company's Put Option to Cobe is reduced to the extent of its purchase.

Upon the sale of \$5,000,000 in preferred stock under the Equity Commitment, the Company becomes entitled to borrow funds under the Convertible Loan Commitment. Such funds may be borrowed by the Company during a funding period that extends from January 1997 to September 1997. Upon the completion of a Qualifying Financing by the Company, the Company has the option to repay outstanding borrowings under the Convertible Loan Commitment, in cash, or to convert such borrowings into preferred stock. The conversion rights of such class of preferred stock will be adjusted to provide for a conversion at 90% of the per share price in the Company's next Qualifying Financing, as adjusted for the Reverse Stock Split. If such financing is not completed by December 1997, then the conversion rights of this class of preferred stock will be set at \$6.98 per share of Common Stock. Interest accrues at 10% on amounts borrowed under the Convertible Loan Commitment, which is due at maturity, and may be retired in a manner consistent with principal. The Company may repay borrowed amounts at anytime prior to the maturity date which is established for all amounts borrowed as one year from the date of the first borrowing.

In connection with the Convertible Loan Commitment, the Company has issued warrants to purchase 69,444 shares of Common Stock for securing the commitment. The Company will issue additional warrants to purchase 8,333 shares of Common Stock for each \$1,000,000 borrowed under the Convertible Loan Commitment, with such additional warrants to be prorated to the level of borrowing. The warrants expire on October 15, 2000 if not exercised, and may be exercised, in whole or in part, at a price equal to the lesser of (a) \$9.00 per share, which price increases by \$3.00 per share on each anniversary of the closing of the offering being made in the Prospectus to which these financial statements are included; or (b) 85% of the fair market value of the Company's Common Stock at the time of exercise.

The Equity Commitment and the Convertible Loan Commitment expire upon the closing of an initial public offering by the Company.

No dealer, salesperson or other person has been authorized to give any information or to make any representations other than those contained in this Prospectus, and, if given or made, such information or representation must not be relied upon as having been authorized by the Company or any of the Underwriters or any other person. This Prospectus does not constitute an offer to sell or a solicitation of an offer to buy any security other than the shares of Common Stock offered, nor does it constitute an offer to sell or a solicitation of an offer to buy any of the securities offered to any person in any jurisdiction or in which it is unlawful to make such offer or solicitation to such person. Neither the delivery of this Prospectus nor any sale made hereunder shall under any circumstances create an implication that the information contained herein is correct as of any date subsequent to the date hereof.

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Until , 1997 (25 days after the date of this Prospectus), all dealers effecting transactions in the Common Stock offered, whether or not participating in this distribution, may be required to deliver a Prospectus. This is in addition to the obligation of dealers to deliver a Prospectus when acting as Underwriters and with respect to their unsold allotments or subscriptions.

3,250,000 Shares

[LOGO] AASTROM BIOSCIENCES INC

Common Stock

PROSPECTUS

COWEN & COMPANY

J.P. MORGAN & CO.

, 1996

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

ITEM 13. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION

Other expenses in connection with the registration of the securities hereunder, which will be paid by the Company, will be substantially as follows:

ITEM ----	AMOUNT -----
Securities and Exchange Commission registration fee.....	\$ 11,326
NASD filing fee.....	4,238
Nasdaq National Market fee.....	50,000
Blue sky qualification fees and expenses.....	20,000
Accounting fees and expenses.....	85,000
Legal fees and expenses.....	350,000
Printing and engraving expenses.....	115,000
Transfer agent and registrar fees.....	7,500
Officers' and Directors' Insurance.....	200,000
Miscellaneous expenses.....	56,936

Total.....	\$900,000 =====

ITEM 14. INDEMNIFICATION OF DIRECTORS AND OFFICERS

Sections 1561 through 1565 of the Michigan Business Corporation Act (the "MBCA") authorize a corporation to grant or a court to award, indemnity to directors, officers, employees and agents in terms sufficiently broad to permit such indemnification under certain circumstances for liabilities (including reimbursement for expenses incurred) arising under the Securities Act of 1933.

The Bylaws of the Company (see Exhibit 3.4), provide that the Company shall, to the fullest extent authorized or permitted by the MBCA, or other applicable law, indemnify a director or officer who was or is a party or is threatened to be made a party to any proceeding by or in the right of the Company to procure a judgment in its favor by reason of the fact that such person is or was a director, officer, employee or agent of the Company, against expenses, including actual and reasonable attorneys' fees, and amounts paid in settlement incurred in connection with the action or suit, if the indemnitee acted in good faith and in a manner the person reasonably believed to be in, or not opposed to, the best interests of the Company or its shareholders. This section also authorizes the Company to advance expenses incurred by any agent of the Company in defending any proceeding prior to the final disposition of such proceeding upon receipt of an undertaking by or on behalf of the agent to repay such amount unless it shall be determined ultimately that the agent is entitled to be indemnified.

The Bylaws also authorize the Company to purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the Company against any liability asserted against or incurred by such person in such capacity or arising out of such person's status as such, regardless of whether the Company would have the power to indemnify such person against such liability under the provisions of the MBCA.

The Company has entered into an indemnification agreement with certain of its directors, officers and other key personnel, which contains provisions that may in some respects be broader than the specific indemnification provisions contained under applicable law. The indemnification agreement may require the Company, among other things, to indemnify such directors, officers and key personnel against certain liabilities that may arise by reason of their status or service as directors, officers or employees of the Company, to advance the expenses incurred by such parties as a result of any threatened claims or proceedings brought against them as to which

they could be indemnified, and, to the maximum extent that insurance coverage of such directors, officers and key employees under the Company's directors' and officers' liability insurance policies is maintained.

Section 1209 of the MBCA permits a Michigan corporation to include in its Articles of Incorporation a provision eliminating or limiting a director's liability to a corporation or its shareholders for monetary damages for breaches of fiduciary duty. The enabling statute provides, however, that liability for breaches of the duty of loyalty, acts or omissions not in good faith or involving intentional misconduct or knowing violation of the law, or the receipt of improper personal benefits cannot be eliminated or limited in this manner. The Company's Restated Articles of Incorporation include a provision which eliminates, to the fullest extent permitted by the MBCA director liability for monetary damages for breaches of fiduciary duty.

Section 6 of the Underwriting Agreement filed as Exhibit 1.1 hereto sets forth certain provisions with respect to the indemnification of certain controlling persons, directors and officers against certain losses and liabilities, including certain liabilities under the Securities Act.

ITEM 15. RECENT SALES OF UNREGISTERED SECURITIES

(a) ISSUANCES OF COMMON STOCK

Since October 1, 1993, the Company has sold the following shares of Common Stock:

In October 1995, the registrant issued 37,500 shares of Common Stock to Albert B. Deisseroth at a price of \$.80 per share.

(b) ISSUANCES OF SHARES OF PREFERRED STOCK

Since October 1, 1993, the Company has sold the following shares of Preferred Stock:

In October 1993, the registrant issued 10,000 shares of Series C Preferred Stock to Cobe at a price of \$1,000 per share.

In April and May 1995, the registrant issued an aggregate of 2,500,001 shares of Series D Preferred Stock to 11 accredited investors at a price of \$4.00 per share.

In December 1995, the registrant issued 62,500 shares of Series D Preferred Stock to Northwest Ohio Venture Fund, L.P. at a purchase price of \$4.00 per share.

In January 1996, the registrant issued an aggregate of 1,411,765 shares of Series E Preferred Stock to SBIC Partners, L.P. and the State Treasurer of the State of Michigan at a purchase price of \$4.25 per share.

Pursuant to a Governance Agreement between the Company and Rhone-Poulenc Rorer Inc. ("RPR"), dated September 15, 1995, RPR terminated its contractual relationship with the Company on September 6, 1996. As a result of such termination, the Company became obligated to issue 205,882 shares of Series E Preferred Stock to RPR at a purchase price of \$17.00 per share.

The Company believes that each such sale and issuance of securities was exempt from registration pursuant to Section 4(2) of the Securities Act of 1933, as amended.

(c) OPTION ISSUANCES TO, AND EXERCISES BY, EMPLOYEES AND DIRECTORS

From January 18, 1990 to the present, the registrant has granted options to purchase a total of 2,945,174 shares of Common Stock at exercise prices ranging from \$.10 to \$2.13 per share to 95 employees and one non-employee director. No consideration was paid to the Registrant by any recipient of any of the foregoing options for the grant of any such options. From October 30, 1992 to the present, the Registrant issued a total of 2,829,735 shares of Common Stock to 26 employees and one non-employee director upon exercise of stock options at exercise prices ranging from \$.10 to \$2.13 per share.

There were no underwriters employed in connection with any of the transactions set forth in Item 15.

The issuances described in Items 15(a) were exempt from registration under the Securities Act in reliance on Section 4(2) of the Securities Act as transactions by an issuer not involving a public offering. The issuances described in Item 15(b) were exempt from registration under the Securities Act in reliance on Rule 701 promulgated thereunder as transactions pursuant to compensatory benefit plans and contracts relating to compensation. The recipients of securities in each such transaction represented their intention to acquire the securities for investment only and not with a view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the share certificates and other instruments issued in such transactions.

ITEM 16. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) Exhibits

- 1.1* Form of Underwriting Agreement.
- 3.1 Restated Articles of Incorporation.
- 3.2* Form of Restated Articles of Incorporation (to be filed with the Secretary of State of the State of Michigan prior to the closing of this offering).
- 3.3 Bylaws, as amended.
- 4.1* Specimen Common Stock Certificate.
- 4.2 Amended and Restated Investors' Rights Agreement dated April 7, 1992.
- 5.1* Opinion of Pepper, Hamilton & Scheetz, counsel to the Company, with respect to the legality of the securities being registered, including their consent to being named in the Registration Statement.
- 10.1 Form of Indemnification Agreement.
- 10.2 1989 Stock Option Plan and form of agreement thereunder.
- 10.3 Ancillary Stock Option Plan and form of agreement thereunder.
- 10.4 401(k) Plan.
- 10.5 Amended and Restated 1992 Incentive and Non-Qualified Stock Option Plan and forms of agreements thereunder.
- 10.6 1996 Outside Directors Stock Option Plan and forms of agreements thereunder.
- 10.7 1996 Employee Stock Purchase Plan and form of agreement thereunder.
- 10.8 Form of Employment Agreement.
- 10.9 Stock Purchase Agreement dated October 22, 1993 between Cobe Laboratories, Inc. and the Company and amendment thereto dated October 29, 1996.
- 10.10** Distribution Agreement dated October 22, 1993 between Cobe BCT, Inc. and the Company and amendments thereto dated March 29, 1995, September 11, 1995 and October 29, 1996.
- 10.11 License Agreement dated July 17, 1992 between J.G. Cremonese and the Company and related addenda thereto dated July 14, 1992 and July 7, 1993.
- 10.12** Collaborative Product Development Agreement dated May 10, 1994 between SeaMED Corporation and the Company.
- 10.13** Collaborative Product Development Agreement dated November 8, 1994 between Ethox Corporation and the Company.

- 10.14** License and Supply Agreement dated April 1, 1996 between Immunex Corporation and the Company.
- 10.15 Lease Agreement dated May 18, 1992 between Domino's Farms Holding, L.P. and the Company and amendments thereto dated February 26, 1993, October 3, 1994, November 16, 1994 and July 29, 1996.
- 10.16 Clinical Trial Agreement dated April 19, 1996 between the Company and the University of Texas M.D. Anderson Cancer Center.
- 10.17 License Agreement dated March 13, 1992 between the Company and the University of Michigan and amendments thereto dated March 13, 1992, October 8, 1993 and June 21, 1995.
- 10.18 Employee Proprietary Information and Invention Agreement effective June 1, 1991 between the Company and R. Douglas Armstrong.
- 10.19 Employment Agreement dated June 19, 1992 between the Company and James Maluta.
- 10.20 Employment Agreement dated December 8, 1995 between the Company and Todd E. Simpson, C.P.A.
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- 10.23 Employment Agreement dated October 26, 1995 between the Company and Alan K. Smith, Ph.D.
- 10.24 Promissory Note dated November 18, 1993 for \$120,000 loan by the Company to R. Douglas Armstrong and amendment thereto dated October 30, 1996.
- 10.25 Promissory Note dated October 20, 1993 for \$47,303 loan by the Company to Stephen G. Emerson, M.D., Ph.D and amendment thereto dated October 30, 1996.
- 10.26 Consulting Agreement dated June 1, 1995 between the Company and Stephen G. Emerson, M.D., Ph.D.
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- 10.29 Convertible Loan Commitment Agreement dated October 15, 1996 between the State Treasurer of the State of Michigan and the Company.
- 10.30* Forms of Subscription Agreement for the purchase of Series D Preferred Stock.
- 10.31* Stock Purchase Agreement dated January 8, 1996 among the Company, SBIC Partners, L.P. and the State Treasurer of the State of Michigan.
- 11.1 Computation of earnings per share.
- 23.1 The consent of Coopers & Lybrand, L.L.P.
- 23.2* The consent of Pepper, Hamilton & Scheetz is contained in their opinion filed as Exhibit 5.1 of the Registration Statement.

24.1 Power of Attorney is contained on the signature page of this Registration Statement (see page II-6).

27.1 Financial Data Schedule.

27.2 Financial Data Schedule.

27.3 Financial Data Schedule.

27.4 Financial Data Schedule.

27.5 Financial Data Schedule.

27.6 Financial Data Schedule.

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*To be filed by Amendment.

**The Company has applied for confidential treatment with respect to certain portions of these documents.

(b)Financial Statement Schedules

Schedules other than those referred to above have been omitted because they are not applicable or not required under the instructions contained in Regulation S-X or because the information is included elsewhere in the Financial Statements or the notes thereto.

ITEM 17. UNDERTAKINGS

The undersigned Registrant hereby undertakes to provide to the Underwriters at the closing specified in the Underwriting Agreement certificates in such denominations and registered in such names as required by the Underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the Registrant, pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

The undersigned Registrant hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act of 1933 shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Ann Arbor, State of Michigan, on the 1st day of November, 1996.

AASTROM BIOSCIENCES, INC.

/s/ R. Douglas Armstrong
By: _____
R. Douglas Armstrong, Ph.D.
President and Chief Executive
Officer
(Principal Executive Officer)

POWER OF ATTORNEY

KNOW ALL MEN BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints R. Douglas Armstrong and Todd E. Simpson, or either of them, as his attorney-in-fact, each with full power of substitution for him in any and all capacities, to sign any and all amendments to this Registration Statement, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each said attorney-in-fact or his substitute or substitutes may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

SIGNATURE -----	TITLE -----	DATE -----
/s/ R. Douglas Armstrong _____ R. Douglas Armstrong, Ph.D.	President, Chief Executive Officer, and Director (Principal Executive Officer)	November 1, 1996
/s/ Todd E. Simpson _____ Todd E. Simpson	Vice President, Finance & Administration and Chief Financial Officer (Principal Financial and Accounting Officer)	November 1, 1996
/s/ Robert J. Kunze _____ Robert J. Kunze	Chairman of the Board and Director	November 1, 1996
/s/ Albert B. Deisseroth _____ Albert B. Deisseroth, M.D., Ph.D.	Director	November 1, 1996
/s/ Stephen G. Emerson _____ Stephen G. Emerson, M.D., Ph.D.	Director	November 1, 1996
/s/ G. Bradford Jones _____ G. Bradford Jones	Director	November 1, 1996
/s/ Horst R. Witzel _____ Horst R. Witzel, Dr.-Ing.	Director	November 1, 1996
/s/ Edward C. Wood _____ Edward C. Wood, Jr.	Director	November 1, 1996

EXHIBIT INDEX

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- 3.2* Form of Restated Articles of Incorporation (to be filed with the Secretary of State of the State of Michigan prior to the closing of this offering).
- 3.3 Bylaws, as amended.
- 4.1* Specimen Common Stock Certificate.
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- 23.2* The consent of Pepper, Hamilton & Scheetz is contained in their opinion filed as Exhibit 5.1 of the Registration Statement.
- 24.1 Power of Attorney is contained on the signature page of this Registration Statement (see page II-6).
- 27.1 Financial Data Schedule.
- 27.2 Financial Data Schedule.
- 27.3 Financial Data Schedule.
- 27.4 Financial Data Schedule.
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*To be filed by Amendment.

**The Company has applied for confidential treatment with respect to certain portions of these documents.

Inside back cover page of Prospectus

[COLOR DIAGRAM OF CELL LINEAGES OF HUMAN BONE MARROW STEM CELLS]

MICHIGAN DEPARTMENT OF COMMERCE - CORPORATION AND SECURITIES BUREAU

Date Received (FOR BUREAU USE ONLY)

Name
T. Knox Bell, Esq.

Address
Gray Cary Ware & Freidenrich
4365 Executive Drive, Suite 1600

City State Zip Code
San Diego CA 92121 EFFECTIVE DATE

Document will be returned to the name and address you enter above

RESTATED ARTICLES OF INCORPORATION
FOR USE BY DOMESTIC PROFIT CORPORATIONS
(Please read information and instructions on the last page)

Pursuant to the provisions of Act 284, Public Acts of 1972, the undersigned corporation executes the following Articles:

1. The present name of the corporation is:
Aastrom Biosciences, Inc.
2. The identification number assigned by the Bureau is: 529-456
3. All former names of the corporation are:
Ann Arbor Stromal, Inc.
4. The date of filing the original Articles of Incorporation was: March 24, 1989

The following Restated Articles of Incorporation supersede the Articles of Incorporation as amended and shall be the Articles of Incorporation for the corporation:

ARTICLE I

The name of the corporation is:
Aastrom Biosciences, Inc.

ARTICLE II

The purpose or purposes for which the corporation is formed are:
To engage in any activity within the purpose for which corporations may be organized under the Michigan Business Corporation Act.

ARTICLE III

The total authorized shares:

Common shares 20,300,000 Preferred shares 10,990,980

A statement of all or any of the relative rights, preferences and limitations of the shares of each class is as follow:

See Rider attached hereto and made a part hereof.

ARTICLE IV

1. The address of the current registered office is:

36th Floor, 100 Renaissance Center, Detroit, Michigan 48243
(Street Address) (Zip Code)

2. The mailing address of the current registered office, if different than above:

Michigan
(Street Address or P.O. Box) (City) (Zip Code)

3. The name of the current resident agent is: Michael B. Staebler

ARTICLE V (Optional. Delete if not applicable)

When a compromise or arrangement or a plan of reorganization of this corporation is proposed between this corporation and its creditors or any class of them or between this corporation and its shareholders or any class of them, a court of equity jurisdiction within the state, on application of this corporation or of a creditor or shareholder thereof, or on application of a receiver appointed for the corporation, may order a meeting of the creditors or class of creditors or of the shareholders or class of shareholders to be affected by the proposed compromise or arrangement or reorganization, to be summoned in such manner as the court directs. If a majority in number representing 3/4 in value of the creditors or class of creditors, or of the shareholders or class of shareholders to be affected by the proposed compromise or arrangement or a reorganization, agree to a compromise or arrangement or a reorganization of this corporation as a consequence of the compromise or arrangement, the compromise or arrangement and the reorganization, if sanctioned by the court to which the application has been made, shall be binding on all the creditors or class of creditors, or on all the shareholders or class of shareholders and also on this corporation.

ARTICLE VI (Optional. Delete if not applicable)

Any action required or permitted by the Act to be taken at an annual or special meeting of shareholders may be taken without a meeting, without prior notice, and without a vote, if consents in writing, setting forth the action so taken, are signed by the holders of outstanding shares having not less than the minimum number of votes that would be necessary to authorize or take the action at a meeting at which all shares entitled to vote on the action were present and voted. The written consents shall bear the date of signature of each shareholder who signs the consent. No written consents shall be effective to take the corporate action referred to unless, within 60 days after the record date for determining shareholders entitled to express consent to or to dissent from a proposal without a meeting, written consents dated not more than 10 days before the record date and signed by a sufficient number of shareholders to take the action are delivered to the corporation. Delivery shall be to the corporation's registered office, its principal place of business, or an officer or agent of the corporation having custody of the minutes of the proceedings of its shareholders. Delivery made to a corporation's registered office shall be by hand or by certified or registered mail, return receipt requested.

Prompt notice of the taking of the corporate action without a meeting by less than unanimous written consent shall be given to shareholders who would have been entitled to notice of the shareholder meeting if the action had been taken at a meeting and who have not consented in writing.

Article VII. (Additional provisions, if any, may be inserted here; attach additional pages if needed.)

See Rider attached hereto and made a part hereof.

5. COMPLETE SECTION (a) IF THE RESTATED ARTICLES WERE ADOPTED BY THE UNANIMOUS CONSENT OF THE INCORPORATOR(S) BEFORE THE FIRST MEETING OF THE BOARD OF DIRECTORS; OTHERWISE, COMPLETE SECTION (b). DO NOT COMPLETE BOTH.

a. [] These Restated Articles of Incorporation were duly adopted on the _____ day of _____,

19 _____, in accordance with the provisions of Section 642 of the Act by the unanimous consent of the incorporator(s) before the first meeting of the Board of Directors.

Signed this _____ day of _____, 19 _____.

(Signatures of Incorporators: Type or Print Name Under Each Signature)

b. [X] These Restated Articles of Incorporation were duly adopted on the 31st day of October, 1996 in accordance with the provisions of Section 642 of the Act and: (check one of the following)

[] were duly adopted by the Board of Directors without a vote of the shareholders. These Restated Articles of Incorporation only restate and integrate and do not further amend the provisions of the Articles of Incorporation as heretofore amended and there is no material discrepancy between those provisions and the provisions of these Restated Articles.

[] were duly adopted by the shareholders. The necessary number of shares as required by statute we voted in favor of these Restated Articles.

[X] were duly adopted by the written consent of the shareholders having not less than the minimum number of votes required by statute in accordance with Section 407(1) of the Act. Written notice to shareholders who have not consented in writing has been given. (Note: Written consent by less than all of the shareholders is permitted only if such provision appears in the Articles of Incorporation.)

[] were duly adopted by the written consent of all the shareholders entitled to vote in accordance with section 407(2) of the Act.

Signed this 31st day of October, 1996.

By /s/ R. Douglas Armstrong

(Only Signature of President, Vice-President, Chairperson, or Vice-Chairperson)

R. Douglas Armstrong, Ph.D. President

(Type or Print Name) (Type or Print Title)

Name of person or organization Preparer's name and business
remitting fees: telephone number:

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- ----- () -----

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INFORMATION AND INSTRUCTIONS

1. The articles of incorporation cannot be restated until this form, or a comparable document, is submitted.
2. Submit one original of this document. Upon filing, the document will be added to the records of the Corporation and Securities Bureau. The original will be returned to the address appearing in the box on the front as evidence of filing.

Since this document will be maintained on optical disk media, it is important that the filing be legible. Documents with poor black and white contrast, or otherwise illegible, will be rejected.

3. This document is to be used pursuant to sections 641 through 643 of the Act for the purpose of restating the articles of incorporation of a domestic profit corporation. Restated articles of incorporation are an integration into a single instrument of the current provisions of the corporation's articles of incorporation, along with any desired amendments to those articles.
4. Restated articles of incorporation which do not amend the articles of incorporation may be adopted by the board of directors without a vote of the shareholders. Restated articles of incorporation which amend the articles of incorporation require adoption by the shareholders. Restated articles of incorporation submitted before the first meeting of the board of directors require adoption by all of the incorporators.
5. Item 2 - Enter the identification number previously assigned by the Bureau. If this number is unknown, leave it blank.
6. The duration of the corporation should be stated in the restated articles of incorporation only if it is not perpetual.
7. This document is effective on the date endorsed "filed" by the Bureau. A later effective date, no more than 90 days after the date of delivery, may be stated as an additional article.
8. If the restated articles are adopted before the first meeting of the board of directors, item 5(a) must be completed and signed in ink by a majority of the incorporators. Other restated articles must be signed by the president, vice-president, chairperson or vice-chairperson.
9. FEES: Make remittance payable to the State of Michigan. Include corporation name and identification number on check or money order.

NONREFUNDABLE FEE..... \$10.00
TOTAL MINIMUM FEE..... \$10.00
ADDITIONAL FEES DUE FOR INCREASED AUTHORIZED SHARES ARE:
each additional 20,000 authorized shares or portion thereof. \$30.00
maximum fee for first 10,000,000 authorized shares..... \$5,000.00
each additional 20,000 authorized shares or portion
thereof in excess of 10,000,000 shares..... \$30.00
maximum fee per filing for authorized shares in excess of
10,000,000 shares..... \$200,000.00

10. Mail form and fee to: The office is located at:

Michigan Department of Commerce	6546 Mercantile Way
Corporation and Securities Bureau	Lansing, MI 48910
Corporation Division	Telephone: (517) 334-6302
P.O. Box 30054	
Lansing, MI 48909-7554	

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RIDER TO ARTICLE III

PART A: COMMON STOCK

Section 1. Voting Rights. The holders of shares of Common Stock shall be entitled to one vote for each share so held with respect to all matters voted on by the shareholders of the corporation, subject in all cases to Section 4 of Part B of this Article III.

Section 2. Liquidation Rights. The rights of the holders of Common Stock upon any voluntary or involuntary liquidation, dissolution or winding up of the affairs of the Corporation shall be as set forth in Section 3 of Part B of this Article III. However, all distributions made or funds paid to the holders of Common Stock upon the occurrence of such an event shall be made on the basis of the number of shares of Common Stock held by each of them.

Section 3. Dividends. Dividends may be paid on the Common Stock as and when declared by the Board of Directors, subject in all cases to Section 2 of Part B of this Article III.

PART B: PREFERRED STOCK

Section 1. Designation. The Preferred Stock shall consist of six series to be designated and known as "Series A Preferred Stock" (or "Series A"), "Series B Preferred Stock" (or "Series B"), "Series C Preferred Stock" (or "Series C"), "Series D Preferred Stock" (or "Series D"), "Series E Preferred Stock" (or "Series E") and "Series F Preferred Stock" (or "Series F"). All series of Preferred Stock shall be identical with each other in all respects except as otherwise provided herein. As used herein, the term "Preferred Stock" without designation shall refer to shares of Series A, Series B, Series C, Series D, Series E and Series F Preferred Stock, or to shares of any series. The number of shares constituting each such series of Preferred Stock shall be as set forth below:

- . Series A Preferred Stock: 2,500,000 shares.
- . Series B Preferred Stock: 3,030,000 shares.
- . Series C Preferred Stock: 10,000 shares.
- . Series D Preferred Stock: 3,000,000 shares.
- . Series E Preferred Stock: 1,617,647 shares.
- . Series F Preferred Stock: 833,333 shares.

Section 2. Dividends. Dividends are payable when and as declared by the Board of Directors subject to the restrictions imposed by the Michigan Business Corporation Act. Dividends on the Preferred Stock shall not be cumulative and no right to such dividends shall accrue to holders of Preferred Stock unless declared by the Board of Directors. Holders of outstanding shares of certain series of Preferred Stock

shall be entitled to receive dividends in preference to any dividend (whether in cash, securities of the Corporation or other property) on certain other shares of capital stock of the Corporation, as set forth below in terms of four "Levels," to be designated and known as "Level 1," "Level 2," "Level 3" and "Level 4." No dividends or other distributions shall be made with respect to a particular Level until all dividends on the preceding Levels have been paid on or set apart for payment. For example, dividends on Level 3 shall not be paid or set apart for payment until full dividends on Level 1 and Level 2 have been paid or set apart for payment. Dividends, if paid, must be paid on, or, if declared and set apart for payment on, must be declared and set apart for payment on, all outstanding shares of capital stock on a particular Level contemporaneously, and if less than full dividends are paid on or if declared and set apart for payment on a particular Level, then the same percentage of the respective dividend rate on all shares on such Level shall be paid or declared and set apart for payment.

- . Level 1: \$0.48 per share of Series F Preferred Stock; and \$0.34 per share of Series E Preferred Stock
- . Level 2: \$0.32 per share of Series D Preferred Stock; \$80.00 per share of Series C Preferred Stock; and \$0.16 per share of Series B Preferred Stock.
- . Level 3: \$0.08 per share of Series A Preferred Stock.
- . Level 4: If a dividend is declared with respect to the Common Stock, then a contemporaneous dividend must be declared with respect to the Series E and Series F Preferred Stock in an amount equal to that which would be received if the Series E and Series F Preferred Stock had been converted to Common Stock on the declaration date of such dividend.

Section 3. Liquidation Preference.

3.1 Preferential Amounts. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Corporation, any distribution of the assets or surplus funds of the Corporation to holders of shares of capital stock of the Corporation by reason of their ownership thereof must take place as set herein. Holders of shares of certain series of Preferred Stock shall be entitled to receive such distributions prior and in preference to any such distributions on certain other shares of capital stock of the Corporation, as set forth below in terms of four "Tiers," to be designated and known as "Tier 1," "Tier 2," "Tier 3" and "Tier 4." No such distributions shall be made with respect to a particular Tier until all such preferential distributions on the preceding Tiers have been made. For example, such distributions on Tier 3 shall not be made until the full preferential distributions on Tier 1 and Tier 2 have been made. If the assets or surplus funds of the Corporation available for distribution to stockholders are insufficient to permit payment in full of amounts to which the holders of the outstanding

shares on a particular Tier are entitled pursuant to this Section 3, then such available assets and funds shall be distributed ratably among the holders of the outstanding shares on such Tier in proportion to the full preferential distribution each such holder is otherwise entitled to receive. The preferential amounts set forth below shall be adjusted for any stock dividends, combinations or splits with respect to such shares.

- . Tier One: \$6.00 per share of Series F Preferred Stock, plus all accrued or declared but unpaid dividends thereon (the "Series F Preferential Amount"); and \$4.25 per share of Series E Preferred Stock, plus all accrued or declared but unpaid dividends thereon (the "Series E Preferential Amount").
- . Tier Two: \$4.00 per share of Series D Preferred Stock, plus all accrued or declared but unpaid dividends thereon (the "Series D Preferential Amount"); \$1,000.00 per share of Series C Preferred Stock, plus all accrued or declared but unpaid dividends thereon (the "Series C Preferential Amount"); and \$2.00 per share of Series B Preferred Stock, plus all accrued or declared but unpaid dividends thereon (the "Series B Preferential Amount").
- . Tier Three: \$1.00 per share of Series A Preferred Stock, plus all accrued or declared but unpaid dividends thereon (the "Series A Preferential Amount").

3.2 Participation of Preferred Stock. After the payment or setting apart for payment of the Series A Preferential Amount, the Series B Preferential Amount, the Series C Preferential Amount, the Series D Preferential Amount, the Series E Preferential Amount and the Series F Preferential Amount, the remaining assets or surplus funds of the Corporation available for distribution upon such liquidation, dissolution or winding up shall be divided pro rata among the holders of Common Stock and Preferred Stock, treating the Preferred Stock as if converted to Common Stock on the date of such liquidation, dissolution or winding up.

3.3 Limits on Participation. In the event of such distribution upon a liquidation, dissolution or winding up of the Corporation, the amount otherwise payable to a holder of Preferred Stock shall not exceed the amount per share set forth opposite the name of the particular series of Preferred Stock, as set forth below and as adjusted for any stock dividends, combinations or splits with respect to such shares.

- . Series A Preferred Stock: \$5.00 per share.
- . Series B Preferred Stock: \$6.00 per share.
- . Series C Preferred Stock: \$2,500.00 per share.
- . Series D Preferred Stock: \$6.00 per share.

. Series E Preferred Stock: \$6.00 per share.
. Series F Preferred Stock : \$9.00 per share.

3.4 Consolidation or Merger. A consolidation or merger of the Corporation with or into another corporation or entity shall be regarded as a liquidation, dissolution or winding up of the Corporation with respect to the Preferred Stock within the meaning of this Section 3 unless such consolidation or merger is not intended to effect a change in the ownership or control of the Corporation or of its assets and is not intended to alter materially the business or assets of the Corporation, including, by way of example and without limiting the generality of the foregoing: (i) a consolidation or merger which merely changes the identity, form or place of organization of the Corporation, or which is between or among the Corporation and any of its direct or indirect subsidiaries, or (ii) following such merger or consolidation, shareholders of the Corporation immediately prior to such event own not less than 51% of the voting power of such corporation immediately after such merger or consolidation on a pro rata basis.

Section 4. Voting Rights.

4.1 General. Except as otherwise required by law, the holder of each share of Preferred Stock issued and outstanding shall have the number of votes equal to the number of shares of Common Stock into which such shares of Preferred Stock could be converted at the record date for determination of the shareholders entitled to vote on such matters, or, if no such record date is established, at the date such vote is taken or any written consent of shareholders is solicited, such votes to be counted together with all other shares of stock of the Corporation having general voting power and not separately as a class.

4.2 Merger or Sale of Assets. Consent of the holders of at least the percentage or ratio of the outstanding shares of the class or series set forth opposite the name of such particular class or series of capital stock of the Corporation, as set forth below, shall be required for any action which results in a consolidation or merger which would be treated as a liquidation, dissolution or winding up of the Corporation under Section 3.4, or the liquidation, sale or assignment of all or substantially all of the assets of the Corporation.

. Common Stock and Preferred Stock, with the exception of
. Series C Preferred Stock: 2/3.
. Series A Preferred Stock: 2/3.
. Series B Preferred Stock: 2/3.
. Series D Preferred Stock: 2/3.
. Series E Preferred Stock: 51%.
. Series F Preferred Stock: 51%.

4.3 Changes Affecting a Particular Series. Consent of the holders of at least the percentage or ratio of the outstanding shares of a particular series of Preferred Stock set forth opposite the name of such series, as set forth below, with only the affected series

voting and with each such affected series voting as a separate class, shall be required for any action which: (a) alters the rights, preferences, privileges or restrictions of such series; (b) increases or decreases the authorized number of shares of such series; or (c) creates any new class or series of capital stock of the Corporation having rights, preferences or privileges senior to or on a parity with such series.

- . Series A Preferred Stock: 2/3.
- . Series B Preferred Stock: 2/3.
- . Series C Preferred Stock: Majority.
- . Series D Preferred Stock: 2/3.
- . Series E Preferred Stock: 51%.
- . Series F Preferred Stock: 51%.

4.4 Other Actions. Consent of the holders of at least the percentage or ratio of the outstanding shares of a particular series of Preferred Stock set forth opposite the name of such series, as set forth below, with each such series voting as a separate class, shall be required for: (a) any purchase or redemption by the Corporation of any shares of Preferred Stock; (b) any repurchase by the Corporation of any shares of Common Stock, other than repurchases from directors, employees and consultants of the Corporation which do not in any consecutive twelve-month period exceed One Hundred Thousand Dollars (\$100,000); (c) any declaration or payment by the Corporation of a dividend or distribution on account of the Common Stock prior to the conversion of all shares of Preferred Stock, other than a dividend or distribution payable in shares of Common Stock or otherwise taken into account by the anti-dilution provisions set forth in these Articles of Incorporation for the benefit of the Preferred Stock; (d) the sale by any wholly-owned subsidiary of the Corporation of any shares of its stock to a third person; and (e) any amendment to these Articles of Incorporation.

- . Series A Preferred Stock: 2/3.
- . Series B Preferred Stock: 2/3.
- . Series D Preferred Stock: 2/3.
- . Series E Preferred Stock: 51%.
- . Series F Preferred Stock: 51%.

4.5 Series C Quorum Requirement. At any meeting of the holders of all outstanding shares of Preferred Stock to vote as a class, the presence in person or by proxy of the holders of a majority of the outstanding shares of Series C Preferred Stock shall be required to constitute a quorum; in the absence of a quorum a majority of the holders present in person or by proxy shall have the power to adjourn the meeting from time to time without notice, other than announcement at the meeting, until a quorum shall be present.

Section 5. Redemption. The Preferred Stock is not redeemable.

Section 6. Conversion of Preferred Stock. The holders of Preferred Stock shall have conversion rights as follows (the "Conversion Rights"):

6.1 Conversion Prices.

6.1.1 Series A, Series B, Series C, Series D and Series E Preferred Stock.

Upon any conversion of Series A, Series B, Series C, Series D and Series E Preferred Stock into Common Stock pursuant to this Section 6, each such share of such series of Preferred Stock shall be converted into such number of fully paid and nonassessable shares of Common Stock as is determined by taking the respective preferential amount for such series of Preferred Stock, as set forth below:

- . Series A Preferred Stock: \$1.00;
- . Series B Preferred Stock: \$2.00;
- . Series C Preferred Stock: \$1,000.00;
- . Series D Preferred Stock: \$4.00;
- . Series E Preferred Stock: \$4.25;

and dividing such preferential amount set forth above by the respective conversion price for such series of Preferred Stock, as set forth below:

- . "Series A Conversion Price": \$1.00;
- . "Series B Conversion Price": \$2.00;
- . "Series C Conversion Price": \$4.00;
- . "Series D Conversion Price": \$4.00;
- . "Series E Conversion Price": \$4.25.

The Applicable Conversion Price (as defined below in Section 6.1.3) for each such series shall be subject to adjustment as provided below in Section 6.5.

6.1.2 Series F Preferred Stock. Upon any conversion of Series F Preferred Stock into Common Stock pursuant to this Section 6, each such share of Series F Preferred Stock shall be converted into such number of fully paid and nonassessable shares of Common Stock as is determined by dividing \$6.00 by the Series F Conversion Price, as such Series F Conversion Price is determined pursuant to Section 6.3.4.

6.1.3 Applicable Conversion Price. The term "Applicable Conversion Price" shall refer to the Series A Conversion Price with respect to the Series A Preferred Stock, the Series B Conversion Price with respect to the Series B Preferred Stock, the Series C Conversion Price with respect to the Series C Preferred Stock, the Series D Conversion Price with respect to the Series D Preferred Stock, the Series E Conversion Price with respect to the Series E Preferred Stock and the Series F Conversion price with respect to the Series F Preferred Stock, subject to adjustment as provided below in Section 6.5.

6.2 Voluntary Conversion.

6.2.1 Series A, Series B, Series D and Series E Preferred Stock.

Each share of Series A, Series B, Series D, and Series E Preferred Stock shall be convertible into Common Stock, at the option of the holder thereof, at any time after the date of issuance of such share at the office of the Corporation or any transfer agent for such stock.

6.2.2 Series C Preferred Stock. Each share of Series C Preferred Stock shall be convertible into Common Stock, at the option of the holder thereof, at any time after April 1, 1998, at the office of the Corporation or any transfer agent for such stock.

6.3 Automatic Conversion.

6.3.1 Series A, Series B and Series D Preferred Stock. Each share of Series A, Series B and Series D Preferred Stock shall automatically be converted into shares of Common Stock at the then effective Applicable Conversion Price immediately upon the closing of the sale of the Corporation's Common Stock in a firm commitment, underwritten public offering registered under the Securities Act of 1933, as amended (the "Securities Act") (other than a registration relating solely to a transaction under Rule 145 under the Securities Act or any successor thereto or to an employee benefit plan of the Corporation) at a public offering price (prior to underwriter commissions and expenses) equal to or exceeding \$4.26 per share of Common Stock, as adjusted for any stock dividends, combinations or splits with respect to such shares, and the gross proceeds of which exceed \$10,000,000. In addition, each share of Series A, Series B and Series D Preferred Stock shall automatically be converted into shares of Common Stock at the then effective Applicable Conversion Price for such particular series upon the conversion of a majority of the shares of such particular series then outstanding.

6.3.2 Series C Preferred Stock. Each share of Series C Preferred Stock shall automatically be converted into shares of Common Stock at the then effective Series C Conversion Price immediately upon the closing of the sale of the Corporation's Common Stock in a firm commitment, underwritten public offering registered under the Securities Act (other than a registration relating solely to a transaction under Rule 145 under the Securities Act or any successor thereto or to an employee benefit plan of the Corporation).

6.3.3 Series E Preferred Stock. Each share of Series E Preferred Stock shall automatically be converted into shares of Common Stock at the then effective Series E Conversion Price immediately upon the closing of the sale of the Corporation's Common Stock in a firm commitment, underwritten public offering registered under the Securities Act (other than a registration relating solely to a transaction under Rule 145 under the Securities Act or any successor thereto or to an employee benefit plan of the Corporation) at a public offering price (prior to underwriter commissions and expenses) equal to or exceeding \$4.26 per share of Common Stock, as adjusted for any stock dividends, combinations or splits with respect to such shares, and the gross proceeds of which exceed \$12,500,000. In addition, each share of Series E Preferred Stock shall

automatically be converted into shares of Common Stock at the then effective Series E Conversion Price upon the conversion of a majority of the shares of Series E Preferred Stock then outstanding.

6.3.4 Series F Preferred Stock. Each share of Series F Preferred Stock shall automatically be converted into shares of Common Stock at the then effective Series F Conversion Price as follows:

(a) Initial Public Offering. Each share of Series F Preferred Stock shall automatically be converted into shares of Common Stock at the then effective Series F Conversion Price immediately upon the closing of the sale of the Corporation's Common Stock in a firm commitment, underwritten public offering registered under the Securities Act (other than a registration relating solely to a transaction under Rule 145 under the Securities Act of any successor thereto or to an employee benefit plan of the Corporation). In the event that the conversion of Series F Preferred Stock shall occur pursuant to this Section 6.3.4(a), the Series F Conversion Price shall equal eighty percent (80%) of the price per share of the Common Stock sold in such initial public offering (prior to any underwriter commissions, fees or discounts), and such conversion shall occur following any adjustment to the Series F Conversion Price pursuant to Section 6.5.

(b) Qualifying Financing. Each share of Series F Preferred Stock shall automatically be converted into shares of Common Stock at the then effective Series F Conversion Price immediately upon the closing of a non-public equity financing (including a transaction with multiple closings for the sale of shares of the same class at the same price per share within any twelve-month period) wherein the aggregate consideration for such issuance received by the Corporation is at least \$10,000,000, of which at least \$1,000,000 is from new investors, and the Corporation is not subjected to any restrictions imposed by the investors in such equity financing upon the use of such funds. In the event that the conversion of the Series F Preferred Stock into shares of Common Stock shall occur pursuant to this Section 6.3.4(b), the Series F Conversion Price shall equal eighty percent (80%) of the price per share (on an "as converted" into Common Stock basis) paid in said non-public equity financing, and such conversion shall occur following any adjustment to the Series F Conversion Price pursuant to Section 6.5.

(c) Merger, etc.. Each share of Series F Preferred Stock shall automatically be converted into shares of Common Stock at the then effective Series F Conversion Price immediately prior to the closing of a consolidation or merger of the Corporation with or into another corporation which would be treated as a liquidation, dissolution or winding up pursuant to Section 3.4 or the sale or conveyance to another corporation of all or substantially all of the assets of the Corporation, which results in aggregate consideration to the Corporation or its shareholders with a fair market value of at least \$85,000,000, as determined in good faith by the Board of Directors of the Corporation. In the event that the conversion of the Series F Preferred Stock into shares of Common Stock shall occur pursuant to this Section 6.3.4(c), the Series F Conversion Price shall equal eighty percent (80%) of the value per share (on an "as

converted" into Common Stock basis) realized by the Company's shareholders from the consideration received in said consolidation or merger, which value shall be determined by the mutual agreement between the Company and the Purchaser. If the Company and the Purchaser do not reach mutual agreement as to said value, then said value shall be determined by a nationally recognized investment banking firm which is mutually selected by the Company and the Purchaser, with the fees for obtaining said valuation determination to be borne equally by the Company and the Purchaser. Such conversion shall occur following any adjustment to the Series F Conversion Price pursuant to Section 6.5.

(d) Operational Plan. Each share of Series F Preferred Stock shall automatically be converted into shares of Common Stock at the then effective Series F Conversion Price immediately upon the adoption by resolution of the Corporation's Board of Directors of an operational plan for the Corporation which provides for the Corporation to continue its operations in the ordinary course of business through revenues, working capital or other resources through at least December 31, 1998 without any further infusion of capital from investors through debt or equity investment in the Corporation; provided, however, that any such operational plan, as determined in good faith by the Corporation's Board of Directors, must be consistent with the intent of the then current annual Product Development Plan pursuant to the Distribution Agreement by and between the Corporation and Cobe BCT, Inc., dated October 22, 1993. In the event that the conversion of the Series F Preferred Stock into shares of Common Stock shall occur pursuant to this Section 6.3.4(d), the Series F Conversion Price shall equal eighty percent (80%) of the fair market value of a share of Series F Preferred Stock, as determined by the mutual agreement of the Company and the Purchaser. If the Company and the Purchaser do not reach mutual agreement as to said value, then said value shall be determined by a nationally recognized investment banking firm which is mutually selected by the Company and the Purchaser, with the fees for obtaining said valuation determination to be borne equally by the Company and the Purchaser. Such conversion shall occur following any adjustment to the Series F Conversion Price pursuant to Section 6.5.

(e) December 1, 1997. If not earlier converted pursuant to this Section 6.3.4, each share of Series F Preferred Stock shall automatically be converted into shares of Common Stock at the then effective Series F Conversion Price on December 1, 1997; provided, however, that in the event that prior to December 1, 1997, the Corporation has entered into a letter of intent (whether or not such letter of intent is intended to be binding or non-binding on the Corporation) which contemplates a transaction which would trigger automatic conversion of the Series F Preferred Stock into Common Stock pursuant to paragraph (a), (b) or (c) of this Section 6.3.4 and contemplates the consummation of the closing of such transaction on or before February 1, 1998, then each share of Series F Preferred Stock shall automatically be converted into shares of Common Stock at then effective Series F Conversion Price on February 2, 1998. In the event that the conversion of the Series F Preferred Stock into shares of Common Stock shall occur pursuant to this Section 6.3.4(e), the Series F Conversion Price shall be \$4.65, as adjusted pursuant to Section 6.5.

6.4 Mechanics of Conversion. No fractional shares of Common Stock shall be issued upon conversion of shares of Preferred Stock. In lieu of any fractional shares to which the holder would otherwise be entitled, the Corporation shall pay cash equal to such fraction multiplied by the then effective Applicable Conversion Price for the series. Before any holder of Preferred Stock shall be entitled to convert the same into shares of Common Stock pursuant to Section 6.2, such holder shall surrender the certificate or certificates therefor at the principal office of the Corporation or of any transfer agent for such stock and shall give written notice to the Corporation at such office that such holder elects to convert the same and shall state therein the name or names of the nominees in which such holder wishes the certificate or certificates for shares of Common Stock to be issued. The Corporation shall, as soon as practicable thereafter, issue and deliver at such office to such holder of Preferred Stock, or to their respective nominee or nominees, a certificate or certificates for the number of shares of Common Stock to which such holder or nominee shall be entitled as aforesaid, together with cash in lieu of any fraction of a share. Such conversion shall be deemed to have been made immediately prior to the close of business on the date of such surrender of the shares of Preferred Stock to be converted, and the person or persons entitled to receive the shares of Common Stock issuable upon such conversion shall be treated for all purposes as the record holder or holders of such shares of Common Stock on such date.

6.5 Adjustments to Conversion Prices.

6.5.1 Special Definitions. For purposes of this Section 6.5, the following definitions shall apply:

(a) "Options" shall mean rights, options or warrants to subscribe for, purchase or otherwise acquire either Common Stock or Convertible Securities (defined below).

(b) "Original Issue Date" shall mean the date on which a share of a particular series of Preferred Stock was first issued.

(c) "Convertible Securities" shall mean any evidence of indebtedness, shares or other securities directly or indirectly convertible into or exchangeable for Common Stock.

(d) "Additional Shares of Common Stock" shall mean all shares of Common Stock issued (or, pursuant to Section 6(D)(3) deemed to be issued) by the Corporation after the Original Issue Date, other than shares of Common Stock issued or issuable:

(i) upon conversion of shares of Preferred Stock;

(ii) to the University of Michigan, Stephen G. Emerson, Bernhard O. Palsson, Michael F. Clarke, or to the officers, employees, consultants or directors of the Corporation pursuant to any stock purchase plan or arrangement, stock

option plan, or other stock incentive plan or agreement approved by the Corporation's Board of Directors; or

(iii) by way of dividend or other distribution on shares excluded from the definition of Additional Shares of Common Stock by the foregoing clauses (i) or (ii), or this clause (iii).

6.5.2 No Adjustment of Applicable Conversion Price. No adjustment in the Applicable Conversion Prices for the series of Preferred Stock shall be made with respect to the issuance of Additional Shares of Common Stock or otherwise, unless the consideration per share (determined pursuant to Section 6.5.5 hereof) for an Additional Share of Common Stock issued or deemed to be issued by the Corporation is less than the Applicable Conversion Price for such series in effect on the date of, and immediately prior to, the issue of such Additional Share of Common Stock.

6.5.3 Deemed Issuances of Additional Shares of Common Stock.

(a) Options and Convertible Securities. In the event the Corporation at any time or from time to time after the Original Issue Date of a particular series shall issue any Options or Convertible Securities or shall fix a record date for the determination of holders of any class of securities entitled to receive any such Options or Convertible Securities, then the maximum number of shares (as set forth in the instrument relating thereto without regard to any provisions contained therein for a subsequent adjustment of such number) of Common Stock issuable upon the exercise of such Options or, in the case of Convertible Securities and Options therefor, the conversion or exchange of such Convertible Securities, shall be deemed to be Additional Shares of Common Stock issued as of the time of such issue or, in case such a record date shall have been fixed, as of the close of business on such record date, provided that Additional Shares of Common Stock shall not be deemed to have been issued with respect to the Preferred Stock unless the consideration per share (determined pursuant to Section 6.5.5 hereof) of such Additional Shares of Common Stock would be less than the Applicable Conversion Price of such series in effect on the date of and immediately prior to such issue, or such record date, as the case may be, and provided further that in any case in which Additional shares of Common Stock are deemed to be issued the following provisions shall apply:

(i) Exercise or Conversion. No further adjustment in the Applicable Conversion Price shall be made upon the subsequent issue of Convertible Securities or shares of Common Stock upon the exercise of such Options or conversion or exchange of such Convertible Securities.

(ii) Increase or Decrease. If such Options or Convertible Securities by their terms provide, with the passage of time or otherwise, for any increase in the consideration payable to the Corporation, or decrease in the number of shares of Common Stock issuable, upon the exercise, conversion or exchange thereof, the Applicable Conversion Price computed upon the original issue thereof (or upon the

occurrence of a record date with respect thereto), and any subsequent adjustments based thereon, shall, upon any such increase or decrease becoming effective, be recomputed to reflect such increase or decrease insofar as it affects such Options or the rights of conversion or exchange under such Convertible Securities.

(iii) Expiration. Upon the expiration of any such Options or any rights of conversion or exchange under such Convertible Securities which shall not have been exercised, the Applicable Conversion Prices computed upon the original issue thereof (or upon the occurrence of a record date with respect thereto), and any subsequent adjustments based thereon, shall, upon such expiration, be recomputed as follows:

(A) Underlying Common Stock. In the case of Convertible Securities or Options for Common Stock, any such subsequent adjustments shall be recomputed as if the only Additional Shares of Common Stock issued were the shares of Common Stock, if any, actually issued upon the exercise of such Options or the conversion or exchange of such Convertible Securities and the consideration received therefor was the consideration actually received by the Corporation for the issue of all such Options, whether or not exercised, plus the consideration actually received by the Corporation upon such exercise, or for the issue of all such Convertible Securities which were actually converted or exchanged, plus the additional consideration, if any, actually received by the Corporation upon such conversion or exchange.

(B) Underlying Convertible Securities. In the case of Options for Convertible Securities, any such subsequent adjustments shall be recomputed as if only the Convertible Securities, if any, actually issued upon the exercise thereof were issued at the time of issue of such Options, and the consideration received by the Corporation for the Additional Shares of Common Stock deemed to have been then issued was the consideration actually received by the Corporation for the issue of all such Options, whether or not exercised, plus the consideration deemed to have been received by the Corporation (determined pursuant to Section 6.5.5 upon the issue of the Convertible Securities with respect to which such Options were actually exercised).

(iv) Limitation. No readjustment pursuant to clause (ii) or (iii) above shall have the effect of increasing the Applicable Conversion Price to an amount which exceeds the lower of (A) such Applicable Conversion Price on the original adjustment date, or (B) such Applicable Conversion Price that would have resulted from any issuance of Additional Shares of Common Stock between the original adjustment date and such readjustment date (nor shall any shares issued upon conversion prior to such readjustment be affected by such readjustment).

(v) Short-Term Options. In the case of any Options that expire by their terms not more than thirty (30) days after the date of issue thereof, no adjustment of the Applicable Conversion Price shall be made until the expiration or exercise of all such Options, whereupon such adjustment shall be made in the same manner as provided in clause (iii) above.

(vi) Date of Issuance. If such record date shall have been fixed and such Options or Convertible Securities are not issued on the date fixed therefor, the adjustment previously made in the Applicable Conversion Price which became effective on such record date shall be cancelled as of the close of business on such record date, and thereafter the Applicable Conversion Price shall be adjusted pursuant to this Section 6.5.3 as of the actual date of their issuance.

(b) Stock Dividends, Stock Distributions and Subdivisions. In the event the Corporation at any time or from time to time after the Original Issue Date shall declare or pay any dividend or make any other distribution on the Common Stock payable in Common Stock, or effect a subdivision of the outstanding shares of Common Stock (by reclassification or otherwise than by payment of a dividend in Common Stock), then and in any such event, Additional Shares of Common Stock shall be deemed to have been issued as follows:

(i) Dividend or Distribution. In the case of any such dividend or distribution, immediately after the close of business on the record date for the determination of holders of any class of securities entitled to receive such dividend or distribution.

(ii) Subdivision. In the case of any such subdivision, at the close of business on the date immediately prior to the date upon which such corporate action becomes effective.

If such record date shall have been fixed and such dividend shall not have been fully paid on the date fixed therefor, the adjustment previously made in the Applicable Conversion Price which became effective on such record date shall be cancelled as of the close of business on such record date, and thereafter the Applicable Conversion Price shall be adjusted pursuant to this Section 6.5.3 as of the time of actual payment of such dividend.

6.5.4 Anti-Dilution Adjustment of Applicable Conversion Price Upon Issuance of Additional Shares of Common Stock.

(a) Series A, Series B and Series E Preferred Stock. In the event the Corporation, at any time after the Original Issue Date, shall issue Additional Shares of Common Stock (including Additional Shares of Common Stock deemed to be issued pursuant to Section 6.5.3 but excluding Additional Shares of Common Stock issued pursuant to Section 6.5.3(b) which event is dealt with in Section 6.5.6 hereof) without consideration or for a consideration per share less than the Series A Conversion Price, Series B Conversion Price or Series E Conversion Price in effect on the date of and immediately prior to such issuance, then and in such event, the Applicable Conversion Price for the affected Series A, Series B and Series E Preferred Stock, respectively, shall be reduced, concurrently with such issuance, in order to increase the number of shares of Common Stock into which shares of such series of Preferred Stock is convertible, to a price (calculated to the nearest cent) determined by the following formula:

$$CP(1) = CP(0) \times \frac{C}{CS + AS} + CP(0)$$

where:

CP(0) = the Applicable Conversion Price for Series A, Series B or Series E Preferred Stock in effect on the date of and immediately prior to such issuance;

CP(1) = the Applicable Conversion Price for Series A, Series B or Series E Preferred Stock as so adjusted;

CS = the number of shares of Common Stock outstanding immediately prior to such issuance (including shares of Common Stock issuable upon conversion or exercise of any Convertible Securities or Options);

C = the aggregate consideration received by the Corporation for the total number of Additional Shares of Common Stock so issued; and

AS = the number of such Additional Shares of Common Stock so issued.

Notwithstanding the foregoing, the Applicable Conversion Price for Series A, Series B or Series E Preferred Stock shall not be so reduced if the amount of such reduction would be an amount less than \$0.01, but any such amount shall be carried forward and applied toward any subsequent reduction which, together with such amount and any other amount or amounts so carried forward, shall aggregate \$0.01 or more.

(b) Series D Preferred Stock.

(i) Ratchet Adjustment. In the event the Corporation shall issue Additional Shares of Common Stock (including Additional Shares of Common Stock deemed to be issued pursuant to Section 6.5.3, but excluding Series D Preferred Stock and Additional Shares of Common Stock issued pursuant to Section 6.5.3(b) (which event is dealt with in Section 6.5.6 hereof)), either without consideration or for a consideration per share less than the Series D Conversion Price in effect on the date of and immediately prior to such issuance, wherein the aggregate consideration for such issuance received by the Corporation is at least \$2,000,000, the following will be applicable:

(A) Single Transaction. In a private financing transaction (including a transaction with multiple closings for the sale of shares of the same class at the same price per share within any twelve-month period), the Series D Conversion Price shall be reduced concurrently with such issuance to a price equal to the consideration per share (as determined pursuant to Section 6.5.5 hereof) received by

the Corporation for such Additional Shares of Common Stock; provided, however, that in no event shall the Series D Conversion Price be reduced to less than \$3.00.

(B) Multiple Transactions. In multiple transactions at different per share prices during any twelve-month period, the Series D Conversion Price shall be reduced to an amount equal to the weighted average consideration received by the Corporation for such Additional Shares of Common Stock during such twelve-month period (but in no event shall the Series D Conversion Price be reduced to less than \$3.00. Such weighted average consideration shall be determined by dividing the aggregate consideration received by the Corporation for the Additional Shares of Common Stock over such twelve-month period by the aggregate number of Additional Shares of Common Stock issued over the same period.

(ii) Formula Adjustment. In the event the Corporation shall issue Additional Shares of Common Stock (including Additional Shares of Common Stock deemed to be issued pursuant to Section 6.5.3 but excluding Series D Preferred Stock and Additional Shares of Common Stock issued pursuant to Section 6.5.3(b), which event is dealt with in Section 6.5.6 for a per share consideration less than the Series D Conversion Price in effect on the date of and immediately prior to such issuance, in a single transaction or in a series of transactions, and for aggregate consideration less than \$2,000,000 during any twelve-month period, then the Series D Conversion Price shall be adjusted for such Additional Shares of Common Stock pursuant to the formula provided in Section 6.5.4(a) as if the Series D Preferred Stock were Series B Preferred Stock (except for the Applicable Conversion Price which shall be the Series D Conversion Price).

(iii) Single Adjustment. For purposes of this Section 6.5.4(b) any issuance of Additional Shares of Common Stock shall be included in only one twelve-month period (and in only one adjustment of the Series D Conversion Price), which period shall be the earliest twelve-month period which may be applicable (and which adjustment shall be the adjustment to be made with respect to the earliest applicable twelve-month period). After the first twelve-month period with respect to which an adjustment is made to the Series D Conversion Price, any new twelve-month period shall be deemed to commence on the date of issuance of Additional Shares of Common Stock first occurring more than twelve months following the date of issuance of Additional Shares of Common Stock which caused the most recent prior twelve-month period to begin.

(c) Series F Preferred Stock. In the event the Corporation shall issue Additional Shares of Common Stock (including Additional Shares of Common Stock deemed to be issued pursuant to Section 6.5.3, but excluding Series F Preferred Stock and Additional Shares of Common Stock issued pursuant to Section 6.5.3(b), which event is dealt with in Section 6.5.6, either without consideration or for a consideration per share less than the Series F Conversion Price in effect on the date of and immediately prior to such issuance, in a private financing transaction (including a transaction with multiple closings for the sale of shares of the same class at the same

price per share within any twelve-month period), wherein the aggregate consideration for such issuance received by the Corporation is at least \$1,000,000, then the Series F Conversion Price shall be adjusted for such Additional Shares of Common Stock pursuant to the formula provided in Section 6.5.4(a) as if the Series F Preferred Stock were Series B Preferred Stock (except the Applicable Conversion Price shall be the Series F Conversion Price); provided, however, that the adjustment to the Series F Conversion Price provided for in this Section 6.5.4(c) shall apply only to the Corporation's first such private financing following the Original Issue Date of the Series F Preferred Stock.

6.5.5 Determination of Consideration. For purposes of this Section 6.5 the consideration received by the Corporation for the issue of any Additional Shares of Common Stock shall be computed as follows:

(a) Cash and Property. Such consideration shall be computed as follows:

(i) Cash. Insofar as it consists of cash, such consideration shall be computed at the aggregate amount of cash received by the Corporation;

(ii) Property. Insofar as it consists of property other than cash, such consideration shall be computed at the fair value thereof at the time of such issue, as determined in good faith by the Board of Directors; and

(iii) Combination. In the event Additional Shares of Common Stock are issued together with other shares or securities or other assets of the Corporation for consideration which covers both, such consideration shall be the proportion of such consideration so received, computed as provided in clauses (i) and (ii) above, as determined in good faith by the Board of Directors.

(b) Options and Convertible Securities. The consideration per share received by the Corporation for Additional Shares of Common Stock deemed to have been issued pursuant to Section 6.5.3(a), relating to Options and Convertible Securities, shall be determined by dividing:

(i) the total amount, if any, received or receivable by the Corporation as consideration for the issue of such Options or Convertible Securities, plus the minimum aggregate amount of additional consideration (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such consideration) payable to the Corporation upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities; by

(ii) the maximum number of shares of Common Stock (as set forth in the instruments relating thereto, without regard to any provision contained

therein for a subsequent adjustment of such number) issuable upon the exercise of such Options or the conversion or exchange of such Convertible Securities.

6.5.6 Adjustment for Dividends or Combinations.

(a) Stock Dividends, Distributions or Subdivisions. In the event the Corporation shall issue Common Stock pursuant to Section 6.5.3(b) in a stock dividend, stock distribution or subdivision, the Applicable Conversion Price in effect immediately prior to such stock dividend, stock distribution or subdivision shall, concurrently with the effectiveness of such stock dividend, stock distribution or subdivision, be proportionately decreased.

(b) Combinations or Consolidations. In the event the outstanding shares of Common Stock shall be combined or consolidated, by reclassification or otherwise, into a lesser number of shares of Common Stock, the Applicable Conversion Price in effect immediately prior to such combination or consolidation shall, concurrently with the effectiveness of such combination or consolidation, be proportionately increased.

6.5.7 Adjustment for Merger or Reorganization. In the event of any consolidation or merger of the Corporation with or into another corporation or the sale or conveyance of all or substantially all of the assets of the Corporation to another corporation, each share of Series A, Series B, Series C, Series D and Series E Preferred Stock shall thereafter be convertible into the number of shares of stock or other securities or property to which a holder of the number of shares of Common Stock of the Corporation deliverable upon conversion of such series would have been entitled upon such consolidation, merger or conveyance, and, in any such case, appropriate adjustment (as determined by the Board of Directors) shall be made in the application of the provisions herein set forth with respect to the rights and interest thereafter of the holders of the series, in order that the provisions set forth herein (including provisions with respect to changes in and other adjustments of the Applicable Conversion Price) shall thereafter be applicable, as nearly as reasonably may be, in relation to any shares of stock or other property thereafter deliverable upon the conversion of that series of Preferred Stock. However, in the case of any merger or consolidation which is treated as a liquidation, dissolution or winding up of the affairs of the Corporation pursuant to Section 3.4, each share of Series A, Series B, Series C, Series D and Series E Preferred Stock shall not be converted into shares of stock or other securities or property of the resulting corporation, but shall be cancelled and surrendered to the Corporation upon distribution to the holders of Series A, Series B, Series C, Series D and Series E Preferred Stock of all cash or other property to which they are entitled pursuant to Section 3 as a result of such transaction being treated as a liquidation, dissolution, or winding up under Section 3.4.

6.5.8 Adjustment to Series C Conversion Price for Distributions to Holders of Common Stock. In the event that the Corporation shall distribute to the holders of its Common Stock (whether pursuant to a reclassification, merger or consolidation or

otherwise) evidences of its indebtedness or assets (including cash, securities, intangible assets or other property), then the Series C Conversion Price shall be adjusted so that the number of shares of Common Stock into which a share of Series C Preferred Stock is convertible equals the number of shares of Common Stock determined as follows: multiply the number of shares of Common Stock into which each share of Series C Preferred Stock is convertible at the then effective Series C Conversion Price by a fraction, the numerator of which shall be the Series C Conversion Price effective on the record date for determination of shareholders entitled to receive such distribution, and the denominator of which shall be such Series C Conversion Price less the fair market value of such property, as determined in good faith by the Board of Directors of the Corporation, distributed with respect to each share of Common Stock. Such adjustment to the Series C Conversion Price shall be made whenever any such distribution is made.

6.6 No Impairment. The Corporation will not, by amendment of these Restated Articles of Incorporation or through any reorganization, transfer of assets, consolidation, merger, dissolution, issue or sale of securities or any other voluntary action, avoid or seek to avoid the observance or performance of any of the terms to be observed or performed hereunder by the Corporation but will at all times in good faith assist in the carrying out of all the provisions of this Section 6 and in the taking of all such action as may be necessary or appropriate in order to protect the Conversion Rights of the holders of the Preferred Stock against impairment.

6.7 Certificate as to Adjustments. Upon the occurrence of each adjustment or readjustment of the Applicable Conversion Prices pursuant to this Section 6, the Corporation at its expense shall promptly compute such adjustments or readjustments in accordance with the terms hereof and furnish to each holder of Preferred Stock a certificate setting forth such adjustment or readjustment and showing in detail the facts upon which such adjustment or readjustment is based. The Corporation shall, upon the written request at any time from any holder of Preferred Stock, furnish or cause to be furnished to such holder a like certificate setting forth (i) such adjustments and readjustments, (ii) the Applicable Conversion Price at the time in effect, and (iii) the number of shares of Common Stock and the amount, if any, of other property which at the time would be received upon the conversion of such holder's shares of Preferred Stock.

6.8 Notices of Record Date. In the event of any taking by the Corporation of a record of the holders of any class of securities (other than Preferred Stock) for the purposes of determining the holders thereof who are entitled to receive any dividend (other than a cash dividend which is the same as cash dividends paid in previous quarters) or other distribution, the Corporation shall mail to each holder of Preferred Stock at least ten (10) days prior to the date specified therein, a notice specifying the date on which any such record is to be taken for the purpose of such dividend or distribution.

6.9 Common Stock Reserved. The Corporation shall reserve and keep available out of its authorized but unissued Common Stock such number of shares of Common

Stock as shall from time to time be sufficient to effect conversion of the Preferred Stock. The Corporation shall not take any corporate action which would require an adjustment in the number of shares of Common Stock into which any share of Preferred Stock is convertible unless either (i) immediately after such corporate action is taken and the transactions contemplated thereby are consummated, the number of authorized and unissued shares of Common Stock would be sufficient to effect the conversion of all outstanding shares of Preferred Stock at the Applicable Conversion Prices then in effect, or (ii) concurrently with the taking of such corporate action, the Corporation shall take such corporate action as, in the opinion of its counsel, may be necessary to increase its authorized and unissued shares of Common Stock to such number as shall be sufficient to provide for such conversion.

6.10 Taxes Upon Conversion of Series C Preferred Stock. The Corporation shall pay any and all taxes that may be payable in respect of the issue or delivery of shares of Common Stock on conversion of shares of Series C Preferred Stock pursuant hereto. The Corporation shall not, however, be required to pay any tax which may be payable in respect of any transfer involved in the issue and delivery of shares of Common Stock in a name other than that in which the shares of Series C Preferred Stock so converted were registered, and no such issue or delivery shall be made unless and until the person requesting such issue has paid to the Corporation the amount of any such tax or has established, to the satisfaction of the Corporation, that such tax has been paid.

ARTICLE VII

1. Director Liability. A director of the Corporation shall not be personally liable to the Corporation or its shareholders for monetary damages for breach of fiduciary duty as a director. However, this provision does not eliminate or limit the liability of a director for any of the following:

(a) any breach of the director's duty of loyalty to the Corporation or its shareholders;

(b) any acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;

(c) a violation of Section 551(1) of the Michigan Business Corporation Act, as amended (the "MBCA");

(d) a transaction from which the director derived an improper personal benefit; or

(e) an act or omission occurring before the date these Articles of Incorporation became effective in accordance with the pertinent provisions of the MBCA.

Any repeal, amendment or other modification of this Article VII shall not adversely affect any right or protection of a director of the Corporation existing at the time of such repeal, amendment or other modification.

If the MBCA is amended, after this Article becomes effective, to authorize corporate action further eliminating or limiting personal liability of directors, then the liability of directors shall be eliminated or limited to the fullest extent permitted by the MBCA as so amended.

2. Control Share Acquisitions. Chapter 7B of the MBCA, known as the "Stacey, Bennett, and Randall shareholder equity act," does not apply to control share acquisitions of shares of the Corporation.

BYLAWS
OF
AASTROM BIOSCIENCES, INC.

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ARTICLE I GENERAL

Section 1.1 The name, location of principal office, and purposes of the Corporation shall be as set forth in the Articles of Incorporation. The powers of the Corporation and of its directors and shareholders, and all matters concerning the conduct and regulation of the business of the Corporation, shall be subject to such provisions in regard thereto, if any, as are set forth in said Articles of Incorporation.

Section 1.2 All references in these Bylaws to the Articles of Incorporation shall be construed to mean the Articles of Incorporation of the Corporation as amended from time to time.

Section 1.3 The registered office of the Corporation may be the same as the principal office of the Corporation, but in any event must be located in the State of Michigan, and must be the business office of the registered agent, as required by the Michigan Business Corporation Act (the "MBCA"). The Corporation may have business offices at such other places, either within or without the State of Michigan, as the Board of Directors may designate or as the business of the Corporation may require from time to time.

ARTICLE II SHAREHOLDERS

Section 2.1 Annual Meeting. The annual meeting of the shareholders of the Corporation shall be held at the principal office of the Corporation, or at such other place as may be set forth in the notice thereof, in August or September of each year, at a date and time as designated by the Board of Directors, for the purpose of election of Directors to succeed those whose terms expire and for the transaction of such other business as may properly come before the meeting. The Board of Directors, for good and sufficient reasons, may schedule the annual meeting at any other time, and notice shall be given or waived as provided in Section 2.4 hereof.

Section 2.2 Special Meetings. Special Meetings of the shareholders (or of any specific class thereof), for any purpose or purposes, unless otherwise prescribed by statute or by the Articles of Incorporation, may be called by the President and shall be called by the President or Secretary at the request in writing of a majority of the Board of Directors, or at the request in writing of a shareholder or shareholders owning at least ten percent (10%) of the number of shares of stock (or, with respect to meetings of a specific class, the number of shares of such specific class thereof) of the Corporation issued and outstanding and entitled to vote. Such request shall state the purpose or purposes of the proposed meeting. Upon the closing of the first sale of the Corporation's common stock

pursuant to a firmly underwritten registered public offering (the "IPO"), special meetings of the shareholders may be called only by the President and shall be called by the President at the request in writing of a majority of the Directors then in office, and shall be held at such place, on such date, and at such time as the President or shall fix. Business transacted at special meetings shall be confined to the purpose or purposes stated in the notice.

Section 2.3 List of Shareholders. The officer who has charge of the stock

ledger of the Corporation shall prepare and make, at least ten (10) days before every meeting of shareholders, a complete list of the shareholders entitled to vote at the meeting, arranged in alphabetical order, and showing the address of each shareholder and the number of shares registered in the name of each shareholder. Such list shall be open to the examination of any shareholder, for any purpose germane to the meeting, during ordinary business hours, for a period of at least ten (10) days prior to the meeting, either at a place within the city where the meeting is to be held, which place shall be specified in the notice of the meeting, or, if not so specified, at the place where the meeting is to be held. The list shall also be produced and kept at the time and place of the meeting during the whole time thereof, and may be inspected by any shareholder who is present.

Section 2.4 Notice of Meetings. Written notice of the time, place and

purposes of the meeting of shareholders shall be given not less than 10 nor more than 60 days before the date fixed for such meeting to each shareholder of record entitled to vote at the meeting. Notice shall be deemed duly served when the same has been personally delivered or deposited in the United States Mail, with postage fully prepaid, addressed to the shareholder at such shareholder's address as it appears on the records of the Corporation. Written notice may also be given by facsimile or telegram, and such notice shall be deemed to be given when the recipient receives the notice personally, or when confirmation of transmission of the notice to the shareholder's address as it appears on the books and records of the Corporation has been delivered to the Corporation or to the equipment transmitting such notice. Such notice shall be given by or under the direction of the Secretary of the Corporation, and in the absence or refusal of the Secretary to give such notice, notice shall be given by or under the direction of any other officer of the Corporation. No notice need be given of an adjourned meeting of the shareholders provided the time and place to which such meeting is adjourned is announced at the meeting at which the adjournment is taken and at the adjourned meeting only such business is transacted as might have been transacted at the original meeting. If the adjournment is for more than thirty (30) days, or if after the adjournment a new record date is fixed for the adjourned meeting, a notice of the adjourned meeting shall be given to each shareholder of record entitled to vote at the meeting. A waiver of such notice in writing, signed by a person entitled to said notice, whether before or after the time of the meeting, shall be deemed equivalent to said notice. Attendance of a person at a meeting of shareholders, in person or by proxy, shall constitute a waiver of such notice, except when the attendance is for the express and sole purpose of objecting to the transaction of any business,

clearly stated at the commencement of the meeting, by reason of a claim that a meeting was not lawfully called or convened.

Section 2.5 Transaction of Business. At an annual or special meeting of

the shareholders, only such business shall be conducted as shall have been properly brought before the meeting. To be properly brought before a meeting, business must be (a) specified in the notice of meeting (or any supplement thereto) given by or at the direction of the Secretary or other officer of the Corporation, (b) properly brought before the meeting by or at the direction of the Board of Directors, (c) properly brought before an annual meeting by a shareholder, or (d) properly brought before a special meeting by a shareholder, but if, and only if, the notice of a special meeting provides for business to be brought before the meeting by shareholders. For business to be properly brought before a meeting by a shareholder, the shareholder must have given timely notice thereof in writing to the Secretary of the Corporation. To be timely, a shareholder proposal to be presented at an annual meeting shall be received at the Corporation's principal executive offices not less than 120 calendar days in advance of the date that the Corporation's (or the Corporation's predecessor's) proxy statement was released to shareholders in connection with the previous year's annual meeting of shareholders, except that if no annual meeting was held in the previous year or the date of the annual meeting has been changed by more than 30 calendar days from the date contemplated at the time of the previous year's proxy statement, or in the event of a special meeting, notice by the shareholder to be timely must be received not later than the close of business on the tenth day following the day on which such notice of the date of the meeting was mailed or such public disclosure was made. A shareholder's notice to the Secretary shall set forth as to each matter the shareholder proposes to bring before the annual or special meeting (a) a brief description of the business desired to be brought before the annual or special meeting and the reasons for conducting such business at the special meeting, (b) the name and address, as they appear on the Corporation's books, of the shareholder proposing such business, (c) the class and number of shares of the Corporation which are beneficially owned by the shareholder, and (d) any material interest of the shareholder in such business.

Section 2.6 Quorum. The holders of a majority of the stock issued and

outstanding and entitled to vote thereat, present in person or represented by proxy, shall constitute a quorum at all meetings of the shareholders (or any specific class thereof) for the transaction of business except as otherwise provided by statute or by the Articles of Incorporation. If, however, such quorum shall not be present or represented by any meeting of the shareholders, the chairman of the meeting or the holders of a majority of shares of stock entitled to vote thereat who are present, in person or represented by proxy, shall have the power to adjourn the meeting from time to time, without notice other than announcement at the meeting, until a quorum shall be present or represented.

Section 2.7 Voting and Record Date. In order that the Corporation

may determine the shareholders entitled to notice of or to vote at any meeting of shareholders or any adjournment thereof, or to express consent to corporate action in writing without a meeting, or entitled to receive payment of any dividend or other distribution of allotment of any rights, or entitled to exercise any rights in respect of any change, conversion or exchange of stock or for the purpose of any other lawful action, the Board of Directors may fix a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted by the Board of Directors, and which record date shall not be (i) more than sixty (60) nor less than ten (10) days before the date of such meeting, nor (ii) more than ten (10) days after the date upon which the resolution fixing the record date is adopted by the Board of Directors for action by shareholder consent in writing without a meeting, nor (iii) more than sixty (60) days prior to any other action. If a record date is not fixed (a) the record date for determination of shareholders entitled to vote at a meeting of shareholders shall be the close of business on the day next preceding the day on which notice of such meeting is given, and (b) the record date for determining shareholders for any purpose other than that specified in subdivision (a) shall be the close of business on the day on which the resolution of the Board relating thereto is adopted. When a determination of shareholders of record entitled to vote at a meeting of shareholders has been made as provided in this Section, the determination applies to any adjournment of the meeting, unless the Board fixes a new record date under this Section for the adjourned meeting.

Section 2.8 Proxies. A proxy, given by a shareholder to another person,

authorizing such other person to vote the shares of such shareholder, shall be in writing and signed by the shareholder or his authorized agent or representative. A proxy shall not be valid after the expiration of three (3) years from its date unless otherwise provided therein. All proxies shall be filed with the Secretary at or before the meeting at which they are intended to be used. A proxy shall be deemed sufficient if it appears on its face to confer the requisite authority and is signed by the owner of the stock to be voted. No witnesses to the execution of any proxy shall be required.

Section 2.9 Inspectors. The Board of Directors, in advance of a

shareholders meeting, may appoint one or more inspectors to act at the meeting or any adjournment thereof. If inspectors are not so appointed, the person presiding at a shareholders meeting may, and on request of a shareholder entitled to vote thereat shall, appoint one or more inspectors. In case a person appointed fails to appear or act, the vacancy may be filled by appointment made by the Board of Directors in advance of the meeting or at the meeting by the person presiding thereat. The inspectors shall determine the number of shares outstanding and the voting power of each, the shares represented at the meeting, the existence of a quorum, the validity and effect of proxies, and shall receive votes, ballots or consents, hear and determine challenges and questions arising in connection with the right to vote, count and tabulate votes, ballots or consents, determine the result, and do such acts as are proper to conduct the election or vote with fairness

to all shareholders. On request of the person presiding at the meeting or a shareholder entitled to vote thereat, the inspectors shall make and execute a written report to the person presiding at the meeting of any of the facts found by them and matters determined by them. The report shall be prima facie evidence of the facts stated and of the vote as certified.

Section 2.10 Action by Written Consent. The shareholders of the

Corporation shall have the ability to take action without a meeting only as provided in the Articles of Incorporation.

Section 2.11 Voting of Shares by Certain Holders.

(a) Voting by Trustee or Fiduciary. Shares standing in the name of

any person as trustee or other fiduciary may be voted and all rights incident thereto may be exercised only by the trustee or other fiduciary, in person or by proxy, and without proof of authority.

(b) Voting of Pledged Stock. Unless the Corporation has specific

written instructions to the contrary, from the pledgee and pledgor, pledged stock may be voted by the pledgor only.

(c) Voting by Guardian of Incompetent. Shares standing in the name

of a person adjudged incompetent may be voted and all rights incident thereto may be exercised only by his guardian, in person or by proxy.

(d) Voting by Executor or Administrator. Shares standing in the

name of a deceased person may be voted and all rights incident thereto may be exercised only by his executor or administrator, in person or by proxy.

(e) Voting by Guardian of Minor. Shares standing in the name of a

minor may be voted and all rights incident thereto may be exercised by his guardian, in person or by proxy, or in the absence of such representation by his guardian, by the minor, in person or by proxy, whether or not the Corporation has notice, actual or constructive, of the nonage or the appointment of a guardian, and whether or not a guardian has been in fact appointed.

(f) Voting of Shares in Name of Corporation. Shares standing in

the name of a corporation, domestic or foreign, may be voted or represented and all rights incident thereto may be exercised on behalf of that corporation by the persons described in any of the following subdivisions:

(1) Any officer of the Corporation authorized so to do by the Bylaws of that Corporation.

(2) Any person authorized so to do by resolution of the Board of Directors or a duly authorized committee of the Board of Directors of that Corporation.

(3) Any person authorized so to do by proxy or power of attorney duly executed by the President or Vice President and Secretary or Assistant Secretary of that Corporation.

However, such shares may be voted or represented by the persons described in any subdivision only in the absence of vote or representation by the persons described in a preceding subdivision of this subparagraph.

(g) Voting Shares in Names of Two or More Persons. Shares standing

in the names of two or more persons shall be voted or represented in accordance with the vote or consent of the majority of the persons in whose names the shares stand. If only one such person is present in person or by proxy, he may vote all the shares, and all the shares standing in the names of such persons are represented for the purpose of determining a quorum. This applies to the voting of shares by two or more administrators, executors, trustees, or other fiduciaries, unless the instrument or order of court appointing them otherwise directs.

ARTICLE III BOARD OF DIRECTORS

Section 3.1 General Powers. The property, affairs and business of the Corporation shall be managed by the Board of Directors.

Section 3.2 Number, Qualification and Term of Office. Unless otherwise provided in the Articles of Incorporation, the Board of Directors shall be divided into three classes, as nearly equal in numbers as the then total number of directors constituting the entire Board of Directors permits, with the term of office of one class expiring each year. The term of office of directors in the first class shall expire at the first annual meeting of shareholders after their election, the term of office of directors in the second class shall expire at the second annual meeting of shareholders after their election, and the term of office of directors in the third class shall expire at the third annual meeting of shareholders after their election. The directors elected at the 1994 Annual Shareholders Meeting will be classified into terms of one, two or three years, by resolution of the Board of Directors. At each annual meeting of shareholders after such classification of the Board of Directors, a number of directors equal to the number of the class whose term expires at the meeting shall be elected to hold office until the third succeeding annual meeting. Directors shall hold office until the next election of the class for which such directors shall have been chosen and until their successors are elected and qualified, except in the case of the death, resignation or removal of any Director. Directors need not be shareholders of the Corporation. The size of the

Board of Directors shall be within the range of five to nine directors, with the exact size to be fixed from time to time by resolution of the Board of Directors.

Section 3.3 Vacancies. The shareholders may, at any meeting called for

such purpose, by a vote of a majority of the capital stock issued and outstanding and entitled to vote thereon, remove any Director from office, with or without cause. Any Director may resign by written notice to the President, such resignation to be effective upon its receipt by the President or at such subsequent time as may be specified in the notice of resignation. Subject to the rights of the holders of any series of Preferred Stock then outstanding, newly created directorships resulting from any increase in the authorized number of Directors or any vacancies in the Board of Directors resulting from death, resignation, retirement, disqualification or other cause may be filled only by a majority vote of the directors then in office, though less than a quorum, and Directors so chosen shall hold office for a term expiring at the next annual meeting of shareholders at which the term of office of the class to which they have been elected expires, except in the case of death, resignation or removal of any Director. No decrease in the number of Directors constituting the Board of Directors shall shorten the term of any incumbent Director. Acceptance of resignation shall not be necessary for it to be effective.

Section 3.4 Meetings of the Board of Directors. The Board of Directors

shall hold an annual meeting immediately following the annual shareholders meeting, for the purpose of electing officers and for the transaction of such other business as may properly come before the meeting. No notice of such annual meeting shall be necessary to the newly elected directors in order legally to constitute the meeting, provided a quorum shall be present, unless said meeting is held, by a consent of a majority of the Directors of such new Board, at a time and place other than at the place of holding and immediately following the annual meeting of shareholders. Special meetings of the Board of Directors may be held at any place either within or without the State of Michigan at any time pursuant to resolution adopted by the Board of Directors or upon call of the President or any two (2) officers.

Section 3.5 Notice of Meetings. Notice of meetings of Directors shall be

given or waived in the same manner as notice of meetings of shareholders, as provided in Section 2.4, except that notice of Directors meetings shall be given not later than two (2) nor more than ten (10) days prior to such meetings.

Section 3.6 Quorum and Required Vote of Board. A majority of the total

number of Directors shall constitute a quorum for the transaction of business, and the act of a majority of the Directors present at any meeting at which a quorum is present shall be the act of the Board of Directors. Amendment of these Bylaws by the Board requires the vote of not less than a majority of the members of the Board then in office.

Section 3.7 Telephonic Meetings. A member of the Board or of a committee

designated by the Board may participate in a meeting by means of conference telephone or similar communications equipment by which all persons participating in the discussion can hear each other. Participation in a meeting pursuant to this provision constitutes presence in person at the meeting.

Section 3.8 Board Action Without Meeting. If all of the Directors then

constituting the Board of Directors of the Corporation or of any committee of the Board of Directors shall severally and/or collectively consent in writing to any action to be taken, such action shall have the same effect as though it had been authorized at a duly called and properly held meeting of the Board of Directors or such committee. Such written consent shall be filed with the minutes of the proceedings of the Board.

Section 3.9 Committees. The Board of Directors may, by resolution or

resolutions, passed by a majority of the whole Board of Directors, designate one or more committees, each committee to consist of two (2) or more of the Directors of the Corporation, which, to the extent provided in said resolution or resolutions or in other provisions of these Bylaws, shall have and may exercise the powers of the Board of Directors in the management of the business and affairs of the Corporation, and may have the power to authorize the seal of the Corporation to be affixed to all papers which may require it. However, such a committee does not have the power or authority to amend the Bylaws of the Corporation, fill vacancies on the Board of Directors, or fix compensation of the Directors serving on the Board of Directors or on a committee; and, unless the resolution of the Board of Directors creating such committee or the Articles of Incorporation expressly so provide, such a committee does not have the power or authority to declare a dividend or to authorize the issuance of stock. Any such committee, and each member thereof, shall serve at the pleasure of the Board of Directors. Such committee or committees shall have such name or names as may be determined from time to time by resolution adopted by the Board of Directors and each committee shall elect a chairman and secretary if one is not named by the Board of Directors. Each committee shall keep regular minutes of its meetings and report to the Board of Directors when required.

Section 3.10 Compensation. By resolution of the Board of Directors, the

Directors may be paid their expenses, if any, of attendance at each meeting of the Board, and may be paid a fixed sum for attendance. No such payment shall preclude any Director from serving the Corporation in any other capacity and receiving compensation therefor. Members of the committees shall be allowed similar compensation for attending committee meetings.

Section 3.11 Presumption of Assent. A Director of the Corporation who is

present at a meeting of the Board at which action on any corporate matter is taken shall be presumed to have assented to the action taken unless his dissent shall be entered in the minutes of the meeting or unless he shall file his written dissent to

such action with the person acting as Secretary of the meeting before the adjournment thereof, or by registered mail to such Secretary immediately after the adjournment thereof. This shall not apply to a Director who voted in favor of such action.

ARTICLE IV OFFICERS AND AGENTS

Section 4.1 General. The Corporation shall have a President, a Secretary,

and a Treasurer, and, if desired, a Chairman of the Board and one or more Vice Presidents, Assistant Secretaries and Assistant Treasurers. All officers of the Corporation shall be elected by the Directors and shall hold office until their successors are elected and qualified. The Corporation may also have such other officers, agents and factors as may be deemed necessary for the transaction of the business of the Corporation, who shall be chosen in such manner and hold their offices for such terms and have such authority and duties as may be determined by the Board of Directors. The Board of Directors may secure the fidelity of any and/or all of such officers by bond or otherwise and may also provide for the qualification of any or all of such officers before any person authorized by law to administer an oath. The Board of Directors, by resolution, may require any or all of the officers of the Corporation to give bonds, in favor of the Corporation, with sufficient surety or sureties, and in such amounts as the Board of Directors may fix, conditioned on the faithful performance of the duties of their respective offices. The President shall be chosen from among the Directors. Any two offices except those of President and Vice President may be held by the same person but no officer shall execute, acknowledge or verify any instrument in more than one capacity. Subject to these Bylaws, each officer shall have in addition to the duties and powers herein set forth, such duties and powers as are commonly incident to his office, and such duties and powers as the Board of Directors shall from time to time designate. In all cases where the duties of any officer, agent or employee are not specifically prescribed by the Bylaws or by the Board of Directors, such officer, agent or employee shall obey the orders and instructions of the President. Compensation of the officers shall be as authorized by the Board of Directors.

Section 4.2 Duties of the President. The President shall, subject to the

direction and under the supervision of the Board of Directors, be the chief executive officer of the Corporation and shall have general and active control of its affairs and business and general supervision over its officers, agents and employees. The President shall also appoint and discharge all subordinate agents and employees and fix their salaries, subject to review by the Board of Directors, and shall designate their duties. He shall preside at all meetings of the shareholders and, unless a Chairman of the Board has been elected, at all meetings of the Board of Directors, at which he is present. The President shall have custody of the Treasurer's bond, if any.

Section 4.3 Duties of the Chairman of the Board. The Board of Directors

may elect or appoint a Chairman of the Board. The Chairman of the Board shall, if

present, preside at all meetings of the Board of Directors and shall exercise and perform such other powers and duties as may be assigned to him from time to time by the Board of Directors or prescribed by these Bylaws.

Section 4.4 Duties of the Vice President. The Board of Directors may

elect or appoint one or more Vice Presidents. The Vice Presidents, if such be elected, shall, subject to the direction and under the supervision of the President, be the assistant chief executive officer of the Corporation and shall assist the President in the general and active control of its affairs in business. The Vice Presidents shall perform all the duties of the President in case of the absence or disqualification of the President. Any of such Vice Presidents shall preside at all meetings of the shareholders in the absence or unavailability of the President.

Section 4.5 Duties of the Secretary. The Secretary shall: (a) keep the

minutes of the proceedings of the shareholders and of the Board of Directors in one or more books provided for that purpose; (b) see that all notices are duly given in accordance with the provisions of these Bylaws or as required by law; (c) be custodian of the corporate records and of the seal of the Corporation and ensure that the seal of the Corporation is affixed to all documents the execution of which on behalf of the Corporation under its seal is duly authorized; (d) keep a register of the post office address of each shareholder which shall be furnished to the Secretary by such shareholder; and (e) perform all duties incident to the office of secretary and such other duties as from time to time may be assigned to him by the President or by the Board of Directors. The Secretary also shall have charge of the stock ledger (which may, however, be kept by any transfer agent or agents of the Corporation under the direction of the Secretary), the original or duplicate of which shall, at all times, during the usual hours for business, be open to the examination of every shareholder at the principal office or place of business of the Corporation in Michigan. In the absence of the Secretary from any meeting, a temporary Secretary shall be chosen, who shall be sworn to the faithful discharge of his duty and shall record the proceedings of such meeting in the aforesaid books.

Section 4.6 Duties of the Treasurer. The Treasurer shall, subject to the

direction and under the supervision of the Board of Directors, the President and the Vice President, have the care and custody of the funds and valuable papers of the Corporation, except his own bond, and he shall have power to endorse for deposit or collection all notes, checks, drafts and other obligations for the payment of money to the Corporation or its order. He shall keep, or cause to be kept, at the principal office of the Corporation accurate books of account, which shall be the property of the Corporation. He shall disburse the funds of the Corporation as may be ordered by the Board of Directors, taking proper vouchers for such disbursements, and shall render to the President and Directors, when they so direct, an account of all his transactions as Treasurer and of the financial condition of the Corporation.

Section 4.7 Assistant Secretaries and Assistant Treasurers. The Assistant

Secretary or Assistant Secretaries, in the absence or disability of the Secretary, shall perform the duties and exercise the powers of the Secretary. The Assistant Treasurer or Assistant Treasurers, in the absence or disability of the Treasurer, shall perform the duties and exercise the powers of the Treasurer. Any Assistant Treasurer, if required by the Board, shall keep in force a bond as provided in Section 4.1. The Assistant Secretaries and Assistant Treasurers, in general, shall exercise and perform such other powers and duties as shall be assigned to them by the Secretary or by the Treasurer, respectively, or by the Board of Directors or the President.

Section 4.8 Vacancies. The Board of Directors may, at any meeting called

for the purpose, by vote of a majority of their number, remove from office any officer of the Corporation, with or without cause. Any officer may resign by written notice to the President, which resignation may be effective upon its receipt by the President or at such subsequent time as may be specified in the notice of resignation, PROVIDED, HOWEVER, that the resignation of the President shall be submitted to the Board of Directors. The Board of Directors may, at any meeting, accept the resignation of any officer or remove or accept the resignation of any agent or member of a committee, and may fill such vacancy for the unexpired term and until the successor thereof shall be duly elected and qualified. Acceptance of resignation shall not be necessary for it to be effective.

ARTICLE V CAPITAL STOCK

Section 5.1 Issuance. The shares of capital stock of the Corporation

shall be issued by the Board of Directors in such amounts, at such times, for such consideration, and on such terms and conditions as the Board shall deem advisable, subject to the provisions of the Articles of Incorporation of the Corporation and the further provisions of these Bylaws.

Section 5.2 Stock Certificates. The shares of the capital stock of the

Corporation shall be represented by certificates signed and sealed in accordance with the provisions of the laws of the State of Michigan. Certificates shall have a form and content complying with the laws of the State of Michigan and approved by the Board of Directors of the Corporation. Certificates of stock shall bear the signature of the President, and shall be signed by the Secretary, Assistant Secretary, or any other officer appointed by the Board of Directors for the purpose, to be known as an Authorized Officer. The signatures of the officers may be facsimiles if the certificate is countersigned by a transfer agent or registered by a registrar other than the Corporation itself or its employee. In case an officer who has signed or whose facsimile signature has been placed upon a certificate ceases to be such officer before the certificate is issued, it may be issued by the Corporation with the same effect as if he were such officer at the date of issue. Each certificate shall recite on its face the stock represented thereby is transferable only upon the books of the Corporation properly endorsed. A certificate

representing shares issued by a corporation which is authorized to issue shares of more than one class shall set forth on its face or back or state that the Corporation will furnish to a shareholder upon request and without charge a full statement of the designation, relative rights, preferences and limitations of the shares of each class authorized to be issued, and if the Corporation is authorized to issue any class of shares in series, the designation, relative rights, preferences and limitations of each series so far as the same have been prescribed and the authority of the Board to designate and prescribe the relative rights, preferences and limitations of other series.

Section 5.3 Transfers. Upon surrender to the Corporation or the transfer

agent of the Corporation of a certificate for shares duly endorsed or accompanied by proper evidence of succession, assignment or authority to transfer, it shall be the duty of the Corporation to issue a new certificate to the person entitled thereto, cancel the old certificate and record the transaction upon its books.

Section 5.4 Ownership. The Corporation shall be entitled to treat the

person in whose name any share of stock is registered as the owner thereof for purposes of dividends and other distributions in the course of business, or in the case of recapitalization, consolidation, merger, reorganization, sale of assets, liquidation or otherwise and for the purpose of votes, approvals and consents by shareholders, and for the purpose of notice to shareholders, and for all other purposes whatever, and shall not be bound to recognize any equitable or other claim to or interest in such shares on the part of any other person, whether or not the Corporation shall have notice thereof, save as expressly required by the laws of the State of Michigan.

Section 5.5 Replacement of Certificates. Upon the presentation to the

Corporation of a proper affidavit attesting the loss, destruction or mutilation of any certificate for shares of stock of the Corporation, the Board of Directors may direct the issuance of a new certificate in lieu of and to replace the certificate so alleged to be lost, destroyed and mutilated. The Board of Directors may require as a condition precedent to the issuance of a new certificate any or all of the following, to wit: (a) Additional evidence of the loss, destruction or mutilation claimed; (b) Advertisement of the loss in such manner as the Board of Directors may direct or approve; (c) A bond or agreement of indemnity, in such form and amount and with such surety (or without surety) as the Board of Directors may direct or approve; or (d) The order or approval of a court.

Section 5.6 Transfer Agent and Registrar. The Board of Directors may

appoint a transfer agent and a registrar for the registration of transfers of its securities.

Section 5.7 Regulations. The Board of Directors shall have power and

authority to make all such rules and regulations as the Board shall deem expedient

regulating the issue, transfer and registration of certificates for shares of this Corporation.

Section 5.8 Dividends. The Board of Directors, in its discretion from

time to time, may declare dividends upon the capital stock from the surplus of the Corporation as permitted by the MBCA, subject to the Articles of Incorporation.

Section 5.9 Reserves. Before payment of any dividend, there may be set

aside out of any funds of the Corporation available for dividends such sum or sums as the Directors from time to time, in their absolute discretion, think proper as a reserve or reserves to meet contingencies, or for equalizing dividends, or for repairing or maintaining any property of the Corporation, or for such other purpose as the Directors shall think conducive to the interest of the Corporation, and the Directors may modify or abolish any such reserve in the manner in which it was created.

ARTICLE VI INDEMNIFICATION OF OFFICERS, DIRECTORS,

EMPLOYEES AND AGENTS

Section 6.1 Indemnification of Directors and Officers: Claims by Third

Parties. The Corporation shall, to the fullest extent authorized or permitted

by the MBCA or other applicable law, as the same presently exists or may hereafter be amended, indemnify a director or officer (the "Indemnitee") who was or is a party or is threatened to be made a party to a threatened, pending, or completed action, suit, or proceeding, whether civil, criminal, administrative, or investigative and whether formal or informal, other than an action by or in the right of the Corporation, by reason of the fact that he or she is or was a director, officer, employee or agent of the Corporation, or is or was serving at the request of the Corporation as a director, officer, partner, trustee, employee, or agent of another foreign or domestic corporation, partnership, joint venture, trust, or other enterprise, whether for profit or not, against expenses, including attorneys' fees, judgments, penalties, fines, and amounts paid in settlement actually and reasonably incurred by him or her in connection with the action, suit, or proceeding, if the Indemnitee acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the Corporation or its shareholders, and with respect to a criminal action or proceeding, if the Indemnitee had no reasonable cause to believe his or her conduct was unlawful. The termination of an action, suit or proceeding by judgment, order, settlement, conviction, or upon a plea of nolo contendere or its equivalent, does not, of itself, create a presumption that the Indemnitee did not act in good faith and in a manner which he or she reasonably believed to be in or not opposed to the best interests of the Corporation or its shareholders, and, with respect to a criminal action or proceeding, had reasonable cause to believe that his or her conduct was unlawful.

Section 6.2 Indemnification of Directors and Officers: Claims Brought By

or In the Right of the Corporation. The Corporation shall, to the fullest

extent authorized or permitted by the MBCA or other applicable law, as the same presently exists or may hereafter be amended, indemnify a director or officer (the "Indemnitee") who was or is a party to or is threatened to be made a party to a threatened, pending, or completed action or suit by or in the right of the Corporation to procure a judgment in its favor by reason of the fact that he or she is or was a director, officer, employee or agent of the Corporation, or is or was serving at the request of the Corporation as a director, officer, partner, trustee, employee, or agent of another foreign or domestic corporation, partnership, joint venture, trust, or other enterprise, whether for profit or not, against expenses, including actual and reasonable attorneys' fees, and amounts paid in settlement incurred by the person in connection with the action or suit, if the Indemnitee acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the Corporation or its shareholders. However, indemnification under this Section shall not be made for a claim, issue, or matter in which the Indemnitee has been found liable to the Corporation unless and only to the extent that the court in which the action or suit was brought has determined upon application that, despite the adjudication of liability but in view of all circumstances of the case, the Indemnitee is fairly and reasonably entitled to indemnification for the expenses which the court considers proper.

Section 6.3 Actions by the Indemnitee. Notwithstanding the provisions of

Sections 6.1 and 6.2, the Corporation shall not indemnify an Indemnitee in connection with any action, suit, proceeding or claim (or part thereof) brought or made by such Indemnitee; unless such action, suit, proceeding or claim (or part thereof) (i) was authorized by the Board of Directors of the Corporation, or (ii) was brought or made to enforce this Article and such Indemnitee has been successful in such action, suit, proceeding or claim (or part thereof).

Section 6.4 Approval of Indemnification. An indemnification under

Sections 6.1 or 6.2 hereof, unless ordered by a court, shall be made by the Corporation only as authorized in the specific case upon its determination that indemnification of the Indemnitee is proper in the circumstances because such Indemnitee has met the applicable standard of conduct set forth in Sections 6.1 and 6.2. This determination shall be made in any of the following ways:

(a) By a majority vote of a quorum of the Board consisting of Directors who were not parties to the action, suit, or proceeding.

(b) If the quorum described in subdivision (a) is not obtainable, then by a majority vote of its committee of Directors who are not parties to the action. The committee shall consist of not less than two (2) disinterested Directors.

(c) By independent legal counsel in a written opinion.

(d) By the shareholders.

Section 6.5 Advancement of Expenses. Expenses incurred in defending a

civil or criminal action, suit, or proceeding described in Section 6.1 or 6.2 above shall be paid by the Corporation in advance of the final disposition of the action, suit, or proceeding upon receipt of an undertaking by or on behalf of the Indemnatee to repay the expenses if it is ultimately determined that the Indemnatee is not entitled to be indemnified by the Corporation. The undertaking shall be by unlimited general obligation of the person on whose behalf advances are made but need not be secured.

Section 6.6 Partial Indemnification. If an Indemnatee is entitled to

indemnification under Section 6.1 or 6.2 for a portion of expenses including attorneys' fees, judgments, penalties, fines, and amounts paid in settlement, but not for the total amount thereof, the Corporation shall indemnify the Indemnatee for the portion of the expenses, judgments, penalties, fines, or amounts paid in settlement for which the Indemnatee is entitled to be indemnified.

Section 6.7 Indemnification of Employees and Agents. Any person who is

not covered by the foregoing provisions of this Article and who is or was an employee or agent of the Corporation, or is or was serving at the request of the Corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise, may be indemnified to the fullest extent authorized or permitted by the MBCA or other applicable law, as the same exists or may hereafter be amended, but in the case of any such amendment, only to the extent such amendment permits the Corporation to provide broader indemnification rights than before such amendment, but in any event only to the extent authorized at any time or from time to time by the Board of Directors.

Section 6.8 Other Rights of Indemnification. The indemnification or

advancement of expenses provided under Sections 6.1 to 6.7 is not exclusive of other rights to which a person seeking indemnification or advancement of expenses may be entitled under the Articles of Incorporation, Bylaws, or a contractual agreement. However, the total amount of expenses advanced or indemnified from all sources combined shall not exceed the amount of actual expenses incurred by the person seeking indemnification or advancement of expenses. The indemnification provided for in Sections 6.1 to 6.7 continues as to a person who ceases to be a director, officer, employee, or agent and shall inure to the benefit of the heirs, executors, and administrators of the person.

Section 6.9 Definitions. "Other enterprises" shall include employee

benefit plans; "fines" shall include any excise taxes assessed on a person with respect to an employee benefit plan; and "serving at the request of the corporation" shall include any service as a director, officer, employee, or agent of the corporation which imposes duties on, or involves services by, the director, officer, employee,

or agent with respect to an employee benefit plan, its participants or beneficiaries; and a person who acted in good faith and in a manner he or she reasonably believed to be in the interest of the participants and beneficiaries of an employee benefit plan shall be considered to have acted in a manner "not opposed to the best interests of the corporation or its shareholders" as referred to in Sections 6.1 and 6.2.

Section 6.10 Application to a Resulting or Surviving Corporation or

Constituent Corporation. The definition for "corporation" found in Section 569

of the MBCA, as the same exists or may hereafter be amended, is and shall be, specifically excluded from application to this Article. The indemnification and other obligations of the Corporation set forth in this Article shall be binding upon any resulting or surviving corporation after any merger or consolidation of the Corporation. Notwithstanding anything to the contrary contained herein or in Section 569 of the MBCA, no person shall be entitled to the indemnification and other rights set forth in this Article for acting as a director or officer of another corporation prior to such other corporation entering into a merger or consolidation with the Corporation.

Section 6.11 Contract With the Corporation. The right to indemnification

conferred in this Article VI shall be deemed to be a contract between the Corporation and each director or officer who serves in any such capacity at any time while this Article VI is in effect, and any repeal or modification of any such law or of this Article VI shall not affect any rights or obligations then existing with respect to any state of facts then or theretofore existing or any action, suit or proceeding theretofore or thereafter brought or threatened based in whole or in part upon any such state of facts. In the event this Article is repealed or modified, the Corporation shall give written notice thereof to the directors and officers and any such repeal or modification shall not be effective for a period of sixty (60) days after such notice is delivered.

Section 6.12 Liability Insurance. The Corporation shall have the power to

purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the Corporation or is or was serving at the request of the Corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise against any liability asserted against and incurred by such person in any such capacity or arising out of such person's status as such, regardless of whether the Corporation would have the power to indemnify such person against such liability under the provisions of the MBCA.

Section 6.13 Severability. Each and every paragraph, sentence, term and

provision of this Article VI shall be considered severable in that, in the event a court finds any paragraph, sentence, term or provision to be invalid or unenforceable, the validity and enforceability, operation, or effect of the remaining paragraphs, sentences, terms, or provisions shall not be affected, and this

Article VI shall be construed in all respects as if the invalid or unenforceable matter had been omitted.

Section 6.14 Enforcement. If a claim under this Article is not paid in

full by the Corporation within thirty days after a written claim has been received by the Corporation, the claimant may at any time thereafter bring suit against the Corporation to recover the unpaid amount of the claim, and, if successful in whole or in part, the claimant shall be entitled to be paid also the expense of prosecuting such claim. It shall be a defense to any such action (other than an action brought to enforce a claim for expenses incurred in defending any proceeding in advance of its final disposition where the required undertaking, if any is required, has been tendered to the Corporation) that the claimant has not met the standards of conduct which make it permissible under the MBCA for the Corporation to indemnify the claimant for the amount claimed, but the burden of proving such defense shall be on the Corporation. Neither the failure of the Corporation (including its Board of Directors, a committee thereof, independent legal counsel, or its shareholders) to have made a determination prior to the commencement of such action that indemnification of the claimant is proper in the circumstances because such claimant has met the applicable standard of conduct set forth in the MBCA nor an actual determination by the Corporation (including its Board of Directors, a committee thereof, independent legal counsel, or its shareholders) that the claimant has not met applicable standard of conduct, shall be a defense to the action or create a presumption that the claimant has not met the applicable standard of conduct.

ARTICLE VII EXECUTION OF PAPERS

The officers of the Corporation may sell any or all of its holdings of stock, bonds, or securities of other corporations, or government securities; sign all deeds, mortgages, assignments of mortgages, discharges of mortgages, bills of sale, leases and other conveyances and transactions of any interest in property, real, personal or mixed, to the extent that the Board of Directors of the Corporation may from time to time specify in resolutions approved by the Board. The Board may in any instance designate the officers and agents who shall have authority to execute any contract, conveyance or other instrument on behalf of the Corporation, and may also ratify and affirm such execution. Any such instrument or document shall be binding on the Corporation if executed by the President or a Vice President. In addition, any such instrument or document shall be binding on the Corporation if signed by any other officer designated by the Board on behalf of the Corporation.

ARTICLE VIII BANKING

Section 8.1 Bank Accounts. The Board of Directors shall by resolution designate the bank or banks in which the funds of the Corporation shall be deposited, and such funds shall be deposited in the name of the Corporation and

shall be subject to checks drawn as authorized by resolution of the Board of Directors.

Section 8.2 Borrowing. To the extent authorized by law, the Corporation

may, wherever its general interests and corporate purpose require the same, borrow money and issue its promissory notes, debentures or bonds for the repayment thereof with interest, and may in like case mortgage, pledge or encumber its property as security for its debts or other lawful engagements.

ARTICLE IX VOTING STOCK IN OTHER CORPORATIONS

Unless otherwise ordered by the Board of Directors, the President shall have full power and authority on behalf of the Corporation to attend and to act and to vote at any meetings of shareholders of any corporation in which this Corporation may hold stock, and at any such meeting shall possess and may exercise any and all of the rights and powers incident to the ownership of such stock, PROVIDED, HOWEVER, that such rights shall be exercised in the best interests of this Corporation. The Board of Directors may, by resolution, from time to time confer like powers upon any other person or persons, but the same shall not be effective unless actually received by such other corporation prior to the meeting of shareholders in which such other person is to act. The President, or in his absence or disability, a Vice President of the Corporation, may authorize from time to time the signature and issuance of proxies to vote such stock of other corporations owned by this Corporation, and all such proxies shall be signed in the name of this Corporation by the President or Vice President and the Secretary or Assistant Secretary, or by any two officers authorized by the Board of Directors.

ARTICLE X SUBSIDIARIES

The Board of Directors may establish, reorganize and/or dissolve wholly- or partly-owned subsidiaries of the Corporation. The Articles of Incorporation and Bylaws of any such subsidiary shall not, without approval of the shareholders of this Corporation, substantially differ from the Articles of Incorporation and Bylaws, respectively, of this Corporation.

ARTICLE XI FISCAL YEAR

Except as from time to time otherwise provided by the Board of Directors, the fiscal year of the Corporation shall end on the last day of June.

ARTICLE XII CORPORATE BOOKS AND RECORDS

The Corporation shall keep books and records of account and minutes of the proceedings of its shareholders, Board of Directors and executive committees, if any. The books, records and minutes may be kept outside this state. The Corporation shall keep at its registered office, or at the office of its

transfer agent within or without this state, records containing the names and addresses of all shareholders, the number, class and series of shares held by each and the dates when they respectively became holders of record thereof. Any of such books, records or minutes may be in written form or in any other form capable of being converted into written form within a reasonable time. The Corporation shall convert into written form without charge any such record not in such form, upon written request of a person entitled to inspect them.

ARTICLE XIII AMENDMENTS

Except as otherwise expressly provided in the Articles of Incorporation or in these Bylaws, these Bylaws may be altered, amended or repealed by any duly adopted resolution of the Board of Directors or at any annual or special meeting of the shareholders. The Board of Directors, however, shall not adopt or alter any Bylaws fixing the number, qualifications, classifications or term of office of Directors. If the amendment is to be adopted at a special meeting of the shareholders, the notice thereof shall specify the subject matter of the proposed alteration, amendment or repeal and the Articles of these Bylaws to be affected thereby. Bylaws adopted by the Directors may be altered or repealed by the Directors or shareholders. Provided, further, that neither the time nor the place for the election of Directors shall be changed within sixty (60) days next preceding the day on which any election of Directors is to be held, and provided further that a notice of any such change shall be given to each shareholder at least twenty (20) days before the next election is held, in person or by letter mailed to his last known post office address.

ATTEST:

/s/ TODD E. SIMPSON

TODD E. SIMPSON, SECRETARY

Includes amendments approved through April 30, 1996

AASTROM BIOSCIENCES, INC.

AMENDED AND RESTATED
INVESTORS' RIGHTS AGREEMENT

April 7, 1992

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AASTROM BIOSCIENCES, INC.
AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT

THIS AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT (the "Agreement") is entered into as of April 7, 1992, by and among AASTROM BioSciences, Inc., a Michigan corporation formerly doing business as Ann Arbor Stromal, Inc. (the "Company"), the investors listed on the Schedule of Investors attached hereto as Exhibit A (individually, an "Investor" and collectively, the "Investors"), as that exhibit may be amended from time to time, Stephen G. Emerson, Bernhard O. Palsson and Michael F. Clarke (individually, a "Founder" and collectively, the "Founders"), Dr. R. Douglas Armstrong ("Armstrong") and the Regents of the University of Michigan, a constitutional corporation of the State of Michigan (the "University"). For the purposes of this Agreement, the Founders and Armstrong shall be collectively referred to as the "Option Holders."

RECITALS:

A. The Company has issued shares of its Common Stock to the University and has granted, and may, in the future, grant, stock options to the Founders pursuant to the Company's Stock Option Plans.

B. The Company has issued two million five hundred thousand (2,500,000) shares of its Series A Preferred Stock to certain of the Investors (the "Series A Investors") pursuant to that certain Series A Preferred Stock Purchase Agreement, dated as of August 17, 1989.

C. Pursuant to that certain Investors' Rights Agreement dated August 17, 1989 among the Company, the Series A Investors, the Founders and the University (the "Investors' Rights Agreement"), the Company granted certain rights and the parties made certain covenants with respect to the Series A Preferred Stock and the Common Stock of the Company.

D. Since the execution of the Investors' Rights Agreement, the Company has engaged Armstrong as its president and has granted, and may, in the future, grant, stock options to Armstrong pursuant to the Company's Stock Option Plans.

E. Certain of the Investors (the "Series B Investors") are purchasing concurrently herewith three million thirty thousand (3,030,000) shares of Series B Preferred Stock and desire to obtain the same rights as are contained in the Investors' Rights Agreement.

F. The Company, the Series A Investors, the Founders and the University desire to grant to the Series B Investors and

Armstrong the same rights as were granted under the Investors' Rights Agreement and to amend and restate such Agreement.

G. The parties intend that this Agreement supersede the Investors' Rights Agreement and, in that regard, the parties to the Investors' Rights Agreement will waive certain rights contained in such Investors' Rights Agreement, specifically (i) the right of first refusal to purchase on a pro rata basis the shares of Series B Preferred Stock being issued concurrently herewith and (ii) the right of the University to obtain certain warrants to purchase Common Stock.

AGREEMENT:

NOW, THEREFORE, in consideration of the mutual promises, representations, warranties, covenants, and conditions set forth in this Agreement and in the agreements pursuant to which the Investors acquired their securities in the Company, the parties mutually agree as follows:

SECTION 1

Definitions

1.1 Certain Definitions. As used in this Agreement, the following terms shall have the following respective meanings:

"Commission" shall mean the Securities and Exchange Commission or any other federal agency at the time administering the Securities Act.

"Securities Act" shall mean the Securities Act of 1933, as amended, or any similar federal statute, and the rules and regulations of the Commission thereunder, all as the same shall be in effect at the time.

"Exchange Act" shall mean the Securities Exchange Act of 1934, as amended, or any similar federal statute and the rules and regulations of the Commission thereunder, all as the same shall be in effect at the time.

"Restricted Securities" shall mean the securities of the Company required to bear the legend set forth in Section 2.2 hereof.

"Shares" shall mean the securities of the Company held by the Investors as described on Exhibit A.

"Options" shall mean any and all stock options granted to any of the

Option Holders, as of the date hereof or thereafter, pursuant to any stock option plan or agreement approved by the Company's Board of Directors.

"Registrable Securities" shall mean any shares of the Company's Common

Stock (i) issued or issuable pursuant to the conversion of the Shares, (ii) held as of August 17, 1989 by the University, (iii) issued or issuable upon exercise of the Options, or (iv) issued as a dividend or other distribution with respect to, or in exchange or in replacement of, the Shares or such Common Stock or Preferred Stock, excluding in all cases, however (including exclusion from the calculation of the number of outstanding Registrable Securities), any Registrable Securities sold by a person in a transaction, including a transaction pursuant to a registration statement under Section 2 hereof or a transaction pursuant to Rule 144, in which such person's rights under Section 2 are not transferred.

The terms "register," "registered" and "registration" refer to a

registration effected by preparing and filing a registration statement in compliance with the Securities Act, and the declaration or ordering of the effectiveness of such registration statement.

"Registration Expenses" shall mean all expenses incurred by the Company in

complying with Sections 2.4, 2.5 and 2.6 hereof, including, without limitation, all registration and filing fees, printing expenses, fees and disbursements of counsel for the Company, reasonable fees and disbursements of a single special counsel for the Holders, blue sky fees and expenses, and the expense of any special audits incident to or required by any such registration other than a registration pursuant to Section 2.4, in which event such special audit expenses will be paid by the holders of the securities so registered pro rata on the basis of the number of shares so registered, (but excluding the compensation of regular employees of the Company which shall be paid in any event by the Company).

"Holder" shall mean any holder of outstanding Registrable Securities or

securities convertible into or exercisable for Registrable Securities.

"Initiating Holders" shall mean the holder or holders of fifty percent

(50%) or more of the combination of the then outstanding Shares and Common Stock issued upon conversion of the Shares.

"New Securities" shall mean any Common Stock or Preferred Stock of the

Company, whether now authorized or not, and rights, options or warrants to purchase said Common Stock or Preferred Stock, and securities of any type whatsoever that are,

or may become, convertible into said Common Stock or Preferred Stock; provided, however, that "New Securities" does not include (i) securities issuable upon conversion of or with respect to the Shares; (ii) securities offered to the public pursuant to a registration statement filed under the Securities Act; (iii) securities issued pursuant to the acquisition of another corporation by the Company by merger, purchase of substantially all of the assets, or other reorganization whereby the Company (or the Company's shareholders immediately prior to such event) owns (or own, on a pro rata basis) not less than fifty-one percent (51%) of the voting power of such corporation immediately after such event; (iv) shares of the Company's Common Stock (or related options) issued to employees, officers or directors of or consultants to the Company (including, but not limited to, shares issued to the Option Holders) pursuant to any employee stock offering, plan, or arrangement approved by the Board of Directors; or (v) shares of the Company's Common Stock or Preferred Stock issued in connection with any stock split, stock dividend, or recapitalization by the Company.

SECTION 2

Restrictions on Transferability of
Securities; Compliance with Securities Act

2.1 Restrictions on Transferability. The Shares, any Common Stock into

which the Shares may be convertible, the Common Stock and Options held by the Option Holders and the University shall not be transferable except upon the conditions specified in this Agreement, which conditions are intended to insure compliance with the provisions of the Securities Act, or, in the case of Section 2.12 hereof, to assist in an orderly distribution. Each Investor will cause any proposed transferee of the Shares (or of the Common Stock into which the Shares may be convertible) held by an Investor to agree to take and hold such securities subject to the provisions and upon the conditions specified in this Agreement. Each Option Holder and the University will cause any proposed transferee of Common Stock held by an Option Holder or the University, respectively, to agree to take and hold such securities subject to the provisions and upon the conditions specified in this Agreement.

2.2 Restrictive Legend. Each certificate representing (i) the Shares,

(ii) shares of the Company's Common Stock issued upon conversion of the Shares, (iii) any securities issued in respect of the Shares or such Common Stock, or (iv) shares of the Company's Common Stock, Preferred Stock or Options held by an Option Holder or the University shall (unless otherwise permitted by the provisions of Section 2.3 below) be stamped or otherwise imprinted with a legend in the following form (in addition to any legend required under applicable state securities laws):

THE SECURITIES EVIDENCED BY THIS CERTIFICATE HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED, HAVE BEEN ISSUED PURSUANT TO A CLAIM OF EXEMPTION FROM THE REGISTRATION OR QUALIFICATION PROVISIONS OF SUCH ACT AND APPLICABLE STATE SECURITIES LAWS, AND MAY NOT BE SOLD, TRANSFERRED, ASSIGNED OR HYPOTHECATED, EXCEPT AS PERMITTED PURSUANT TO 17 C.F. R SECTION 230.144, OR THERE IS IN EFFECT A REGISTRATION STATEMENT UNDER SUCH ACT AND APPLICABLE STATE SECURITIES LAWS COVERING SUCH SECURITIES, OR THE ISSUER RECEIVES AN OPINION OF COUNSEL FOR THE HOLDER OF SUCH SECURITIES REASONABLY SATISFACTORY TO THE ISSUER, STATING THAT SUCH SALE, TRANSFER, ASSIGNMENT OR HYPOTHECATION IS EXEMPT FROM THE REGISTRATION, QUALIFICATION AND PROSPECTUS DELIVERY REQUIREMENTS OF SUCH ACT AND APPLICABLE STATE SECURITIES LAWS.

SALE OR OTHER TRANSFER OF THE SECURITIES EVIDENCED BY THIS CERTIFICATE IS ALSO RESTRICTED BY THE TERMS OF STOCK PURCHASE AGREEMENTS BETWEEN THE ISSUER AND THE PURCHASERS LISTED THEREIN AND BY THE TERMS OF THAT CERTAIN AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT BETWEEN THE ISSUER AND THE OTHER PARTIES THERETO. COPIES OF SUCH DOCUMENTS MAY BE OBTAINED AT NO COST BY WRITTEN REQUEST MADE BY THE HOLDER OF THIS CERTIFICATE TO THE SECRETARY OF THE ISSUER AT ITS PRINCIPAL EXECUTIVE OFFICES.

2.3 Notice of Proposed Transfers. The holder of each certificate

representing Restricted Securities by acceptance thereof agrees to comply in all respects with the provisions of this Section 2.3. Prior to any proposed transfer of any Restricted Securities unless there is in effect a registration statement under the Securities Act covering the proposed transfer, the holder thereof shall give written notice to the Company of such holder's intention to effect such transfer. Each such notice shall describe the manner and circumstances of the proposed transfer in sufficient detail, and shall be accompanied (except in the following cases, with respect to which the requirements set forth in the balance of this sentence need not be complied with: transactions in compliance with Rule 144 so long as the Company is furnished with evidence of compliance with such Rule, including without limitation, an opinion of counsel to such effect; transactions involving the pro rata distribution of Restricted Securities by any holder which is a general or limited partnership to any of its partners, or retired partners, or to the estate of any of its partners or retired partners; transactions involving the transfer of Restricted Securities by any holder who is an individual to his family members or to a trust for the benefit of such holder or his family members; or transfers not involving a change in beneficial ownership) by which the requirements set forth in the balance of this sentence need not be complied with: transactions in compliance with Rule 144 so long as the Company is furnished with evidence of compliance with such Rule, including without limitation, an opinion of counsel to such effect; transactions involving the pro rata distribution of Restricted Securities by any holder which is a general or limited partnership to any of its partners, or retired partners, or to the estate of any of its partners or retired partners; transactions involving the transfer of Restricted Securities by any holder who is an individual to his family members or to a trust for the benefit of such holder or his family members; or transfers not involving a change in beneficial ownership) by

either (i) an unqualified written opinion of legal counsel who shall be reasonably satisfactory to the Company addressed to the Company and reasonably satisfactory in form and substance to the Company's counsel, to the effect that the proposed transfer of the Restricted Securities may be effected without registration under the Securities Act, (ii) a "no action" letter from the Commission to the effect that the distribution of such securities without registration will not result in a recommendation by the staff of the Commission that action be taken with respect thereto, or (iii) such other showing that may be reasonably satisfactory to legal counsel to the Company, whereupon the holder of such Restricted Securities shall be entitled to transfer such Restricted Securities in accordance with the terms of the notice delivered by the holder to the Company. Each certificate evidencing the Restricted Securities transferred as above provided shall bear the appropriate restrictive legend set forth in Section 2.2 above, except that such certificate shall not bear such restrictive legend if in the opinion of counsel for the Company such legend is not required in order to establish compliance with any provisions of the Securities Act.

2.4 Requested Registration.

(a) Request for Registration. In case the Company shall receive from

Initiating Holders after the first anniversary of the Company's initial public offering, or after January 1, 1994, whichever shall occur first, a written request that the Company effect any registration (other than a registration on Form S-3 or any related form of Registration Statement) covering the registration of at least twenty percent (20%) of their Registrable Securities (or a lesser percentage if the anticipated aggregate offering price net of underwriting discounts and commissions, would exceed \$2,000,000), the Company will:

(i) promptly give written notice of the proposed registration to all other Holders; and

(ii) as soon as practicable, use its diligent best efforts to effect such registration (including, without limitation, the execution of an undertaking to file post-effective amendments, appropriate qualification under applicable blue sky or other state securities laws and appropriate compliance with applicable regulations issued under the Securities Act) as may be so requested and as would permit or facilitate the sale and distribution of all or such portion of such Registrable Securities as are specified in such request, together with all or such portion of the Registrable Securities of any Holder or Holders joining in such request as are specified in a written request given within fifteen (15) days after receipt of such written notice from the Company; provided that prior to the Company's initial public offering, no Initiating Holder may make a written request that the Company effect any registration

unless the aggregate anticipated offering price would exceed, net of underwriting discounts and commissions, \$5,000,000; and provided further that the Company shall not be obligated to take any action to effect any such registration, qualification or compliance pursuant to this Section 2.4:

(A) In any particular jurisdiction in which the Company would be required to execute a general consent to service of process in effecting such registration, qualification or compliance unless the Company is already subject to service in such jurisdiction and except as may be required by the Securities Act; or

(B) During the period starting with the date sixty (60) days prior to the Company's estimated date of filing of, and ending on a date six (6) months following the effective date of, a registration statement pertaining to an underwritten public offering of securities filed for the account of the Company (other than a registration relating solely to employee benefit plans or a registration relating solely to a Commission Rule 145 transaction), provided that the Company is actively employing in good faith all reasonable efforts to cause such registration statement to become effective and the Company's estimate of the date of filing such registration statement is made in good faith; or

(C) After the Company has effected one registration pursuant to this Section 2.4 and such registration has been declared or ordered effective.

Subject to the foregoing clauses (A), (B) and (C) and to Section 2.4(c), the Company shall file a registration statement covering the Registrable Securities so requested to be registered as soon as practicable after receipt of the request of the Initiating Holders.

(b) Underwriting. If the Holders intend to distribute the Registrable

Securities covered by their request by means of an underwriting, they shall so advise the Company as a part of their request made pursuant to Section 2.4 and the Company shall include such information in the written notice referred to in Section 2.4(a)(i). The right of any Holder to registration pursuant to Section 2.4 shall be conditioned upon such Holder's participation in such underwriting and the inclusion of such Holder's Registrable Securities in the underwriting to the extent requested (unless otherwise mutually agreed by a majority in interest of the Holders and such Holder) to the extent provided herein. The Company shall (together with all Holders proposing to distribute their securities through such underwriting) enter into an underwriting agreement in customary form with the underwriter or underwriters of recognized national standing selected for such underwriting by the Company with the

approval of a majority in interest of the participating Holders.

Notwithstanding any other provision of this Section 2.4, if the underwriter determines that marketing factors require a limitation of the number of shares to be underwritten or that applicable state law prohibits the registration of any Holders' Registrable Securities because of the failure or lack of obligation of such Holder to contribute to the cost of such registration and so advises the participating Holders in writing, then the Company shall so advise all Holders (except those Holders who have indicated to the Company their decision not to distribute any of their Registrable Securities through such underwriting) and the number of shares of Registrable Securities that may be included in the registration and underwriting shall be allocated among all such Holders in proportion, as nearly as practicable, to the respective amounts of Registrable Securities owned by such Holders at the time of filing the registration statement. No Registrable Securities excluded from the underwriting by reason of the underwriter's marketing limitation or such state law shall be included in such registration.

If any Holder disapproves of the terms of the underwriting, such person may elect to withdraw therefrom by written notice to the Company, the underwriter and the other Holders. The Registrable Securities and/or other securities so withdrawn from such underwriting shall also be withdrawn from such registration; provided, however, that, if by the withdrawal of such Registrable Securities a greater number of Registrable Securities held by other Holders may be included in such registration (up to the maximum of any limitation imposed by the underwriters), then the Company shall offer to all Holders who have included Registrable Securities in the registration the right to include additional Registrable Securities in the same proportion used above in determining the underwriter limitation.

If the underwriter has not limited the number of Registrable Securities to be underwritten, the Company may include securities for its own account or the account of others in such registration if the underwriter so agrees and if the number of Registrable Securities which would otherwise have been included in such registration and underwriting will not thereby be limited.

(c) Delay of Registration. If the Company shall furnish to the

Holders a certificate signed by the President of the Company stating that, in the good faith judgment of the Board of Directors of the Company, it would be seriously detrimental to the Company and its shareholders for such registration statement to be filed on or before the date filing would be required and it is therefore essential to defer the filing of such registration statement, then the Company may direct that such request for registration be delayed not in excess of one hundred

and fifty (150) days, such right to delay a request to be exercised by the Company not more than twice in any one-year period.

2.5 Company Registration.

(a) If at any time or from time to time, the Company shall determine to register any of its Common Stock, for its own account or for the account of others (other than the Holders), other than a registration relating solely to employee benefit plans or a registration relating solely to a Commission Rule 145 transaction or a registration on any registration form which does not include substantially the same information as would be required to be included in a registration statement covering the sale of Registrable Securities, the Company will:

(i) promptly give to each Holder written notice thereof (which shall include a list of the jurisdictions in which the Company intends to attempt to qualify such securities under the applicable blue sky or other state securities laws); and

(ii) include in such registration (and any related qualification under blue sky laws or other compliance), and in any underwriting involved therein, all the Registrable Securities specified in a written request or requests, made within twenty (20) days after receipt of such written notice from the Company, by any Holder or Holders. The rights of a particular Holder under this Section 2.5 shall terminate five (5) years after the effective date of the Company's initial underwritten public offering.

(b) Underwriting. If the registration of which the Company gives

notice is for a registered public offering involving an underwriting, the Company shall so advise the Holders as a part of the written notice given pursuant to Section 2.5(a)(i). In such event the right of any Holder to registration pursuant to Section 2.5 shall be conditioned upon such Holder's participation in such underwriting and the inclusion of such Holder's Registrable Securities in the underwriting to the extent provided herein. All Holders proposing to distribute their securities through such underwriting shall (together with the Company and the other holders distributing their securities through such underwriting) enter into an underwriting agreement in customary form with the underwriter or underwriters selected for such underwriting by the Company.

Notwithstanding any other provision of this Section 2.5, if the underwriter determines that marketing factors require a limitation of the number of shares to be underwritten, the underwriter may exclude some or all Registrable Securities from such registration and underwriting. The Company shall so advise

all Holders (except those Holders who have indicated to the Company their decision not to distribute any of their Registrable Securities through such underwriting), and the number of shares of Registrable Securities that may be included in the registration and underwriting shall be allocated among such Holders in proportion, as nearly as practicable, to the respective amounts of Registrable Securities owned by such Holders at the time of filing the registration statement. No Registrable Securities excluded from the underwriting by reason of the underwriter's marketing limitation shall be included in such registration.

If any Holder disapproves of the terms of any such underwriting, such person may elect to withdraw therefrom by written notice to the Company and the underwriter. The Registrable Securities and/or other securities so withdrawn from such underwriting shall also be withdrawn from such registration; provided, however, that, if by the withdrawal of such Registrable Securities a greater number of Registrable Securities held by other Holders may be included in such registration (up to the maximum of any limitation imposed by the underwriters), then the Company shall offer to all Holders who have included Registrable Securities in the registration the right to include additional Registrable Securities in the same proportion used above in determining the underwriter limitation.

2.6 Registrations on Form S-3.

(a) If (i) Holders of Registrable Securities request in writing (specifying that the request is being made pursuant to this Section 2.6) that the Company file a registration statement on Form S-3 (or any successor form to Form S-3 regardless of its designation) for a public offering of shares of Registrable Securities the reasonably anticipated aggregate proceeds of which would exceed \$500,000, and (ii) the Company is a registrant entitled to use Form S-3 to register such shares, and (iii) the Company has not filed a registration statement pursuant to this Section 2.6 within the twelve (12) months immediately prior to the requested filing date, then the Company shall cause such shares, and any additional shares included pursuant to Section 2.6(b), to be registered on Form S-3 (or any successor form to Form S-3).

(b) Prior to effecting a registration of Registrable Securities pursuant to Section 2.6(a), the Company shall (i) give to each Holder written notice of the intended registration and (ii) include in such registration any additional Registrable Securities specified in any written request or requests by additional Holders received within fifteen (15) days after such written notice is given.

(c) All expenses incurred in connection with any registrations requested pursuant to this Section 2.6 including, without limitation, all registration, qualification, printing, and accounting fees, and fees and disbursements of counsel for the Company, shall be borne by the Holder or Holders participating in such registration on the basis of the amount of securities so registered.

(d) The Holders' rights to registration under this Section 2.6 are in addition to, and not in lieu of, their rights to registration under Sections 2.4 and 2.5.

2.7 Expenses of Registration.

(a) All Registration Expenses (exclusive of underwriting discounts and commissions and more than a single special counsel to the selling shareholders) incurred in connection with the first registration pursuant to Section 2.4 shall be borne by the Company. The Company shall not, however, be required to pay for expenses of any registration proceeding begun pursuant to Section 2.4, the request of which has been subsequently withdrawn by the Initiating Holders (unless the withdrawal is based upon material adverse information concerning the Company of which the Initiating Holders were not aware at the time of such request and the Holders of a majority of Registrable Securities agree to forfeit their right to one requested registration pursuant to Section 2.4 in which event such right shall be forfeited by all Holders), in which case such expenses shall be borne by the holders of securities (including Registrable Securities) requesting such registration in proportion to the number of shares for which registration was requested and such registration shall not be counted as a registration pursuant to Section 2.4 for purposes of Section 2.4(a)(ii)(B).

(b) All Registration Expenses (exclusive of underwriting discounts and commissions and more than a single special counsel to the selling shareholders) incurred in connection with the first two registrations pursuant to Section 2.5 shall be borne by the Company. In each subsequent registration of Registrable Securities effected pursuant to Section 2.5, the Holders who include Registrable Securities in such registration shall bear any additional registration and qualification fees and expenses (including underwriters' discounts and commissions), and any additional costs and disbursements of counsel for the Company that result from the inclusion of the Registrable Securities in such registration, with such additional expenses of the registration being borne by all such Holders pro rata on the basis of the amount of Registrable Securities so registered; provided, however, that if any such cost or expense is attributable solely to one selling Holder and does not constitute a normal cost or expense of such a

registration, such cost or expense shall be allocated to that selling Holder. In addition, each selling Holder shall bear the fees and costs of its own counsel.

2.8 Registration Procedures. In the case of each registration,

qualification or compliance effected by the Company pursuant to this Section 2, the Company will keep each Holder advised in writing as to the initiation of each registration, qualification and compliance and as to the completion thereof. At its expense the Company will:

(a) Keep such registration, qualification or compliance effective for a period of one hundred and twenty (120) days or until the Holder or Holders have completed the distribution described in the registration statement relating thereto, whichever first occurs; and

(b) Furnish such number of prospectuses and other documents incident thereto as a Holder from time to time may reasonably request.

2.9 Indemnification.

(a) The Company will indemnify each Holder, each of its officers, directors, employees, agents, partners and legal counsel, and each person controlling such Holder, with respect to which registration, qualification or compliance has been effected pursuant to this Section 2, and each underwriter, if any, and each person who controls any underwriter against all claims, losses, damages and liabilities (or actions in respect thereof) arising out of or based on (i) any untrue statement (or alleged untrue statement) of a material fact contained in any prospectus, offering circular or other similar document (including any related registration statement, notification or the like) incident to any such registration, qualification or compliance, or based on any omission (or alleged omission) to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading in the light of the circumstances under which they were made, or (ii) any violation by the Company of any federal, state or common law rule or regulation applicable to the Company in connection with any such registration, qualification or compliance, and will reimburse each such Holder, each of its officers, directors, employees, agents, partners and legal counsel, and each person controlling such Holder, each such underwriter and each person who controls any such underwriter, for any legal and any other expenses reasonably incurred in connection with investigating or defending any such claim, loss, damage, liability or action, as incurred, provided that the Company will not be liable in any such case to the extent that any such claim, loss, damage, liability or expense arises out of or is based on any untrue statement or omission based upon written information furnished to the Company

by an instrument duly executed by such Holder or underwriter and specifically for use therein.

(b) Each Holder will, if Registrable Securities held by such Holder are included in the securities as to which such registration, qualification or compliance is being effected, indemnify the Company, each of its directors, officers, employees and agents each legal counsel and independent accountant of the Company, each underwriter, if any, of the Company's securities covered by such a registration statement, each person who controls the Company or such underwriter within the meaning of the Securities Act, and each other such Holder, each of its officers, directors, and partners and each person controlling such Holder, against all claims, losses, damages and liabilities (or actions in respect thereof) arising out of or based on any untrue statement (or alleged untrue statement) of a material fact contained in any such registration statement, prospectus, offering circular or other similar document, or any omission (or alleged omission) to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading in the light of the circumstances under which they were made, and will reimburse the Company, such Holders, such directors, officers, employees, agents, persons, underwriters or control persons for any legal or any other expenses reasonably incurred in connection with investigating or defending any such claim, loss, damage, liability or action, as incurred, in each case to the extent, but only to the extent, that such untrue statement (or alleged untrue statement) or omission (or alleged omission) is made in such registration statement, prospectus, offering circular or other document in reliance upon and in conformity with written information furnished to the Company by an instrument duly executed by such Holder and specifically for use therein; provided, however, that the obligations of such Holders hereunder shall be limited to an amount equal to the proceeds to each such Holder of Registrable Securities sold as contemplated herein.

(c) Each party entitled to indemnification under this Section 2.9 (the "Indemnified Party") shall give notice to the party required to provide indemnification (the "Indemnifying Party") promptly after such Indemnified Party has received written notice of any claim as to which indemnity may be sought, and shall permit the Indemnifying Party to assume the defense of any such claim or any litigation resulting therefrom, provided that counsel for the Indemnifying Party, who shall conduct the defense of such claim or litigation, shall be approved by the Indemnified Party (whose approval shall not unreasonably be withheld). The Indemnified Party may participate in such defense at such party's expense; provided, however, that the Indemnifying Party shall bear the expense of such defense of the Indemnified Party if representation of both parties by the same counsel would be inappropriate due to actual or potential conflicts of

interest. The failure of any Indemnified Party to give notice as provided herein shall relieve the Indemnifying Party of its obligations under this Section 2 only to the extent that such failure to give notice shall materially adversely prejudice the Indemnifying Party in the defense of any such claim or any such litigation. No Indemnifying Party, in the defense of any such claim or litigation, shall, except with the consent of each Indemnified Party, consent to entry of any judgment or enter into any settlement which does not include as an unconditional term thereof the giving by the claimant or plaintiff to such Indemnified Party of a release from all liability in respect to such claim or litigation (without any obligation of performance or admission by the Indemnified Party).

(d) Notwithstanding anything contained in this Section 2.9 to the contrary, the Company shall have the right and the ability to provide the necessary undertakings to the Commission in connection with any registration.

2.10 Information by Holder. The Holder or Holders of Registrable

Securities included in any registration shall furnish to the Company such information regarding such Holder or Holders and the distribution proposed by such Holder or Holders as the Company may request in writing and as shall be required in connection with any registration, qualification or compliance referred to in this Section 2.

2.11 Rule 144 Reporting. With a view to making available the benefits of

certain rules and regulations of the Commission which may at any time permit the sale of the Restricted Securities to the public without registration, after such time as a public market exists for the Common Stock of the Company, the Company agrees to:

(a) Use its best efforts to facilitate the sale of the Restricted Securities to the public, without registration under the Securities Act, pursuant to Rule 144 under the Securities Act, provided that this shall not require the Company to file reports under the Securities Act and the Exchange Act at any time prior to the Company's being otherwise required to file such reports.

(b) Use its best efforts to make and keep public information available, as those terms are understood and defined in Rule 144 under the Securities Act at all times after ninety (90) days after the effective date of the first registration under the Securities Act filed by the Company for an offering of its securities to the general public;

(c) Use its best efforts to then file with the Commission in a timely manner all reports and other documents required of the Company under the Securities Act and the Exchange

Act, as amended (at any time after it has become subject to such reporting requirements);

(d) So long as any Holder holds any Restricted Securities to furnish to the Holder forthwith upon request a written statement by the Company as to its compliance with the reporting requirements of said Rule 144 (at any time after ninety (90) days after the effective date of the first registration statement filed by the Company for an offering of its securities to the general public), and of the Securities Act and the Exchange Act (at any time after it has become subject to such reporting requirements), a copy of the most recent annual or quarterly report of the Company, and such other reports and documents so filed by the Company as a Holder may reasonably request in availing itself of any rule or regulation of the Commission allowing a Holder to sell any such securities without registration.

2.12 "Market Stand-off" Agreement. Each Holder of more than one percent

(1%) of the Company's outstanding voting stock agrees not to sell or otherwise transfer or dispose of any Common Stock (or other securities) of the Company held by it during the one hundred fifty (150) day period following the effective date of a registration statement of the Company filed under the Securities Act if so requested by the Company and underwriter of Common Stock (or other securities) of the Company, provided that:

(a) such agreement shall apply only to the first underwritten registered public offering of the Company; and

(b) all officers and directors of the Company and all other holders of at least one percent (1%) of the Company's voting securities enter into similar agreements. The Company may impose stop-transfer instructions with respect to the shares (or securities) subject to the foregoing restriction until the end of such period.

2.13 Transfer of Registration Rights. The rights to cause the Company to

register securities granted under this Section 2 may be assigned or otherwise conveyed by (i) any Holder (other than an Option Holder) only to a transferee or assignee in a private transaction to whom not less than 100,000 shares of Registrable Securities are conveyed (as presently constituted and subject to subsequent adjustments for stock splits, stock dividends, reverse stock splits, and the like) or (ii) an Option Holder in the manner set forth above or otherwise only to another Holder or to a family member or to a trust for the benefit of such Option Holder or family members in a private transaction to whom not less than 20,000 shares of Registrable Securities are conveyed (as presently constituted and subject to subsequent adjustments as set forth above); provided that the Company is given written notice by such transferee at the time of or within

a reasonable time after said transfer, stating the name and address of said transferee and said transferee's agreement to be bound by the provisions of this Agreement.

2.14 Suspension of Registration Rights. The registration rights granted

pursuant to this Section 2 shall not be exercisable by any Holder during the period in which such Holder has the ability to sell all of the Shares held by such Holder under Rule 144 or Rule 144A during a single ninety (90) day period.

2.15 Certain Limitations in Connection with Future Grants of Registration

Rights. From and after the date of this Agreement, the Company shall not enter

into any agreement with any holder or prospective holder of any securities of the Company providing for the granting to such holder of registration rights unless such agreement:

(a) includes the equivalent of Section 2.12 as a term; and

(b) contains provisions substantially similar to those contained in Sections 2.4(b) and 2.5(b) with respect to the allocation of Registrable Securities to be included in an underwritten public offering if marketing factors require a limitation on the number of such securities to be included.

Notwithstanding the foregoing, from and after the date hereof the Company shall not enter into any agreement with any person or persons providing for the granting to such holder registration rights superior to those granted to Holders pursuant to this Section 2, or of registration rights which might cause a reduction in the number of shares includable by the Holders in any offering pursuant to Section 2.4 or in any offering subject to Section 2.5.

SECTION 3

Affirmative Covenants

Notwithstanding any provision of the Company's Bylaws regarding delivery or non-delivery of financial information to shareholders of the Company, the Company hereby covenants and agrees as follows:

3.1 Financial Information. The Company will furnish the following

information to each Holder (other than the Option Holders) for so long as it is a holder of any Shares or Common Stock issued upon conversion thereof, or of 450,000 shares or more of Common Stock:

(a) As soon as practicable after the end of each fiscal year, and in any event within one hundred and twenty (120) days thereafter, a consolidated balance sheet of the Company and its subsidiaries, if any, as of the end of such fiscal year, and consolidated statements of income, shareholders' equity and cash flows of the Company and its subsidiaries, if any, for such year, prepared in accordance with generally accepted accounting principles and setting forth in each case in comparative form the figures for the previous fiscal year, all in reasonable detail and with an audit opinion thereon from independent public accountants of recognized national standing selected by the Company.

(b) As soon as practicable after the end of the first, second and third quarterly accounting periods in each fiscal year of the Company, and in any event within forty-five (45) days thereafter, a consolidated balance sheet of the Company and its subsidiaries, if any, as of the end of each such quarterly period, and consolidated statements of income, shareholders' equity and cash flows of the Company and its subsidiaries, if any, for such period and for the current fiscal year to date, prepared in accordance with generally accepted accounting principles, with the exception that no notes need be attached to such statements and year-end audit adjustments may not have been made. Said financial statements shall be signed by an officer of the Company who shall state that such financial statements are in accordance with generally accepted accounting principles, with the exception that no notes need be attached to such statements and year-end audit adjustments may not have been made.

3.2 Other Information. The Company shall furnish the following

information to each Holder (other than the Option Holders) for so long as it (together with its affiliates) holds 450,000 or more Shares (on an as-converted-to-Common-Stock basis) or shares of Common Stock.

(a) As soon as practicable after the end of each fiscal month, and in any event within thirty (30) days thereafter, a consolidated balance sheet of the Company and its subsidiaries, if any, as at the end of such month, and a consolidated statement of income of the Company and its subsidiaries, if any, for such month, and for the current fiscal year to date, in each case setting forth in comparative form the Company's and its subsidiaries', if any, projected consolidated balance sheets and projected consolidated statements of income for the corresponding periods as set forth in the annual budget (as prepared pursuant to Section 3.2(b)), prepared in accordance with generally accepted accounting principles, all in reasonable detail and certified subject to changes resulting from year-end audit adjustments, by the principal financial officer of the Company; provided, however, that any financial statements provided hereunder need not contain any footnotes. To such

financial statements there shall be appended a discussion and analysis, in reasonable detail, of such financial statements and the general business condition and prospects of the Company by management of the Company so as to assist the recipients in understanding and interpreting such financial statements.

(b) After adoption by the Board of Directors, but not later than thirty (30) days prior to beginning of each fiscal year, an annual budget for such year which shall include monthly capital and operating expense budgets, cash flow statements, projected balance sheets and profit and loss statements for each month and for the end of such year itemized in such detail as the Board of Directors may reasonably determine. Approval of such budgets, statements and projections shall be required by a majority of the Board of Directors.

(c) Within thirty (30) days after a material change has been made in the annual budget specified in Section 3.2(b) previously delivered, revised budgets, statements or projections (as so specified).

(d) Copies of all reports, registration statements and other material filed by the Company or any subsidiary with the Commission or with any national securities exchange on which securities of the Company or any subsidiary may be listed.

(e) The covenants provided in this Section 3.2 shall be suspended for so long as the Company is subject to the reporting requirements of Section 13(a) or 15(d) of the Exchange Act.

3.3 Inspection Rights. Each holder (other than the Option Holders)

of any Shares or Common Stock issued upon conversion thereof, or of 450,000 or more shares of Common Stock shall have the right to visit and inspect any of the properties of the Company or any of its subsidiaries, and to discuss their affairs, finances and accounts with their officers, all at such reasonable times and as often as may be reasonably requested.

3.4 Assignment of Rights to Information. The rights granted pursuant

to Sections 3.1, 3.2 and 3.3 may be assigned or otherwise conveyed by any Holder or by any subsequent transferee of any such rights; provided that the Company is given notice of the assignment or conveyance; and provided further that if the Company reasonably believes that it is necessary to protect proprietary information, the Company may edit such information delivered to a transferee.

3.5 Confidentiality. Each Holder agrees that it will keep

confidential and will not, except as required by law, including without limitation freedom of information acts, disclose or divulge any confidential, proprietary or secret information which

such Holder may obtain from the Company, and which the Company has prominently marked "confidential", "proprietary" or "secret" or has otherwise identified as being such, pursuant to financial statements, reports and other materials submitted by the Company as required hereunder, or pursuant to visitation or inspection rights granted hereunder unless such information is or becomes known to the Holder from a source other than the Company (unless such Holder knows that such information was improperly obtained from the Company) or is or becomes publicly known, or unless the Company gives its written consent to the Holder's release of such information, except that no such written consent shall be required (and Holder shall be free to release such information) if such information is to be provided to Holder's lawyer or accountant, or to an officer, director or partner of a Holder.

3.6 Employee Agreements. Those current and future employees and

officers of and consultants to the Company designated by the Board of Directors shall be required to execute a proprietary information agreement substantially in the form attached hereto as Exhibit B with such amendments thereto as the Board of Directors may from time to time deem appropriate.

3.7 Insurance. As soon as possible after the date hereof the Company

shall obtain and keep adequate insurance on its properties, by financially sound and reputable insurers, of a character and in such amounts and on such terms usually insured by corporations engaged in the same or a similar business against loss or damage resulting from fire or other risks insured against by extended coverage and of the kind customarily insured against by such corporations, and maintain in full force and effect public liability insurance against claims for personal injury, death or property damage occurring upon, in, about or in connection with the use of any of its properties, and maintain such other insurance as may be required by law or other agreements to which the Company is or shall become a party.

3.8 Board of Directors. The Company shall reimburse directors of the

Company for their reasonable expenses (including travel, meals and lodging) incurred in the service of the Company, including the attendance at Board of Directors meetings, pursuant to policies established by the Board of Directors.

SECTION 4

Right of First Refusal

4.1 Right of First Refusal. The Company hereby grants to each Holder

the right of first refusal to purchase, pro rata, New Securities that the Company may, from time to time, propose to sell and issue. Each Holder's pro rata share, for purposes of this right of first refusal, is the ratio of the number of

shares of Common Stock (and shares of Common Stock issuable upon conversion of securities convertible into shares of Common Stock), excluding the number of shares of Common Stock which may be issued upon exercise of any Option, actually held by such Holder, to the total number of outstanding shares of Common Stock (calculated on a fully diluted basis) of the Company. This right of first refusal shall be subject to the following provisions:

(a) In the event that the Company proposes to undertake an issuance of New Securities, it shall give each Holder written notice of its intention, describing the type of New Securities, the price, and the general terms upon which the Company proposes to issue the same. Each Holder shall have ten (10) business days from the date of receipt of any such notice to agree to purchase its pro rata share of such New Securities for the price and upon the general terms specified in the notice by giving written notice to the Company and stating therein the quantity of New Securities to be purchased. Each Holder shall have a right of over allotment such that if any Holder fails to exercise its right hereunder to purchase its pro rata portion of New Securities, the Company shall so notify the other Holders and the other Holders may purchase the non-purchasing Holder's portion on a pro rata basis, within ten (10) days from the date of such notice.

(b) In the event that a Holder fails to exercise in full the right of first refusal within said ten (10) day period (plus ten (10) day period, if applicable) the Company shall have ninety (90) days thereafter to sell the New Securities respecting which the Holders' rights were not exercised, at a price and upon general terms no more favorable to the purchasers thereof than specified in the Company's notice. In the event the Company has not sold the New Securities within such ninety (90) day period, the Company shall not thereafter issue or sell any New Securities, without first offering such securities to the Holders in the manner provided above.

(c) The right of first refusal granted under this Agreement shall expire upon the closing of the first firmly underwritten public offering of Common Stock of the Company pursuant to a registration statement filed with, and declared effective by, the Commission under the Securities Act, covering the offer and sale of Common Stock to the public at a per-share price (prior to underwriters' commissions and expenses) of at least \$5.00 (as adjusted for any combinations, consolidations, stock distributions or stock dividends with the respect to such stock) and at an aggregate offering price of not less than \$10,000,000.

(d) This right of first refusal is assignable only in connection with a sale of Shares or Common Stock issued on conversion thereof.

4.2 Waiver. The Series A Investors, the Founders and the University

each hereby waive their respective rights under Section 4.1 of the Investors' Rights Agreement to purchase their pro rata share of the Series B Preferred Stock being issued to the Series B Investors pursuant to that certain Series B Preferred Stock Purchase Agreement of even date herewith (the "Series B Agreement").

SECTION 5

University Warrants

5.1 Termination of Warrant Rights. The right of the University to

obtain warrants to purchase Common Stock of the Company, contained in Section 5.1 of the Investors' Rights Agreement, is hereby terminated.

SECTION 6

Miscellaneous

6.1 Amendment of Investors' Rights Agreement. Effective and

contingent upon the closing of the sale of the Series B Preferred Stock pursuant to the Series B Agreement, all of the provisions of the Investors' Rights Agreement shall be null and void and superseded by this Agreement. The parties to such Investors' Rights Agreement forever release, waive and disclaim any and all rights under such Agreement. The parties hereto further agree that this Agreement constitutes the full and entire understanding and agreement between the parties with regard to the subjects hereof and thereof, except that no provision, condition or term of this Agreement, including but not limited to Section 6.8 below, is intended to explicitly or implicitly alter or allow to be altered any provision, condition or term of the UM-Ann Arbor Stromal Agreement.

6.2 Governing Law. This agreement shall be governed by and construed

in accordance with the laws of the State of Michigan applicable to contracts between Michigan residents entered into and to be performed entirely within the State of Michigan.

6.3 Successors and Assigns. Except as otherwise provided herein, the

provisions hereof shall inure to the benefit of, and be binding upon, the successors, assigns, heirs, executors and administrators of the parties hereto.

6.4 Notices. All notices and other communications required or

permitted hereunder shall be in writing and shall be effective five (5) days after mailed by first-class mail, postage prepaid,

or otherwise delivered by hand or by messenger, addressed (a) if to an Investor at such Investor's address set forth on Exhibit A, or at such other address as such Investor shall have furnished to the Company in writing, or (b) if to any other Holder, at such address as such Holder shall have furnished the Company in writing, or, until any such Holder so furnishes an address to the Company, then to and at the address of the last holder of such Registerable Securities who has so furnished an address to the Company, or (c) if to the Company, at such address as the Company shall have furnished to each Holder in writing.

6.5 Delays or Omissions. No delay or omission to exercise any right,

power or remedy accruing to any holder of any Registerable Securities, upon any breach or default of the Company under this Agreement, shall impair any such right, power or remedy of such Holder nor shall it be construed to be a waiver of any such breach or default, or an acquiescence therein, or of or in any similar breach or default thereunder occurring; nor shall any waiver of any single breach or default be deemed a waiver of any other breach or default theretofore or thereafter occurring. Any waiver, permit, consent or approval of any kind or character on the part of any holder of any breach or default under this Agreement, or any waiver on the part of any holder of any provisions or conditions of this Agreement, must be in writing and shall be effective only to the extent specifically set forth in such writing. All remedies, either under this agreement, or by law or otherwise afforded to any Holder, shall be cumulative and not alternative.

6.6 Counterparts. This Agreement may be executed in any number of

counterparts, each of which may be executed by less than all of the Holders, each of which shall be enforceable against the parties actually executing such counterparts, and all of which together shall constitute one instrument.

6.7 Severability. In the case any provision of this Agreement shall

be invalid, illegal or unenforceable, the validity, legality and enforceability of the remaining provisions shall not in any way be affected or impaired thereby.

6.8 Amendments. The provisions of this Agreement may be amended at

any time and from time to time, and particular provisions of this Agreement may be waived, with and only with an agreement or consent in writing signed by the Company and by the Holders of a majority of the number of shares of Registrable Securities (or securities convertible into Registrable Securities) outstanding as of the date of such amendment or waiver. Each party to this Agreement acknowledges that by the operation of this Section the holders of a majority of the outstanding Registrable Securities may have the right and power to diminish or eliminate all rights of such holder under this Agreement.

IN WITNESS WHEREOF, the parties have caused this Agreement to be duly executed and delivered as of the date first above written.

COMPANY:

AASTROM BIOSCIENCES, INC.

By /s/ R. DOUGLAS ARMSTRONG

Dr. R. Douglas Armstrong
President

INVESTORS:

H&Q LIFE SCIENCE TECHNOLOGY FUND I

By /s/ JACKIE BERTERRETCHÉ

Title Attorney-In-Fact

H&Q LONDON VENTURES

By /s/ JACKIE BERTERRETCHÉ

Title Attorney-In-Fact

STATE TREASURER OF THE STATE OF MICHIGAN
CUSTODIAN OF PUBLIC SCHOOL EMPLOYEES'
RETIREMENT SYSTEM; STATE EMPLOYEES'
RETIREMENT SYSTEM; MICHIGAN STATE POLICE
RETIREMENT SYSTEM; JUDGES' RETIREMENT
SYSTEM; AND PROBATE JUDGES' RETIREMENT
SYSTEM

By /s/ PAUL E. RICE

Title Paul E. Rice, Administrator

Venture Capital and LBO Division

BRENTWOOD ASSOCIATES V, L.P.
By: Brentwood V Ventures, L.P.
Its General Partner

By /s/ G. BRADFORD JONES

WIND POINT PARTNERS II, L.P.

By /s/ ROBERT CUMMINGS

Title General Partner

GC&H PARTNERS

By /s/ EDWIN E. HUDDLESON, JR.

Title General Partner

/s/ MICHAEL B. STAEBLER

Michael B. Staebler, Esq.

OPTION HOLDERS:

/s/ STEPHEN G. EMERSON

Stephen G. Emerson

/s/ BERNHARD O. PALSSON

Bernhard O. Palsson

/s/ MICHAEL F. CLARKE

Michael F. Clarke

/s/ R. DOUGLAS ARMSTRONG

R. Douglas Armstrong

THE REGENTS OF THE UNIVERSITY OF MICHIGAN:

By /s/ NORMAN G. HERBERT

Norman G. Herbert

Title Investment Officer/Treasurer

By /s/ C.W. MATTHEWS

C.W. Matthews

Title Associate Vice President for

Finance and Controller

EXHIBIT A

Series A Investors - -----	Shares -----
H&Q Life Science Technology Fund I One Bush Street, 18th Floor San Francisco, CA 94104	875,000
H&Q London Ventures One Bush Street, 18th Floor San Francisco, CA 94104	875,000
State Treasurer of the State of Michigan, Custodian of Certain Retirement Systems c/o Venture Capital Division 430 West Allegan, First Floor Treasury Building Lansing, MI 48933	750,000
TOTAL	----- 2,500,000
Series B Investors - -----	Shares -----
Brentwood Associates, V., L.P. 11150 Santa Monica, Blvd. Suite 1200 Los Angeles, CA 90025 Attn: Brad Jones	850,000
Wind Point II, L.P. 321 North Clark Street Chicago, IL 60610 Attn: Robert Cummings	750,000
H&Q Life Science Technology Fund I One Bush Street, 18th Floor San Francisco, CA 94104 Attn: Robert Kunze	540,000
H&Q London Ventures One Bush Street, 18th Floor San Francisco, CA 94104 Attn: Robert Kunze	360,000

State Treasurer of the State of Michigan, Custodian of Certain Retirement Systems c/o Venture Capital Division 430 West Allegan Lansing, Michigan 48992 Attn: Joseph Taylor	500,000
GC&H Partners c/o Cooley Godward Castro Huddleson & Tatum One Maritime Plaza 20th Floor San Francisco, CA 94111 Attn: Jeanne Meyer	25,000
Michael B. Staebler, Esq. c/o Pepper, Hamilton & Scheetz 100 Renaissance Center Suite 3600 Detroit, Michigan 48243	5,000
TOTALS	----- 3,030,000

EXHIBIT "A"

AASTROM BIOSCIENCES, INC.
P.O. Box 130469
Ann Arbor, Michigan 48113-0469

Gentlemen:

1. The following is a complete list of all inventions or improvements relevant to the subject matter of my service as a director of AASTROM BIOSCIENCES, INC. (the "Company") that have been made or conceived or first reduced to practice by me alone or jointly with others prior to my becoming a director of the Company:

_____ No inventions or improvements.

_____ See below:

_____ Due to confidentiality agreements with prior employer, I cannot disclose certain inventions that would otherwise be included on the above-described list.

_____ Additional sheets attached.

2. I propose to bring to my service as a director the following devices, materials and documents of a former employer or other person to whom I have an obligation of confidentiality that are not generally available to the public, which materials and

documents may be used in my service as a director pursuant to the express written authorization of my former employer or such other person (a copy of which is attached hereto):

_____ No materials.

_____ See below.

_____ Additional sheets attached.

Dated: _____, 19____.

Very truly yours,

A-2

EXHIBIT B

AASTROM BIOSCIENCES, INC.

DIRECTOR PROPRIETARY INFORMATION AND INVENTION AGREEMENT

In consideration of my service as a director or continued service as a director of AASTROM Biosciences, Inc. ("the Company"), I hereby agree as follows:

1. Recognition of Company's Rights; Nondisclosure. At all times during

the term of my service as a director and thereafter, I will hold in strictest confidence and will not disclose or use any of the Company's Proprietary Information (defined below), except as such disclosure or use may be required in connection with my work for the Company, or unless an officer of the Company expressly authorizes such disclosure or use. I assign to the Company any rights I may have or acquire in such Proprietary information and recognize that all Proprietary information shall be the sole property for the Company and its successors and assigns, and the Company and its successors and assigns shall be the sole owner of all patents, copyrights, and other rights in connection therewith.

The term "Proprietary Information" shall mean all of the confidential or proprietary information of the Company, including, but not limited to:

a. inventions, trade secrets, ideas, processes, formulas, source codes, data, programs, other original works or authorship, know-how, improvements, discoveries, developments, designs and techniques, (hereinafter collectively referred to as "Inventions"); and

b. plans for research, development, new products, marketing and selling; financial statements; licenses; prices and costs; information concerning suppliers and customers; and information regarding the skills and compensations of employees of the Company.

Notwithstanding the foregoing, Proprietary information shall not include:

a. information which at the time of disclosure to the undersigned is in the public domain,

b. information which was received by the undersigned from a third party having the legal right to transmit the same to the undersigned, or

c. information which was independently developed by the undersigned without reliance on any information received from the Company.

I understand, in addition, that the Company has received and in the future will receive from third parties confidential or proprietary information ("Third Party Information") subject to a duty on the Company's part to maintain the confidentiality of such information and to use it only for certain limited purposes. During the term of my service as director and thereafter, I will hold Third Party Information in the strictest confidence and will not disclose or use Third Party Information except as permitted by the agreement between the Company and such third party, unless expressly authorized to act otherwise by an officer of the Company.

2. Assignment of Proprietary Rights. I hereby assign to the Company and

its successors and assigns all my right, title and interest in and to any and all inventions whether or not patentable or registrable under copyright or similar statutes, made or conceived or reduced to practice or learned by me, either alone or jointly with others, during the term of my service as a director with the Company. I agree that all such inventions are the sole property of the Company and its successors and assigns.

I also assign to or as directed by the Company all my right, title and interest in and to any and all inventions, full title to which is required to be in the United States by a contract between the Company and the United States or any of its agencies. Inventions assigned to or as directed by the Company by this paragraph 2 are hereinafter referred to as "Company Inventions."

Provided however, the foregoing assignment of inventions applies only to inventions related to the technology and business of the Company, but not to any

other inventions which I may make independent from my service with the Company, or that I may make as part of a formalized collaboration with the Company that is outside of my role as a director (any such collaboration being established and mutually agreed to in writing).

3. Enforcement of Proprietary Rights. I will assist the Company in

every proper way to obtain and from time to time enforce United States and foreign patents, copyright and other rights and protections relating to Company inventions in any and all countries. To that end I will execute, verify and deliver such documents and perform such other acts (including appearances as a witness) as the Company may reasonably request for use in applying for, obtaining, sustaining and enforcing such patents, copyrights and other rights and protections on Company inventions. In addition, I will execute, verify and deliver assignments of such patents, copyrights, and other rights and protections to the Company or its designee. My obligation to assist the Company in obtaining and enforcing patents, copyrights, and other rights and protections relating to such Company Inventions in any and all countries shall continue beyond the termination of my service as a director, but the Company shall compensate me at a reasonable

rate after my termination for the time actually spent by me at the Company's request on such assistance.

In the event the Company is unable, after reasonable effort, to secure my signature on any document needed to apply for or prosecute any patent, copyright, or other right or protection relating to a Company Invention, I hereby irrevocably designate and appoint the Company and its duly authorized officers and agents as my agent and attorney in fact, to act for an in my behalf to execute, verify and file any such applications and to do all other lawfully permitted acts to further the prosecution and issuance of patents, copyrights, and other rights and protections thereon with the same legal force and effect as if executed by me.

4. Obligation to Keep Company Informed. During the term of my service

as a director, I will disclose to the Company promptly, fully and in writing any and all inventions. in addition, after termination of my service as a director, I will disclose all patent applications filed by me within a year after termination of my service as a director. I agree that any patent application filed within a year after termination of my service as a director shall be presumed to relate to an invention made during the term of my service as a director unless I can sustain the burden of proving the contrary.

5. Prior Inventions. Inventions if any, patented or unpatented, which I

made prior to the commencement of my service as a director with the Company, are excluded from the scope of this Agreement. To preclude any possible uncertainty, I have set forth on Exhibit A attached hereto, a complete list of all inventions that I have, alone or jointly with other, conceived, developed or reduced to practice or caused to be conceived, developed, or reduced to practice, prior to the commencement of my service as a director with the Company, that I consider to not be Company property and that I wish to have excluded from the scope of this Agreement.

6. No Improper Use of Materials. During my service as a director at the

Company, I will not improperly use or disclose any confidential information or trade secrets, if any, of any former or current employer, and I will not bring onto the premises of the Company any unpublished documents or any property belonging to any former or current employer unless consented to in writing by that employer.

7. No Conflicting Obligation. I represent that my performance of all

terms of this Agreement and as a director of the Company does not and will not breach any agreement to keep in confidence information acquired by me in confidence or in trust prior to my service as a director by the Company. I have not

entered into, and I agree I will not enter into, any agreement either written or oral in conflict herewith.

8. Effect of Termination. Upon the termination of my service as a

director with the Company, I understand that the Company and I shall be released from all obligations and liabilities to the other occurring or arising after the date of such termination, except that any termination of my service as a director with the Company shall not relieve me of my obligations under Sections 1, 2, 3, 4, and 6 hereof, nor shall any such termination relieve me or the Company from any liability arising from any breach of the provisions contained herein. When I discontinue my service as a director of the Company, I will deliver to the Company any and all drawings, notes, memoranda, specifications, devices, documents, together with all copies thereof, and any other material containing or disclosing any Company Inventions, Third Party Information or Proprietary Information of the Company.

9. Legal and Equitable Remedies. Because my services are personal and

unique and because I may have access to and become acquainted with the Proprietary Information of the Company, the Company shall have the right to enforce this Agreement and any of its provisions by injunction, specific performance or other equitable relief without prejudice to any other rights and remedies that the Company may have for a breach of this Agreement.

10. Notices. Any notices required or permitted hereunder shall be given

to the appropriate party at the address specified below or at such other address as the party shall specify in writing.

Such notice shall be deemed given upon personal delivery to the appropriate address or sent by certified or registered mail, three days after the date of mailing.

11. Miscellaneous. I agree that, with respect to the subject matter

hereof, this Agreement constitutes my entire agreement with the Company, superseding any previous oral or written communications, representations, understandings, or agreements with the Company or any officer or representative thereof. This Agreement shall inure to the benefit of the successors and assigns of the company, and shall be binding upon my successors and assigns. To the extent that any of the agreements set forth herein, or any word, phrase, clause, or sentence hereof shall be found to be illegal or unenforceable for any reason, such agreement, word, phrase, clause, or sentence shall be modified or deleted in such a manner so as to make the Agreement, as modified, legal and enforceable under applicable laws. This Agreement shall be governed by the laws of the State of Michigan, as those laws are applied by Michigan courts to

contracts between Michigan residents made and to be performed within the state of Michigan, which state shall have jurisdiction of the subject matter hereof. This Agreement may not be changed, modified, released, discharged, abandoned, or otherwise amended, in whole or in part, except by an instrument in writing signed by the company and me.

This Agreement shall be effective as of the first day of my service as a director with the company, namely: _____, 19____.

Date: _____

Address

INDEMNIFICATION AGREEMENT

This Agreement is made as of _____, between Aastrom Biosciences, Inc., a Michigan corporation (the "Company"), and those certain officers and directors of the Company designated on the signature page of this Agreement as Indemnitees (hereinafter referred to individually as an "Indemnatee" and collectively as the "Indemnitees").

RECITALS

A. It is essential to the Company to attract and retain as directors and officers the most capable persons available.

B. Both the Company and Indemnitees recognize the increased risk of litigation and other claims being asserted against directors and officers of companies in today's environment.

C. While basic protection against undue risk of personal liability of directors and officers may be provided through insurance coverage, it has become increasingly difficult to obtain such insurance on terms providing reasonable protection at reasonable cost.

D. The Restated Articles of Incorporation and the Bylaws of the Company permit the Company to indemnify and advance expenses to its directors and officers to the full extent permitted by law; and Indemnitees have been serving and continue to serve as directors and officers of the Company in part in reliance on such Restated Articles of Incorporation and Bylaws.

E. In recognition of Indemnitees' need for substantial protection against personal liability, the increasing difficulty in obtaining satisfactory insurance coverage, and Indemnitees' reliance on the aforesaid Restated Articles of Incorporation and Bylaws, and in part to provide Indemnitees with specific contractual assurance that the protection promised by the Restated Articles of Incorporation and Bylaws will be available to Indemnitees (regardless of, among other things, any amendment to or revocation of such Restated Articles of Incorporation or Bylaws or any change in the composition of the Company's Board of Directors), the Company wishes to provide in this Agreement for the indemnification of and the advancing of expenses to Indemnitees to the fullest extent permitted by law and as set forth in this Agreement, and, to the extent insurance coverage is maintained, for the continued coverage of Indemnitees under the Company's directors' and officers', liability insurance policies.

NOW, THEREFORE, in consideration of Indemnitees' service to the

Company, or Indemnitees' service to another enterprise at the request of the Company, the parties hereto agree as follows:

1. Certain Definitions. As used herein, the following terms shall

refer to the following events or have the following meanings, as the case may be:

a. Change in Control is an event which shall be deemed to have

occurred if any one or more of the following events occur: (i) any "person" (as such term is used in Sections 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended) hereafter becomes the "beneficial owner" (as defined in Rule 13d-3 under said Act), directly or indirectly, of securities of the Company representing twenty percent or more of the total voting power represented by the Company's then outstanding Voting Securities, excluding, however, a trustee or other fiduciary holding securities under an employee benefit plan of the Company or a corporation owned directly or indirectly by the shareholders of the Company in substantially the same proportions as their ownership of stock of the Company; or (ii) during any period of two consecutive years, individuals who, at the beginning of such period, constitute the Board of Directors of the Company and any new director whose election by the Board of Directors or nomination for election by the Company's shareholders was approved by a vote of at least two-thirds of the directors then still in office, cease for any reason to constitute a majority of the Board of Directors; or (iii) the shareholders of the Company approve a merger or consolidation of the Company with any other corporation, other than a merger or consolidation which would result in the Voting Securities of the Company outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into Voting Securities of the surviving entity) at least 80 percent of the total voting power represented by the Voting Securities of the Company or such surviving entity outstanding immediately after such merger or consolidation; or (iv) the shareholders of the Company approve a plan of complete liquidation of the Company or an agreement for the sale or disposition by the Company (in one transaction or a series of transactions) of all or substantially all the Company's assets.

b. Claim means (i) any threatened, pending or completed action,

suit or proceeding, whether civil, criminal, administrative or investigative, or (ii) any inquiry or investigation, whether instituted by the Company or any other party, that any of the Indemnitees in good faith believes might lead to the institution of any such action, suit or proceeding.

c. Expenses means, without limitation, attorneys' fees and all

other costs, expenses and obligations paid or incurred in connection with (i) investigating, defending, being a witness in or participating in (including on appeal), any Claim relating to any Indemnifiable Event, or (ii) preparing to defend, be a witness in or participate in any Claim relating to any Indemnifiable Event.

d. Indemnifiable Event means any event or occurrence related to

the fact that any of the Indemnitees is or was a director, officer, employee, agent, trustee or fiduciary of the Company, or is or was serving at the request of the Company as a director, officer, employee, trustee, agent or fiduciary of another corporation, partnership, joint venture, employee benefit plan, trust or other enterprise, or by reason of anything done or not done by any of the Indemnitees in any such capacity for which under applicable law a California corporation may indemnify Indemnitees, as such law exists from time to time.

e. Indemnitees means the officers and directors of the Company

as of the date of this Agreement and any future duly elected officers and directors of the Company designated on and executing the signature page of this Agreement as Indemnitees. "Indemnitee" means any one of the Indemnitees.

f. Independent Legal Counsel means an attorney or firm of

attorneys, selected in accordance with the provisions of Section 3, who shall not have otherwise performed services within the last three years for the Company or the Indemnitee seeking indemnification (other than services with respect to matters concerning the rights of any of the Indemnitees under this Agreement).

g. Reviewing Party means (i) Independent Legal Counsel or (ii)

any appropriate person or body consisting of a member or members of the Company's Board of Directors or any other person or body appointed by the Board who is not a party to the particular Claim for which Indemnitee is seeking indemnification.

h. Voting Securities means any securities of the Company

which entitle their holders to vote generally in the election of directors.

2. Basic Indemnification Arrangement.

a. Indemnification. In the event Indemnitee was, is or

becomes a party to or witness or other participant in, or is threatened to be made a party to or witness or other participant in, a Claim by reason of an Indemnifiable Event, the Company shall indemnify Indemnitee, to the fullest extent permitted by law and as soon as practicable (but in any event no later than thirty days after written demand is presented to the Company), against any and all Expenses, judgments, fines, penalties and amounts paid in settlement (including all interest, assessments and other charges paid or payable in connection with or in respect of such Expenses, judgments, fines, penalties or amounts paid in settlement) of such Claim. If requested by Indemnitee, the Company shall advance (within two business days of such request) any and all Expenses to Indemnitee (an "Expense Advance").

b. Exception; Determination That Indemnification or

Advances Not Permitted. Except as provided in Section 2(c), the obligations of

the Company

under Section 2(a) shall be subject to the condition that a Reviewing Party shall not have determined that Indemnitee would not be permitted to be indemnified under applicable law. Except as provided in Section 2(c), the obligation of the Company under Section 2(a) to make an Expense Advance shall be subject to the condition that, if, when and to the extent a Reviewing Party determines that Indemnitee would not be permitted to be indemnified under applicable law, the Indemnitee shall reimburse the Company for all such Expense Advances theretofore paid. For purposes of this Section 2(b), if the Reviewing Party is Independent Legal Counsel, then any such determination shall be rendered in the form of a written opinion.

c. Initiation of Action Concerning Right to Indemnification. In

the event Indemnitee has commenced or thereafter commences legal proceedings in a court of competent jurisdiction to secure a determination that Indemnitee should be indemnified under applicable law, any determination made by a Reviewing Party that Indemnitee would not be permitted to be indemnified under applicable law shall not be binding and Indemnitee shall not be required to reimburse the Company for any Expense Advance until a final judicial determination is made with respect thereto. Indemnitee shall have the right to commence litigation in any court in the State of Michigan having subject matter jurisdiction and in which venue is proper in order to seek an initial determination by the court as to whether Indemnitee is entitled to indemnification and Expense Advances hereunder or in order to challenge an unfavorable determination by a Reviewing Party, including the legal or factual bases for such unfavorable determination. The Company hereby consents to service of process and to appear in any such proceeding. Unless contested by the Indemnitee as contemplated by this Section 2(c), any determination by a Reviewing Party shall be conclusive and binding on the Company and Indemnitee.

d. Reviewing Party. For purposes of this Section 2, the

Reviewing Party shall be selected by the Board of Directors in circumstances where there has not been a Change in Control. In circumstances where there has been a Change in Control (other than a Change in Control which has been approved by a majority of the Company's Board of Directors who were directors immediately prior to such Change in Control), the Reviewing Party shall be the Independent Legal Counsel referenced in Section 3.

3. Change in Control. The Company agrees that if there is a Change

in Control of the Company (other than a Change in Control which has been approved by a majority of the Company's Board of Directors who were directors immediately prior to such Change in Control), then with respect to all matters thereafter arising concerning the rights of Indemnitee under this Agreement or any other agreement or Company Bylaw now or hereafter in effect relating to Claims for Indemnifiable Events, the Company shall seek legal advice only from Independent Legal Counsel selected by Indemnitee and approved by the Company (which approval shall not be unreasonably withheld). Such Independent Legal Counsel, among other things, shall render its

written opinion to the Company and Indemnatee as to whether and to what extent the Indemnatee would be permitted to be indemnified under applicable law. The Company agrees to pay the reasonable fees of Independent Legal Counsel and to fully indemnify such counsel against any and all expenses (including attorneys' fees), claims, liabilities and damages arising out of or relating to this Agreement or such counsel's engagement pursuant hereto.

4. Indemnification for Additional Expenses. In connection with any

action brought by Indemnatee for (i) indemnification or advance payment of Expenses under this Agreement or any other agreement or Company Bylaw now or hereafter in effect relating to Claims for Indemnifiable Events and/or (ii) recovery under any directors' and officers' liability insurance policy maintained by the Company, regardless of whether Indemnatee ultimately is determined to be entitled to such indemnification, advance payment of Expenses or insurance recovery, as the case may be, the Company shall indemnify Indemnatee against any and all expenses (including attorneys' fees) which are incurred by Indemnatee and, if requested by Indemnatee, shall (within two business days of such request) advance such expenses to Indemnatee.

5. Partial Indemnity; Expenses. If Indemnatee is entitled under

any provision of this Agreement to indemnification by the Company for some or a portion of Expenses, judgments, fines, penalties or amounts paid in settlement of a Claim but not, however, for all of the total amount thereof, the Company shall nevertheless indemnify Indemnatee for the portion to which Indemnatee is entitled. Moreover, notwithstanding any other provision of this Agreement, to the extent that Indemnatee has been successful on the merits or otherwise in defense (including dismissal without prejudice) of any or all Claims relating in whole or in part to an Indemnifiable Event, or in defense of any issue or matter relating in whole or in part to an Indemnifiable Event, Indemnatee shall be indemnified against all Expenses incurred in connection therewith.

6. Burden of Proof. In connection with any determination by a

Reviewing Party as to whether Indemnatee is entitled to be indemnified hereunder, the burden of proof shall be on the Company to establish that Indemnatee is not entitled to indemnification.

7. No Presumptions. For purposes of this Agreement, the

termination of any claim, action, suit or proceeding by judgment, order, settlement (whether with or without court approval) or conviction, or upon a plea of nolo contendere or its equivalent, shall not create a presumption that Indemnatee did not meet any particular standard of conduct or did have any particular belief or that a court has determined that indemnification is not permitted by applicable law. Neither the failure of a Reviewing Party to have made a determination as to whether Indemnatee has met any particular standard of conduct or had any particular belief, nor an actual determination by a Reviewing Party that Indemnatee has not met such standard of conduct or did not have

such belief, prior to the commencement of legal proceedings by Indemnitee as contemplated in Section 2(c), shall be a defense to Indemnitee's claim or create a presumption that Indemnitee has not met any particular standard of conduct or did not have any particular belief.

8. Nonexclusivity, Etc. The rights of the Indemnitees hereunder

shall be in addition to any other rights Indemnitees may have under the Company's Restated Articles of Incorporation, Bylaws, the applicable corporate law, or otherwise. To the extent that a change in the applicable corporate law (whether by statute or judicial decision) permits greater indemnification by agreement than would be afforded currently under the Company's Restated Articles of Incorporation, Bylaws and this Agreement, it is the intent of the parties hereto that Indemnitees shall enjoy by this Agreement the greater benefits so afforded by such change.

9. Liability Insurance. To the extent the Company maintains an

insurance policy or policies providing directors' and officers' liability insurance, Indemnitees shall be covered by such policy or policies, in accordance with its or their terms, to the maximum extent of the coverage available for any Company director or officer.

10. Period of Limitations. No legal action shall be brought and no

claim or cause of action shall be asserted by or in the right of the Company against any of the Indemnitees, Indemnitees' spouses, heirs, executors or personal or legal representatives after the expiration of two years from the date of accrual of such claim or cause of action. Any claim or cause of action of the Company shall be extinguished and deemed released unless asserted by the timely filing of a legal action within such two-year period; provided, however, that if any shorter period of limitations is otherwise applicable to any such claim or cause of action, such shorter period shall govern.

11. Amendments, Etc. Any amendment to this Agreement necessitated

by the election of a person who is not a party to this Agreement to the position of director and/or officer of the Company need only be executed by the Company and such person as an Indemnitee; provided, however, that no other supplement, modification or amendment of this Agreement shall be binding unless executed in writing by all of the parties hereto. No waiver of any of the provisions of this Agreement shall be deemed or shall constitute a waiver of any other provisions hereof (whether or not similar), nor shall such waiver constitute a continuing waiver.

12. Subrogation. In the event of payment under this Agreement, the

Company shall be subrogated to the extent of such payment to all of the rights of recovery of any of the Indemnitees. Indemnitees shall execute all papers required and shall do everything that may be necessary to secure such rights, including the execution of such documents necessary to enable the Company effectively to bring suit to enforce such rights.

13. No Duplication of Payments. The Company shall not be liable

under this Agreement to make any payment in connection with any Claim made against any of the Indemnitees to the extent any of the Indemnitees has otherwise actually received payment (under any insurance policy, Bylaw or otherwise) of the amounts otherwise indemnifiable hereunder.

14. Binding Effect, Etc. This Agreement shall be binding upon and

inure to the benefit of and be enforceable by the parties hereto and their respective successors (including any direct or indirect successor by purchase, merger, consolidation or otherwise to all or substantially all of the business and/or assets of the Company), assigns, spouses, heirs, executors and personal and legal representatives. This Agreement shall continue in effect regardless of whether Indemnitees continue to serve as officers and directors of the Company or of any other enterprise at the Company's request.

15. Severability. The provisions of this Agreement shall be

severable in the event that any of the provisions hereof (including any provision within a single section, paragraph or sentence) is held by a court of competent jurisdiction to be invalid, void or otherwise unenforceable in any respect. The validity and enforceability of any such provision in every other respect and of the remaining provisions hereof shall not be in any way impaired and shall remain enforceable to the fullest extent permitted by laws.

16. Counterparts. This Agreement may be executed in any number of

identical counterparts, each of which shall be deemed to be an original, and all of which together shall be deemed to be one and the same instrument when each party has signed one such counterpart.

17. Governing Law. This Agreement shall be governed by and

construed and enforced in accordance with the laws of the State of Michigan.

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date set forth above.

AASTROM BIOSCIENCES, INC.

By: _____
R. Douglas Armstrong, Ph.D.,
President

The following officers and directors are covered by this Agreement as Indemnitees:

Name:
Title:

Name:
Title:

Name:
Title:

Name:
Title:

Name:
Title:

Name:
Title:

ANN ARBOR STROMAL, INC.

1989 STOCK OPTION PLAN

Adopted August 15, 1989

1. PURPOSE.

(a) The purpose of the Plan is to provide a means which selected key employees and directors (if declared eligible under paragraph 4) of and consultants to Ann Arbor Stromal, Inc., a Michigan corporation (the "Company"), and its Affiliates, as defined in subparagraph 1(b), may be given an opportunity to purchase stock of the Company.

(b) The word "Affiliate" as used in the Plan means any parent corporation or subsidiary corporation of the Company, as those terms are defined in Sections 425(e) and (f), respectively, of the Internal Revenue Code of 1986, as amended from time to time (the "Code").

(c) The Company, by means of the Plan, seeks to retain the services of persons now employed by or serving as consultants or directors to the Company, to secure and retain the services of new employees/persons capable of filling such positions, and to provide incentives for such persons to exert maximum efforts for the success of the Company.

(d) The Company intends that the options issued under the Plan shall, in the discretion of the Board of Directors of the Company (the "Board") or any committee to which responsibility for administration of the Plan has been delegated

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pursuant to subparagraph 2(c), be either incentive stock options as that term is used in Section 422A of the Code ("Incentive Stock Options"), or options which do not qualify as incentive stock options ("Supplemental Stock Options"). All options shall be separately designated Incentive Stock Options or Supplemental Stock Options at the time of grant, and in such form as issued pursuant to paragraph 5, and a separate certificate or certificates shall be issued for shares purchased on exercise of each type of option. An option designated as a Supplemental Stock Option shall not be treated as an incentive stock option.

2. ADMINISTRATION.

(a) The Plan shall be administered by the Board unless and until the Board delegates administration to a committee, as provided in subparagraph 2(c). Whether or not the Board has delegated administration, the Board shall have the final power to determine all questions of policy and expediency that may arise in the administration of the Plan.

(b) The Board shall have the power, subject to, and within the limitations of, the express provisions of the Plan:

(1) To determine from time to time which of the persons eligible under the Plan shall be granted options; when and how the option shall be granted; whether the option will be an Incentive Stock Option or a Supplemental Stock Option; the provisions of each option granted (which need not be identical), including the time or times during the term of each option within which all or portions of such option may be exercised; and the

number of shares for which an option shall be granted to each such person.

(2) To construe and interpret the Plan and options granted under it, and to establish, amend and revoke rules and regulations for its administration. The Board, in the exercise of this power, may correct any defect, omission or inconsistency in the Plan or in any option agreement, in a manner and to the extent it shall deem necessary or expedient to make the Plan fully effective.

(3) To amend the Plan as provided in paragraph 10.

(4) Generally, to exercise such powers and to perform such acts as the Board deems necessary or expedient to promote the best interests of the Company.

(c) The Board may delegate administration of the Plan to a committee composed of not fewer than three (3) members (the "Committee"), all of the members of which Committee shall be disinterested persons, if required and as defined by the provisions of subparagraph 2(d). If administration is delegated to a Committee, the Committee shall have, in connection with the administration of the Plan, the powers theretofore possessed by the Board, subject, however, to such resolutions, not inconsistent with the provisions of the Plan, as may be adopted from time to time by the Board. The Board may abolish the Committee at any time and revest in the Board the administration of the Plan. Additionally, prior to the date of the first

registration of an equity security of the Company under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and notwithstanding anything to the contrary contained herein, the Board may delegate administration of the Plan to any person or persons and the term "Committee" shall apply to any person or persons to whom such authority has been delegated.

(d) The term "disinterested person," as used in this Plan, shall mean an administrator of the Plan, whether a member of the Board or of any Committee to which responsibility for administration of the Plan has been delegated pursuant to subparagraph 2(c): (i) who is not at the time he or she exercises discretion in administering the Plan eligible and has not at any time within one year prior thereto been eligible for selection as a person to whom stock may be allocated or to whom stock options or stock appreciation rights may be granted pursuant to the Plan or any other plan of the Company or any of its affiliates entitling the participants therein to acquire stock, stock options or stock appreciation rights of the Company or any of its affiliates; or (ii) who is otherwise considered to be a "disinterested person" in accordance with the rules, regulations or interpretations of the Securities and Exchange Commission. Any such person shall otherwise comply with the requirements of Rule 16b-3 promulgated under the Securities Exchange Act of 1934, as amended (the "Exchange Act").

(e) Any requirement that an administrator of the Plan be a "disinterested person" shall not apply (i) prior to the date of the first registration of an equity security of the Company under Section 12 of the Exchange Act, or (ii) if the Board or the Committee expressly declares that such requirement shall not apply.

3. SHARES SUBJECT TO THE PLAN.

(a) Subject to the provisions of paragraph 9 relating to adjustments upon changes in stock, the stock that may be sold pursuant to options granted under the Plan shall not exceed in the aggregate one million three hundred sixty-three thousand six hundred thirty-six (1,363,636) shares of the Company's common stock. If any option granted under the Plan shall for any reason expire or otherwise terminate without having been exercised in full, the stock not purchased under such option shall again become available for the Plan.

(b) The stock subject to the Plan may be unissued shares or reacquired shares, bought on the market or otherwise.

(c) An Incentive Stock Option may be granted to an eligible person under the Plan only if the aggregate fair market value (determined at the time the option is granted) of the stock with respect to which incentive stock options (as defined in the Code) granted after 1986 are exercisable for the first time by such optionee during any calendar year under all incentive stock option plans of the Company and its Affiliates does not exceed one hundred thousand dollars (\$100,000). Should it be determined

that an option granted under the Plan exceeds such maximum for any reason other than the failure of a good faith attempt to value the stock subject to the option, such option shall be considered a Supplemental Stock Option to the extent, but only to the extent, of such excess; provided, however, that should it be determined that an entire option or any portion thereof does not qualify for treatment as an incentive stock option by reason of exceeding such maximum, such option or the applicable portion shall be considered a Supplemental Stock Option.

4. ELIGIBILITY.

(a) Incentive Stock Options may be granted only to employees (including officers) of the Company or its Affiliates. A director of the Company shall not be eligible to receive Incentive Stock Options unless such director is also an employee (including an officer) of the Company or any Affiliate. Supplemental Stock Options may be granted only to key employees (including officers) of, directors of or consultants to the Company or its Affiliates. A director of the Company shall not be eligible for a Supplemental Stock Option unless such director is also a key employee (including an officer) of or consultant to the Company or any Affiliate.

(b) A director shall in no event be eligible for the benefits of the Plan unless and until such director is expressly declared eligible to participate in the Plan by action of the Board or the Committee, and only if, at any time discretion is exercised by the Board in the selection of a director as a person

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to whom options may be granted, or in the determination of the number of shares which may be covered by options granted to a director: (i) a majority of the Board and a majority of the directors acting in such matter are disinterested persons, as defined in subparagraph 2(d); (ii) the Committee consists solely of "disinterested persons" as defined in subparagraph 2(d); or (iii) the Plan otherwise complies with the requirements of Rule 16b-3 promulgated under the Exchange Act, as from time to time in effect. The Board shall otherwise comply with the requirements of Rule 16b-3 promulgated under the Exchange Act, as from time to time in effect. This subparagraph 4(b) shall not apply prior to the date of the first registration of an equity security of the Company under Section 12 of the Exchange Act.

(c) No person shall be eligible for the grant of an option under the Plan if, at the time of grant, such person owns (or is deemed to own pursuant to Section 425(d) of the Code) stock possessing more than ten percent (10%) of the total combined voting power of all classes of stock of the Company or of any of its Affiliates unless the exercise price of such option is at least one hundred ten percent (110%) of the fair market value of such stock at the date of grant and the term of the option does not exceed five (5) years from the date of grant.

5. OPTION PROVISIONS.

Each option shall be in such form and shall contain such terms and conditions as the Board or the Committee shall deem appropriate. The provisions of separate options need not be

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identical, but each option shall include (through incorporation of provisions hereof by reference in the option or otherwise) the substance of each of the following provisions:

(a) The term of any option shall not be greater than twelve (12) years from the date it was granted.

(b) The exercise price of each Incentive Stock Option shall be not less than one hundred percent (100%) of the fair market value of the stock subject to the option on the date the option is granted. The exercise price of each Supplemental Stock Option shall be not less than eighty-five percent (85%) of the fair market value of the stock subject to the option on the date the option is granted.

(c) The purchase price of stock acquired pursuant to an option shall be paid, to the extent permitted by applicable statutes and regulations, either (i) in cash at the time the option is exercised, or (ii) at the discretion of the Board or the Committee, either at the time of the grant or exercise of the option, (A) by delivery to the Company of other common stock of the Company, (B) according to a deferred payment or other arrangement (which may include, without limiting the generality of the foregoing, the use of other common stock of the Company) with the person to whom the option is granted or to whom the option is transferred pursuant to subparagraph 5(d), or (C) in any other form of legal consideration that may be acceptable to the Board or the Committee.

In the case of any deferred payment arrangement, interest shall be payable at least annually and shall be charged at the minimum rate of interest necessary to avoid the treatment as interest, under any applicable provisions of the Code, of any amounts other than amounts stated to be interest under the deferred payment arrangement.

(d) An option shall not be transferable except by will or by the laws of descent and distribution, and shall be exercisable during the lifetime of the person to whom the option is granted only by such person.

(e) The total number of shares of stock subject to an option may, but need not, be allotted in periodic installments (which may, but need not, be equal). From time to time during each of such installment periods, the option may become exercisable ("vest") with respect to some or all of the shares allotted to that period, and may be exercised with respect to some or all of the shares allotted to such period and/or any prior period as to which the option was not fully exercised. During the remainder of the term of the option (if its term extends beyond the end of the installment periods), the option may be exercised from time to time with respect to any shares then remaining subject to the option. The provisions of this subparagraph 5(e) are subject to any option provisions governing the minimum number of shares as to which an option may be exercised.

(f) The Company may require any optionee, or any person to whom an option is transferred under subparagraph 5(d), as a condition of exercising any such option, (1) to give written assurances satisfactory to the Company as to the optionee's knowledge and experience in financial and business matters and/or to employ a purchaser representative reasonably satisfactory to the Company who is knowledgeable and experienced in financial and business matters, and that he or she is capable of evaluating, alone or together with the purchaser representative, the merits and risks of exercising the option; and (2) to give written assurances satisfactory to the Company stating that such person is acquiring the stock subject to the option for such person's own account and not with any present intention of selling or otherwise distributing the stock. These requirements, and any assurances given pursuant to such requirements, shall be inoperative if (i) the issuance of the shares upon the exercise of the option has been registered under a then currently effective registration statement under the Securities Act of 1933, as amended (the "Securities Act"), or (ii) as to any particular requirement, a determination is made by counsel for the Company that such requirement need not be met in the circumstances under the then applicable securities laws.

(g) An option shall terminate three (3) months after termination of the optionee's employment or relationship as a consultant or director with the Company or an Affiliate, unless (i) such termination is due to such person's permanent and total

disability, within the meaning of Section 422A(c)(7) of the Code, in which case the option may, but need not, provide that it may be exercised at any time within one (1) year following such termination of employment or relationship as a consultant or director; or (ii) the optionee dies while in the employ of or while serving as a consultant or director to the Company or an Affiliate, or within not more than three (3) months after termination of such relationship, in which case the option may, but need not, provide that it may be exercised at any time within eighteen (18) months following the death of the optionee by the person or persons to whom the optionee's rights under such option pass by will or by the laws of descent and distribution; or (iii) the option by its terms specifies either (a) that it shall terminate sooner than three (3) months after termination of the optionee's employment or relationship as a consultant or director, or (b) that it may be exercised more than three (3) months after termination of the relationship with the Company or an Affiliate. This subparagraph 5(g) shall not be construed to extend the term of any option or to permit anyone to exercise the option after expiration of its term, nor shall it be construed to increase the number of shares as to which any option is exercisable from the amount exercisable on the date of termination of the optionee's employment or relationship as a consultant or director.

(h) The option may, but need not, include a provision whereby the optionee may elect at any time during the term of his

or her employment or relationship as a consultant or director with the Company or any Affiliate to exercise the option as to any part or all of the shares subject to the option prior to the stated vesting date of the option or of any installment or installments specified in the option. Any shares so purchased from any unvested installment or option may be subject to a repurchase right in favor of the Company or to any other restriction the Board or the Committee determines to be appropriate.

(i) To the extent provided by the terms of an option, the optionee may satisfy any federal, state or local tax withholding obligation relating to the exercise of such option by any of the following means or by a combination of such means: (1) tendering a cash payment; (2) authorizing the Company to withhold from the shares of the common stock otherwise issuable to the participant as a result of the exercise of the stock option a number of shares having a fair market value less than or equal to the amount of the withholding tax obligation; or (3) delivering to the Company owned and unencumbered shares of the common stock having a fair market value less than or equal to the amount of the withholding tax obligation.

6. COVENANTS OF THE COMPANY.

(a) During the terms of the options granted under the Plan, the Company shall keep available at all times the number of shares of stock required to satisfy such options.

(b) The Company shall seek to obtain from each regulatory commission or agency having jurisdiction over the Plan such authority as may be required to issue and sell shares of stock upon exercise of the options granted under the Plan; provided, however, that this undertaking shall not require the Company to register under the Securities Act either the Plan, any option granted under the Plan or any stock issued or issuable pursuant to any such option. If, after reasonable efforts, the Company is unable to obtain from any such regulatory commission or agency the authority which counsel for the Company deems necessary for the lawful issuance and sale of stock under the Plan, the Company shall be relieved from any liability for failure to issue and sell stock upon exercise of such options unless and until such authority is obtained.

7. USE OF PROCEEDS FROM STOCK.

Proceeds from the sale of stock pursuant to options granted under the Plan shall constitute general funds of the Company.

8. MISCELLANEOUS.

(a) The Board or the Committee shall have the power to accelerate the time during which an option may be exercised or the time during which an option or any part thereof will vest pursuant to subparagraph 5(e), notwithstanding the provisions in the option stating the time during which it may be exercised or the time during which it will vest.

(b) Neither an optionee nor any person to whom an option is transferred under subparagraph 5(d) shall be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares subject to such option unless and until such person has satisfied all requirements for exercise of the option pursuant to its terms.

(c) Throughout the term of any option granted pursuant to the Plan, the Company shall make available to the holder of such option, not later than one hundred twenty (120) days after the close of each of the Company's fiscal years during the option term, upon request, such financial and other information regarding the Company as comprises the annual report to the shareholders of the Company provided for in the bylaws of the Company.

(d) Nothing in the Plan or any instrument executed or option granted pursuant thereto shall confer upon any eligible employee or optionee any right to continue in the employ of the Company or any Affiliate (or to continue acting as a consultant or director) or shall affect the right of the Company or any Affiliate to terminate the employment or consulting relationship or directorship of any eligible employee or optionee with or without cause. In the event that an optionee is permitted or otherwise entitled to take a leave of absence, the Company shall have the unilateral right to (i) determine whether such leave of absence will be treated as a termination of employment for purposes of paragraph 5(g) hereof and corresponding provisions of

any outstanding options, and (ii) suspend or otherwise delay the time or times at which the shares subject to the option would otherwise vest.

9. ADJUSTMENTS UPON CHANGES IN STOCK.

(a) If any change is made in the stock subject to the Plan, or subject to any option granted under the Plan (through merger, consolidation, reorganization, recapitalization, stock dividend, dividend in property other than cash, stock split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or otherwise), the Plan and outstanding options will be appropriately adjusted in the class(es) and maximum number of shares subject to the Plan and the class(es) and number of shares and price per share of stock subject to outstanding options.

(b) In the event of: (1) a dissolution or liquidation of the Company; (2) a merger or consolidation in which the Company is not the surviving corporation; or (3) a reverse merger in which the Company is the surviving corporation but the shares of the Company's common stock outstanding immediately preceding the merger are converted by virtue of the merger into other property, whether in the form of securities, cash or otherwise then to the extent permitted by applicable law: (i) any surviving corporation shall assume any options outstanding under the Plan or shall substitute similar options for those outstanding under the Plan, or (ii) such options shall continue in full force and effect. In the event any surviving corporation

refuses to assume or continue such options, or to substitute similar options for those outstanding under the Plan, then, with respect to options held by persons then performing services as employees or as consultants or directors for the Company as the case may be, the time during which such options may be exercised shall be accelerated and the options terminated if not exercised prior to such event.

10. AMENDMENT OF THE PLAN.

(a) The Board at any time, and from time to time, may amend the Plan. However, except as provided in paragraph 9 relating to adjustments upon changes in stock, no amendment shall be effective unless approved by the shareholders of the Company within twelve (12) months before or after the adoption of the amendment, where the amendment will:

(i) Increase the number of shares reserved for options under the Plan;

(ii) Modify the requirements as to eligibility for participation in the Plan (to the extent such modification requires shareholder approval in order for the Plan to satisfy the requirements of Section 422A(b) of the Code); or

(iii) Modify the Plan in any other way if such modification requires shareholder approval in order for the Plan to satisfy the requirements of Section 422A(b) of the Code or to comply with the requirements of Rule 16b-3 promulgated under the Exchange Act.

(b) It is expressly contemplated that the Board may amend the Plan in any respect the Board deems necessary or advisable to provide optionees with the maximum benefits provided or to be provided under the provisions of the Code and the regulations promulgated thereunder relating to employee incentive stock options and/or to bring the Plan and/or incentive stock options granted under it into compliance therewith.

(c) Rights and obligations under any option granted before amendment of the Plan shall not be altered or impaired by any amendment of the Plan unless (i) the Company requests the consent of the person to whom the option was granted and (ii) such person consents in writing.

11. TERMINATION OR SUSPENSION OF THE PLAN.

(a) The Board may suspend or terminate the Plan at any time. Unless sooner terminated, the Plan shall terminate ten (10) years from the date the Plan is adopted by the Board or approved by the shareholders of the Company, whichever is earlier. No options may be granted under the Plan while the Plan is suspended or after it is terminated.

(b) Rights and obligations under any option granted while the Plan is in effect shall not be altered or impaired by suspension or termination of the Plan, except with the consent of the person to whom the option was granted.

12. EFFECTIVE DATE OF PLAN.

The Plan shall become effective as determined by the Board, but no options granted under the Plan shall be exercised

unless and until the Plan has been approved by the shareholders of the Company.

INCENTIVE STOCK OPTION AGREEMENT

OPTIONEE:

AASTROM Biosciences, Inc., formerly known as Ann Arbor Stromal, Inc., (the "Company"), pursuant to its 1989 Stock Option Plan (the "Plan"), hereby grants to you, the Optionee named above, an option to purchase shares of the common stock of the Company ("Common Stock"). This option is intended to qualify as an "incentive stock option" within the meaning of Section 422A of the Internal Revenue Code of 1986, as amended from time to time (the "Code"). The date of grant of this option is _____.

The grant hereunder is in connection with and in furtherance of the Company's compensatory benefit plan for participation of the Company's employees (including officers), directors or consultants and is intended to comply with the provisions of Rule 701 promulgated by the Securities and Exchange Commission under the Securities Act of 1933, as amended (the "Act").

The details of your option are as follows:

1. The total number of shares of Common Stock subject to this option is _____. Subject to the limitations contained herein, this option shall be exercisable with respect to each installment shown below on or after the date of vesting applicable to such installment, as follows:

Number of Shares	Date of Earliest Exercise
-----	-----
(Installment)	(Vesting)

provided, however, you will be entitled to exercise this option with respect to all of the shares of Common Stock subject to this

option is your employment by the Company is terminated upon or at any time within six (6) months after the date of a "change of control" of the Company (as defined below), unless such termination is for cause (as defined below). For purposes of this Agreement, a "change of control" shall be deemed to have occurred if in a single transaction or a series of related transactions occurring within a twelve month period: all or substantially all of the business or assets of the Company is sold, transferred or leased; the Company is merged into or consolidated with another entity and, as a result, the shareholders of the Company immediately prior to the merger own less than 51% of the voting capital stock of the successor corporation; there is a change of control of 51% or more of the outstanding capital stock of the Company on a fully diluted basis; or a new shareholder acquires the right to elect a majority of the board of directors. The date of such "change of control" for purposes of this Agreement shall be the date of the closing of the transaction which is deemed to constitute a change of control under the foregoing sentence, or if a series of related transactions is deemed to constitute a change of control, the date of the closing of the last transaction in the series. For purposes of this Agreement, "cause" shall include disclosure of any proprietary information of the Company or of any third party in violation of the Proprietary Information and Invention Agreement between you and the Company; any commission of a felony; willful misconduct; or any commission of any act or series of acts of dishonesty which are injurious to the best interests of the Company.

2. a. The exercise price of this option is _____ per share, being not less than the fair market value of the Common Stock on the date of grant of this option.
- b. Payment of the exercise price per share is due in full in cash (including check) upon exercise of the option with respect to all or any part of each installment which has become exercisable by you. Notwithstanding the foregoing, this option may be exercised pursuant to a program developed under Regulation T as promulgated by the Federal Reserve Board which results in the receipt of cash (or

check) by the Company prior to the issuance of Common Stock.

3. The minimum number of shares with respect to which this option may be exercised at any one time is one hundred (100) except (a) as to an installment subject to exercise, as set forth in paragraph 1, which amounts to fewer than one hundred (100) shares, in which case, as to the exercise of that installment, the number of shares in such installment shall be the minimum number of shares, and (b) with respect to the final exercise of this option this paragraph 3 shall not apply.
4. Notwithstanding anything to the contrary contained herein, this option may not be exercised unless the shares issuable upon exercise of this option are then registered under the Act or if such shares are not then so registered, the Company has determined that such exercise and issuance is exempt from the registration requirements of the Act.
5. The term of this option commences on the date hereof and, unless sooner terminated as set forth below or in the Plan, terminates ten (10) years from the date this option is granted. This option shall terminate prior to the expiration of its term as follows: this option shall terminate three (3) months after the termination of your employment with the Company or an affiliate of the Company (as defined in the Plan) for any reason or for no reason (including without limitation a termination in connection with a "change of control" of the Company, as defined in paragraph 1 hereof) unless:
 - a. such termination of your employment is due to your permanent and total disability (within the meaning of Section 422A(c)(7) of the Code), in which event the option shall terminate on the earlier of the termination date set forth above or one (1) year following such termination of employment; or
 - b. such termination of employment is due to your death, in which event the option shall terminate on the earlier of the termination date set forth above or eighteen (18) months after your death; or
 - c. during any part of such three (3) month period the option is not exercisable solely because of the condition set forth in paragraph 4 above, in which

event the option shall not terminate until the earlier of the termination date set forth above or until it shall have been exercisable for an aggregate period of three (3) months after termination of employment; or

- d. exercise of the option within three (3) months after termination of your employment with the Company or with an affiliate would result in liability under section 16(b) of the Securities Exchange Act of 1934, in which case the option will terminate on the earlier of (i) the termination date set forth above, (ii) the tenth (10th) day after the last date upon which exercise would result in such liability or (iii) six (6) months and ten (10) days after the termination of your employment with the Company or an affiliate.

However, this option may be exercised following termination of employment only as to that number of shares as to which it was exercisable under the provisions of paragraph 1 of this option on the date of termination of employment.

- 6. a. This option may be exercised, to the extent specified above, by delivering a notice of exercise (in a form designated by the Company) together with the exercise price to the Secretary of the Company, or to such other person as the Company may designate, during regular business hours, together with such additional documents as the Company may then require pursuant to subparagraph 5(f) of the Plan.

- b. By exercising this option you agree that:

- (i) The Company may require you to enter an arrangement providing for the payment by you to the Company of any tax withholding obligation of the Company arising by reason of (1) the exercise of this option; (2) the lapse of any substantial risk of forfeiture to which the shares are subject at the time of exercise; or (3) the disposition of shares acquired upon such exercise;
- (ii) you will notify the Company in writing within fifteen (15) days after the date of any

disposition of any of the shares of the Common Stock issued upon exercise of this option that occurs within two (2) years after the date of grant of the option hereunder or within one (1) year after such shares of Common Stock are transferred upon exercise of this option; and

- (iii) the Company (or a representative of the underwriters) may, in connection with the first underwritten registration of the offering of any securities of the Company under the Act, require that you do not sell or otherwise transfer or dispose of any shares of Common Stock or other securities of the Company during such period (not to exceed one hundred fifty (150) days) following the effective date (the "Effective Date") of the registration statement of the Company filed under the Act as may be requested by the Company or the representative of the underwriters; provided, however, that such restriction shall apply only if, on the Effective Date, you are an officer, director, or owner of more than one percent (1%) of the outstanding securities of the Company. For purposes of this restriction, you will be deemed to own securities which (i) are owned directly or indirectly by you, including securities held for your benefit by nominees, custodians, brokers or pledgees; (ii) may be acquired by you within sixty (60) days of the Effective Date; (iii) are owned directly or indirectly, by or for your brothers or sisters (whether by whole or half blood), spouse, ancestors and lineal descendants; or (iv) are owned, directly or indirectly, by or for a corporation, partnership, estate or trust of which you are a shareholder, partner or beneficiary but only to the extent of your proportionate interest therein as a shareholder, partner or beneficiary thereof. You further agree that the Company may impose stop-transfer instructions with respect to securities subject to the foregoing restrictions until the end of such period.

7. This option is not transferable, except by will or by the laws of descent and distribution, and is exercisable during your life only by you.
8. This option is not an employment contract and nothing in this option shall be deemed to create in any way whatsoever any obligation on your part to continue in the employ of the Company, or of the Company to continue your employment with the Company.
9. Any notices provided for in this option or the Plan shall be given in writing and shall be deemed effectively given upon receipt or, in the case of notices delivered by the Company to you, five (5) days after deposit in the United States mail, postage prepaid, addressed to you at the address specified below or at such other address as you hereafter designate by written notice to the Company.
10. This option is subject to all the provisions of the Plan, a copy of which is attached hereto and its provisions are hereby made a part of this option, including without limitation the provisions of paragraph 5 of the Plan relating to option provisions, and is further subject to all interpretations, amendments, rules and regulations which may from time to time be promulgated and adopted pursuant to the Plan. In the event of any conflict between the provisions of this option and those of the Plan, the provisions of the Plan shall control; provided, however, that you shall be entitled to receive stock options on additional shares of the Corporation's common stock to protect you against dilution of your share holding to the full extent provided by your Employment Agreement with the Company.

Dated as of the ____ day of _____, 19__.

Very truly yours,

AASTROM BIOSCIENCES, INC.

By:

Duly authorized on behalf of
the Board of Directors.

The undersigned:

- a. Acknowledges receipt of the foregoing and the attachments referenced therein and understands that all rights and liabilities with respect to this option are set forth in the option and the Plan; and
- b. Acknowledges that as of the date of grant of this option, it sets forth the entire understanding between the undersigned optionee and the Company and its affiliates regarding the acquisition of stock in the Company and supersedes all prior oral and written agreements on that subject.

OPTIONEE

Address:

Attachment:

1989 Stock Option Plan

Stock Transfer Restriction and Buy-Out Agreement

ANCILLARY STOCK OPTION PLAN

THIS ANCILLARY STOCK OPTION PLAN (the "Ancillary Plan") is made as of August 6, 1991, by Aastrom Biosciences, Inc. (the "Company"), with respect to the facts set forth below.

RECITALS

A. On August 15, 1989, the Company formally approved the 1989 Stock Option Plan (the "1989 Plan"), pursuant to which the Board of Directors of the Company (the "Board") is authorized to grant tax qualified "incentive stock options" to employees of the Company or its affiliates and tax nonqualified "supplemental stock options" to employees, officers, employed directors and consultants of the Company or its affiliates.

B. In order to advance the growth and prosperity of the Company, the Board believes that it is in the best interests of the Company to also grant stock options on certain occasions to certain parties and persons selected by the Board who are not otherwise eligible to receive stock options under the terms of the 1989 Plan.

AGREEMENT

NOW, THEREFORE, Company hereby authorizes and establishes this Ancillary Plan, pursuant to the terms and conditions set forth below.

1. Purpose. The purpose of the Ancillary Plan is to advance the growth and prosperity of the Company and its shareholders by providing incentives to certain parties and persons selected by the Board who are not otherwise eligible to receive stock options under the 1989 Plan. The stock options granted pursuant to this Ancillary Plan shall be treated as "nonqualified tax options" under the U.S. Internal Revenue Code.

2. Term. The term of this Ancillary Plan shall commence on the date set forth above and shall terminate upon resolution by the Board.

3. Shares of Stock Subject to this Ancillary Plan. The shares of Common Stock which may be issued pursuant to the Ancillary Plan upon exercise of stock options shall not exceed in the aggregate Fifty Thousand (50,000) shares of the Company's Common Stock, unless otherwise approved by the Board by vote of not less than two thirds (2/3) of the Board. Such shares of Common Stock shall be authorized and unissued shares. The shares allocated to this Ancillary Plan and the stock options granted pursuant to this Ancillary Plan are in addition to, and not part of, the shares allocated to and granted pursuant to the 1989 Plan.

4. Administration of the Plan. The Board shall administer the Ancillary Plan, select the persons to whom stock options shall be granted, determine the number of shares of Common Stock to be optioned and awarded, determine the purchase price per share of Common Stock deliverable upon the exercise of a stock option, determine the method of payment upon the exercise of an option, and interpret, construe and implement the provisions of this Ancillary Plan. An option may be exercisable at any time from time to time, subject to such timing, performance criteria, conditions and restrictions as determined by the Board on a case by case basis for each option as set forth in the Stock Option Agreements.

5. Stock Option Agreements. The granting of stock options shall be evidenced by a Stock Option Agreement, containing such terms and conditions as the Board of Directors shall deem appropriate. The provisions of the Stock Option Agreements granted pursuant to this Ancillary Plan need not be identical, may be similar to or different from the form of Stock Option Agreements granted under the 1989 Plan, and may be customized as determined by the Board on a case by case basis.

6. Amendment of this Ancillary Plan. This Ancillary Plan may, at any time or from time to time, be terminated, modified or amended by the Board.

7. Approval. Approved by the Board on August 6, 1991.

/s/ R. DOUGLAS ARMSTRONG

R. Douglas Armstrong, Ph.D
President/CEO

ANCILLARY STOCK OPTION AGREEMENT

Optionee:

AASTROM Biosciences, Inc., formerly known as Ann Arbor Stromal, Inc., (the "Company"), pursuant to its Ancillary Stock Option Plan dated August 6, 1991 (the "Plan"), has granted to you, the Optionee named above, an option to purchase shares of the common stock of the Company ("Common Stock"). This option is not intended to qualify and will not be treated as an "incentive stock option" within the meaning of Section 422A of the Internal Revenue code of 1986, as amended from time to time (the "Code"). The date of grant of this option is as of _____, ____.

The grant hereunder is a matter of separate inducement and agreement in connection with your services to the Company and not in lieu of any other compensation for services, and is intended to comply with the provisions of Rule 701 promulgated by the Securities and Exchange Commission under the Securities Act of 1933, as amended (the "Act"), and applicable state law exemptions from registration.

The details of your option are as follows:

1. The total number of shares of Common Stock subject to this option is _____. Subject to the limitations contained herein, including without limitation Section 5 hereof, this option shall be exercisable with respect to each installment shown below on or after the date of vesting applicable to such installment, as follows:

Number of Shares

(Installment)

Date of Earliest Exercise

(Vesting)

2. a. The exercise price of this option is _____ per share, being not less than the fair market value of the Common Stock on the date of grant of this option.
- b. Payment of the exercise price per share is due in full in cash (including check) upon exercise of all or any part of each installment which has become exercisable by you. Notwithstanding the foregoing, this option may be exercised pursuant to a program developed under Regulation T as promulgated by the Federal Reserve Board which results in the receipt of cash (or check) by the Company prior to the issuance of Common Stock.
3. The minimum number of shares with respect to which this option may be exercised at any one time is one hundred (100) except (a) as to an installment subject to exercise, as set forth in paragraph 1, which amounts to fewer than one hundred (100) shares, in which case, as to the exercise of that installment, the number of shares in such installment shall be the minimum number of shares, and (b) with respect to the final exercise of this option this paragraph 3 shall not apply.
4. Notwithstanding anything to the contrary contained herein, this option may not be exercised unless the shares issuable upon exercise of this option are then registered under the Act or if such shares are not then so registered, the exercise and issuance of such shares would be exempt from the registration requirements of the Act.
5. The term of this option commences on the date hereof and, unless sooner terminated as set forth below, terminates twelve (12) years from the date this option is granted. This option shall terminate prior to the expiration of its term as follows: this option shall terminate three (3) months after the termination of your participation in the University of Michigan ex vivo bone marrow project more fully described in that certain Option Agreement dated March 24, 1989, between the Company, the University of Michigan and H&Q Life Science Technology Fund 1 (hereinafter such participation in the ex vivo bone marrow project

shall be referred to as "Employment") for any reason or for no reason unless:

- a. such termination of your Employment is due to your permanent and total disability (within the meaning of Section 422A(c)(7) of the Code), in which event the option shall terminate on the earlier of the termination date set forth above or one (1) year following such termination of Employment; or
- b. such termination of Employment is due to your death, in which event the option shall terminate on the earlier of the termination date set forth above or eighteen (18) months after your death; or
- c. during any part of such three (3) month period the option is not exercisable solely because of the condition set forth in paragraph 4 above, in which event the option shall not terminate until the earlier of the termination date set forth above or until it shall have been exercisable for an aggregate period of three (3) months after the termination of Employment; or
- d. exercise of the option within three (3) months after termination of your Employment would result in liability under section 16 (b) of the Securities Exchange Act of 1934, in which case the option will terminate on the earlier of (i) the tenth (10th) day after the last date upon which exercise would result in such liability or (ii) six (6) months and ten (10) days after the termination of your Employment; or
- e. such termination of your Employment is a temporary leave of absence occasioned by your resuming studies at the University of Michigan toward a doctorate degree, in which event vesting of installments of this option as set forth in Section 1 scheduled for any date after the date on which the leave of absence commenced (the "Leave Date") will be suspended, and the vesting schedule set forth in Section 1 shall be deemed to have been amended as follows. Should you Employment

resume at any time during the two (2) year period after the Leave Date, vesting of installments of this option will resume, with the first suspended installment vesting on the date that your Employment resumes, the second suspended installment vesting 3 months thereafter, and so on, so that each succeeding suspended installment vests 3 months after the date on which the previous suspended installment vested. If your Employment does not resume during the two (2) year period after the Leave Date, this option will be deemed to have terminated on the Leave Date, and only those shares that vested on or prior to the Leave Date will be exercisable.

- f. The termination of this option pursuant to this Section 5 shall apply only to those shares not yet vested according to the schedule contained in Section 1 herein, and any provision herein or in the Plan notwithstanding, shall not apply to such vested shares. Any shares that have vested hereunder shall remain exercisable for the twelve (12) year period specified in this Section 5.

However, this option may be exercised following termination of Employment only as to that number of shares as to which it was exercisable under the provisions of paragraph 1 of this option on the date of termination of Employment.

6. a. This option may be exercised, to the extent specified above, by delivering a notice to exercise (in a form designated by the Company) together with the exercise price to the Secretary of the Company, or to such other person as the Company may designate, during regular business hours, together with such additional documents as the Company may then require pursuant to subparagraph 5(f) of the Plan.

b. By exercising this option you agree that:

- (i) the Company may require you to enter an arrangement providing for the cash payment by you to the Company of any tax withholding obligation of the Company arising by reason of (1) the exercise of this option; (2) the lapse of any substantial risk of forfeiture to which the shares are subject at the time of exercise; or (3) the disposition of shares acquired upon such exercise;
- (ii) the Company (or a representative of the underwriters) may, in connection with the first underwritten registration of the offering of any securities of the Company under the Act, require that you not sell or otherwise transfer or dispose of any shares of Common Stock or other securities of the Company during such period (not to exceed one hundred fifty (150) days) following the effective date (the "Effective Date") of the registration statement of the Company filed under the Act as may be requested by the Company or the representative of the underwriters; provided, however, that such restriction shall apply only if, on the Effective Date, you are an officer, director, or owner of more than one percent (1%) of the outstanding securities of the Company. For purposes of this restriction, you will be deemed to own securities which (i) are owned directly or indirectly by you, including securities held for your benefit by nominees, custodians, brokers or pledgees; (ii) may be acquired by you within sixty (60) days of the Effective Date; (iii) are owned directly or indirectly, by or for your brothers or sisters (whether by whole or half blood), spouse, ancestors and lineal descendants; or (iv) are owned, directly or indirectly, by or for a corporation, partnership, estate or trust of which you are a shareholder, partner or

beneficiary, but only to the extent of your proportionate interest therein as a shareholder, partner or beneficiary thereof. You further agree that the Company may impose stop-transfer instructions with respect to securities subject to the foregoing restrictions until the end of such period.

7. This option is not transferable, except by will or by the laws of descent and distribution, and is exercisable during your life only by you.
8. Upon exercise of the option in whole or in part, you will be required to execute a Stock Transfer Restriction and Buy-Out Agreement substantially in the form attached hereto, which sets forth restrictions on transfer of the Stock and gives the Company the right to purchase the Stock under certain circumstances.
9. This option is not an employment contract and nothing in this option shall be deemed to create in any way whatsoever any obligation on your part to continue Employment, or of the Company to employ you.
10. Any notices provided for in this option or the Plan shall be given in writing and shall be deemed effectively given upon receipt or, in the case of notices delivered by the Company to you, five (5) days after deposit in the United States mail, postage prepaid, addressed to you at the address specified below or at such other address as you hereafter designate by written notice to the Company.
11. This option is subject to all the provisions of the Plan, a copy of which is attached hereto and its provisions are hereby made a part of this option, including without limitation the provisions of paragraph 5 of the Plan relating to stock option agreements, and is further subject to all interpretations, amendments, rules and regulations which may from time to time be promulgated and adopted pursuant to the Plan. In the event of any conflict between the provisions of this option and those of the Plan, the provisions of the Plan shall control.

Dated as of the ____ day of _____, 19__.

Very truly yours,
AASTROM BIOSCIENCES, INC.

By: _____
R. Douglas Armstrong, Ph.D.
President/CEO

Duly authorized on behalf of the
Board of Directors

The undersigned:

- a. Acknowledges receipt of this Agreement and the attachments referenced therein and understands that all rights and liabilities with respect to this option are set forth in this Agreement and the Plan; and
- b. Acknowledges that as of the date of grant of this option, this Agreement sets forth the entire understanding between the undersigned optionee and the Company its affiliates regarding the acquisition of stock in the Company and supersedes all prior oral and written agreements on that subject.

OPTIONEE

Address: _____

Attachments:

- Ancillary Stock Option Plan dated August 6, 1991
- Stock Transfer Restriction and Buy-Out Agreement

MERRILL LYNCH

SPECIAL

PROTOTYPE DEFINED

CONTRIBUTION PLAN

401(k) PLAN

EMPLOYEE THRIFT PLAN

PROFIT-SHARING PLAN

ADOPTION AGREEMENT

THIS PROTOTYPE PLAN AND ADOPTION AGREEMENT ARE IMPORTANT LEGAL INSTRUMENTS WITH LEGAL AND TAX IMPLICATIONS FOR WHICH THE SPONSOR, MERRILL LYNCH, PIERCE, FENNER & SMITH, INCORPORATED DOES NOT ASSUME RESPONSIBILITY. THE EMPLOYER IS URGED TO CONSULT WITH ITS OWN ATTORNEY WITH REGARD TO THE ADOPTION OF THIS PLAN AND ITS SUITABILITY TO ITS CIRCUMSTANCES.

ADOPTION OF PLAN
- - - - -

The Employer named below hereby establishes or restates a profit-sharing plan that includes a ☒ 401(k), ☐ profit-sharing and/or ☐ thrift plan feature (the "Plan") by adopting the Merrill Lynch Special Prototype Defined Contribution Plan and Trust as modified by the terms and provisions of this Adoption Agreement.

EMPLOYER AND PLAN INFORMATION
- - - - -

Employer Name:* Aastrom Biosciences. Inc.

Business Address: P.O. Box 376

 Ann Arbor. MI 48106

Telephone Number: (313) 930-5555

Employer Taxpayer I.D. Number: 94-3096597

Employer Taxable Year ends on: June 30th

Plan Name: Aastrom Biosciences, Inc. 401(k) Plan

Plan Number: 001

	401(k)	PROFIT- SHARING	THRIFT
Effective Date of Adoption:	01/01/94	-----	-----
Tax Reform Act of 1986 Restatement Date:	-----	-----	-----
Original Effective Date:	-----	-----	-----

IF THIS PLAN IS A CONTINUATION OR AN AMENDMENT OF A PRIOR PLAN, ALL OPTIONAL FORMS OF BENEFITS PROVIDED IN THE PRIOR PLAN MUST BE PROVIDED UNDER THIS PLAN TO ANY PARTICIPANT WHO HAD AN ACCOUNT BALANCE, WHETHER OR NOT VESTED, IN THE PRIOR PLAN.

- - - - -
* If there are any Participating Affiliates in this Plan, list below the proper name of each Participating Affiliate.

ARTICLE I. DEFINITIONS

A. "COMPENSATION"

(1) With respect to each Participant except as provided below, Compensation shall mean the (select all those applicable for each column):

401(k) AND/
OR THRIFT PROFIT
 SHARING

- ☒ ☐ (a) amount reported in the "Wages Tips and Other Compensation" Box on Form W-2 for the applicable period selected in Item 5 below.
- ☐ ☐ (b) compensation for Code Section 415 safe-harbor purposes (as defined in section 3.9.1(H)(i) of basic plan document #03) for the applicable period selected in Item 5 below.
- ☐ ☐ (c) amount reported pursuant to Code Section 3401 (a) for the applicable period selected in Item 5 below.
- ☐ ☐ (d) all amounts received (under either option (a) or (b) above) for personal services rendered to the Employer but excluding (select one):
- ☐ overtime
- ☐ bonuses
- ☐ commissions
- ☐ amounts in excess of \$ _____
- ☐ other (specify) _____.

(2) Treatment of Elective Contributions (select one):

- ☒ (a) For purposes of contributions, Compensation shall include Elective Deferrals and amounts excludable from the gross income of the Employee under Code Section 125, Code Section 402(e)(3), Code Section 402(h) or Code Section 403(b) ("elective contributions").
- ☐ (b) For purposes of contributions, Compensation shall not include "elective contributions."

(3) CODA Compensation (select one):

- ☒ (a) For purposes of the ADP and ACP Tests, Compensation shall include "elective contributions."
- ☐ (b) For purposes of the ADP and ACP Tests, Compensation shall not include "elective contributions."

- (4) With respect to Contributions to an Employer Contributions Account, Compensation shall include all Compensation (select one):

☐ (a) during tile Plan Year in which the Participant enters the Plan.

☒ (b) after the Participant's Entry Date.

- (5) The applicable period for determining Compensation shall be (select one):

☒ (a) the Plan Year.

☐ (b) the Limitation Year.

☐ (c) the consecutive 12-month period ending on _____.

B. "DISABILITY"

- (1) Definition

Disability shall mean a condition which results in the Participant's (select one):

☐ (a) inability to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment that can be expected to result in death or which has lasted or can be expected to last for a continuous period of not less than 12 months.

☐ (b) total and permanent inability to meet the requirements of the Participant's customary employment which can be expected to last for a continuous period of not less than 12 months.

☐ (c) qualification for Social Security disability benefits.

☒ (d) qualification for benefits under the Employer's long-term disability plan.

- (2) Contributions Due to Disability (select one):

☒ (a) No contributions to an Employer Contributions Account will be made on behalf of a Participant due to his or her Disability.

☐ (b) Contributions to an Employer Contributions Account will be made on behalf of a Participant due to his or her Disability provided that

the Employer elected option (a) or (c) above as the definition of Disability, contributions are not made on behalf of a Highly Compensated Employee, the contribution is based on the Compensation each such Participant would have received for the Limitation Year if the Participant had been paid at the rate of Compensation paid immediately before his or her Disability, and contributions made on behalf of such Participant will be nonforfeitable when made.

C "EARLY RETIREMENT" is (select one):

[] (1) not permitted.

[X] (2) permitted if a Participant terminates Employment before Normal Retirement Age and has (select one):

[] (a) attained age ----- .
[X] (b) attained age 55 and completed 10 Years of Service.
[] (c) attained age -- and completed -- Years of Service

as a Participant.

D. "ELIGIBLE EMPLOYEES" (select one):

[X] (1) All Employees are eligible to participate in the Plan.

[] (2) The following Employees are not eligible to participate in the Plan (select all those applicable):

[] (a) Employees included in a unit of Employees covered by a collective bargaining agreement between the Employer or a Participating Affiliate and the Employee representatives (not including any organization more than half of whose members are Employees who are owners, officers, or executives of the Employer or Participating Affiliate) in the negotiation of which retirement benefits were the subject of good faith bargaining, unless the bargaining agreement provides for participation in the Plan.

[] (b) non-resident aliens who received no earned income from the Employer or a Participating Affiliate which constitutes income from sources within the United States.

[] (c) Employees of an Affiliate.

[] (d) Employees employed in or by the following specified division, plant, location, job category or other identifiable individual or group of Employees:

B. "ENTRY DATE"

Entry Date shall mean (select as applicable):

401(k)
AND/OR PROFIT-
THRIFT SHARING

- ☐ ☐ (1) If the initial Plan Year is less than twelve months, the
day of ----- and thereafter:

- ☐ ☐ (2) the first day of the Plan Year following the date the
Employee meets the eligibility requirements. if the Employer
elects this option (2) establishing only one Entry Date, the
eligibility "age and service" requirements elected in Article
II must be no more than age 20-1/2 and 6 months of service.
- ☒ ☐ (3) the first day of the month following the date the Employee
meets the eligibility requirements.
- ☐ ☐ (4) the first day of the Plan Year and the first day of the
seventh month of the Plan Year following the date the
Employee meets the eligibility requirements.
- ☐ ☐ (5) the first day of the Plan Year, the first day of the fourth
month of the Plan Year, the first day of the seventh month of
the Plan Year, and the first day of the tenth month of the
Plan Year following the date the Employee meets the
eligibility requirements.
- ☐ ☐ (6) other: -----

provided that the Entry Date or Dates selected are no later
than any of the options above.

F. "HOURS OF SERVICE"

Hours of Service for the purpose of determining a Participant's Period of
Severance and Year of Service shall be determined on the basis of the method
specified below:

- (1) Eligibility Service: For purposes of determining whether a Participant

has satisfied the eligibility requirements, the following method shall
be used (select one):

401(k)
AND/OR PROFIT-
THRIFT SHARING

- ☒ ☐ (a) elapsed time method
☐ ☐ (b) hourly records method

(2) Vesting Service: A Participant's nonforfeitable interest shall be

determined on the basis of the method specified below (select one):

- ☐ (a) elapsed time method
☒ (b) hourly records method
☐ (c) if this item (c) is checked, the Plan only provides for contributions that are always 100% vested and this item (2) will not apply.

(3) Hourly Records: For the purpose of determining Hours of Service under

the hourly record method (select one):

- ☒ (a) only actual hours for which an Employee is paid or entitled to payment shall be counted.

☐ (b) an Employee shall be credited with 45 Hours of Service if such Employee would be credited with at least 1 Hour of Service during the week.

G. "INTEGRATION LEVEL"

- ☒ (1) This Plan is not integrated with Social Security.

☐ (2) This Plan is integrated with Social Security. The Integration Level shall be (select one):

☐ (a) the Taxable Wage Base.
☐ (b) \$ _____ (a dollar amount less than the Taxable Wage Base).

☐ (c) _____ % of the Taxable Wage Base (not to exceed 100%).

☐ (d) the greater of \$10,000 or 20% of the Taxable Wage Base.

H. "LIMITATION COMPENSATION"

For purposes of Code Section 415, Limitation Compensation shall be compensation as determined for purposes of (select one):

- ☐ (1) Code Section 415 Safe-Harbor as defined in Section 3.9.1(H)(i) of basic plan document #03.

☒ (2) the "Wages, Tips and Other Compensation" Box on Form W-2.

☐ (3) Code Section 3401(a) Federal Income Tax Withholding.

I. "LIMITATION YEAR"

For purposes of Code Section 415, the Limitation Year shall be (select one):

- ☒ (1) the Plan Year.
☐ (2) the twelve consecutive month period ending on the _____ day of the
month of _____.

J. "NET PROFITS" are (select one):

☒ (1) not necessary for any contribution.

☐ (2) necessary for (select all those applicable):

- ☐ (a) Profit-Sharing Contributions.
☐ (b) Matching 401(k) Contributions.
☐ (c) Matching Thrift Contributions.

K. "NORMAL RETIREMENT AGE"

Normal Retirement Age shall be (select one):

☒ (1) attainment of age 65 (not more than 65) by the Participant.

☐ (2) attainment of age _____ (not more than 65) by the Participant or the _____ anniversary (not more than the 5th) of the first day of the _____ Plan Year in which the Eligible Employee became a Participant whichever is later.

☐ (3) attainment of age _____ (not more than 65) by the Participant or the _____ anniversary (not more than the 5th) of the first day on _____ which the Eligible Employee performed an hour of Service, whichever is later.

L. "PARTICIPANT DIRECTED ASSETS" are:

401(k) AND/ PROFIT-
OR THRIFT SHARING

☒ ☐ (1) permitted.

☐ ☐ (2) not permitted.

M. "PLAN YEAR"

The Plan Year shall end on the 31ST day of DECEMBER.

N. "PREDECESSOR SERVICE"

Predecessor service will be credited (select one):

☒ (1) only as required by the Plan.

☐ (2) to include, in addition to the Plan requirements and subject to the limitations set forth below, service with the following predecessor employer(s) determined as if such predecessors were the Employer:

Service with such predecessor employer applies [select either or both (a) and/or (b); (c) is only available in addition to (a) and/or (b)]:

- ☐ (a) for purposes of eligibility to participate;
☐ (b) for purposes of vesting;
☐ (c) except for the following service: -----

O. "VALUATION DATE"

Valuation Date shall mean (select one for each column, as applicable):

401(k) AND/ PROFIT-
OR THRIFT SHARING

- ☐ ☐ (1) the last business day of each month.
☐ ☐ (2) the last business day of each quarter within the Plan Year.
☐ ☐ (3) the last business day of each semi-annual period within the Plan Year.
☐ ☐ (4) the last business day of the Plan Year.
☒ ☐ (5) other: DAILY.

ARTICLE II. PARTICIPATION

PARTICIPATION REQUIREMENTS

An Eligible Employee must meet the following requirements to become a Participant (select one or more for each column, as applicable):

401(k) AND/ PROFIT-
OR THRIFT SHARING

- ☐ ☐ (1) Performance of one Hour of Service.
☐ ☐ (2) Attainment of age (maximum 20 1/2) and completion of

----- (not more than 1/2) Years of Service. If this

item is selected, no Hours of Service shall be counted.
☒ ☐ (3) Attainment of age (maximum 21) and completion of 1/4

Year(s) of Service. if more than one Year of Service is
selected, tile immediate 100% vesting schedule must be
selected in Article VII of this Adoption Agreement.

☐ (4) Attainment of age (maximum 21) and completion of

Years of Service. If more than one Year of Service

is selected, the immediate 100% vesting schedule must be
selected in Article VII of this Adoption Agreement.

☒ (5) Each Employee who is an Eligible Employee on 01/01/94

will be deemed to have satisfied the participation
requirements on the effective date without regard to
such Eligible Employee's actual age and/ or service.

ARTICLE III. 401(k) CONTRIBUTIONS AND ACCOUNT ALLOCATION -----

A. ELECTIVE DEFERRALS -----

If selected below, a Participant's Elective Deferrals will be (select all
applicable):

- ☒ (1) a dollar amount or a percentage of Compensation, as specified by
the Participant on his or her 401(k) Election form, which may not
exceed 15% of his or her Compensation.
- ☐ (2) with respect to bonuses, such dollar amount or percentage as
specified by the Participant on his or her 401(k) Election form with
respect to such bonus.

B. MATCHING 401(k) CONTRIBUTIONS -----

If selected below, the Employer may make Matching 401(k) Contributions for
each Plan Year (select one):

☒ (1) Discretionary Formula:

Discretionary Matching 401(k) Contribution equal to such a dollar
amount or percentage of Elective Deferrals, as determined by the
Employer, which shall be allocated (select one):

- ☐ (a) based on the ratio of each Participant's Elective Deferral
for the Plan Year to the total Elective Deferrals of all
Participants for the Plan Year. If inserted, Matching
401(k) Contributions shall be subject to a maximum amount
of \$ ----- for each Participant or ---- % of each
Participant's Compensation.

☒ (b) in an amount not to exceed _____ % of each Participants
first _____ % of Compensation contributed as Elective
_____ Deferrals for the Plan Year. If any Matching 401(k)
Contribution remains, it is allocated to each such
Participant in an amount not to exceed _____ % of the next
_____ % of each Participant's Compensation contributed as
_____ Elective Deferrals for the Plan Year.

Any remaining Matching 401(k) Contribution shall be allocated to each such
Participant in the ratio that such Participant's Elective Deferral for the
Plan Year bears to the total Elective Deferrals of all such Participants for
the Plan Year. If inserted, Matching 401(k) Contributions shall be subject
to a maximum amount of \$ _____ for each Participant or _____ % of each
Participant's Compensation.

☐ (2) Nondiscretionary Formula:

A nondiscretionary Matching 401(k) Contribution for each Plan Year
equal to (select one):

☐ (a) _____ % of each Participant's Compensation contributed as
_____ Elective Deferrals. If inserted, Matching 401(k)
Contributions shall be subject to a maximum amount of
\$ _____ for each Participant or _____ % of each Participant's
_____ Compensation.

☐ (b) _____ % of the first _____ % of the Participant's
_____ Compensation contributed as Elective Deferrals and _____ %
of the next _____ % of the Participant's Compensation
_____ contributed as Elective Deferrals. If inserted, Matching
401(k) Contributions shall be subject to a maximum amount
of \$ _____ for each Participant or _____ % of each
_____ Participant's Compensation.

C. PARTICIPANTS ELIGIBLE FOR MATCHING 401(k) CONTRIBUTION ALLOCATION

The following Participants shall be eligible for an allocation to their
Matching 401(k) Contributions Account (select all those applicable):

☐ (1) Any Participant who makes Elective Deferrals.

☐ (2) Any Participant who satisfies those requirements elected by the
Employer for an allocation to his or her Employer Contributions
Account as provided in Article IV Section C.

☐ (3) Solely with respect to a Plan in which Matching 401(k)
Contributions are made quarterly (or on any other regular interval
that is more frequent than annually) any Participant whose 401(k)
Election is in effect throughout such entire quarter (or other
interval).

D. QUALIFIED MATCHING CONTRIBUTIONS

If selected below, the Employer may make Qualified Matching Contributions for each Plan Year (select all those applicable):

- (1) In its discretion, the Employer may make Qualified Matching Contributions on behalf of (select one):

☐ (a) all Participants who make Elective Deferrals in that Plan Year.

☒ (b) only those Participants who are Nonhighly Compensated Employees and who make Elective Deferrals for that Plan Year.

- (2) Qualified Matching Contributions will be contributed and allocated to each Participant in an amount equal to:

☐ (a) % of the Participant's Compensation contributed as

Elective Deferrals. If inserted, Qualified Matching
Contributions shall not exceed % of the Participant's

Compensation.

☒ (b) Such an amount determined by the Employer, which is needed to meet the ACP Test.

- (3) In its discretion, the Employer may elect to designate all or any part of Matching 401(k) Contributions as Qualified Matching Contributions that are taken into account as Elective Deferrals -- included in the ADP Test and excluded from the ACP Test -- on behalf of (select one):

☐ (a) all Participants who make Elective Deferrals for that Plan Year.

☒ (b) Only Participants who are Nonhighly Compensated Employees who make Elective Deferrals for that Plan Year.

E. QUALIFIED NONELECTIVE CONTRIBUTIONS

If selected below, the Employer may make Qualified Nonelective Contributions for each Plan Year (select all those applicable):

- (1) In its discretion, the Employer may make Qualified Nonelective Contributions on behalf of (select one):

☐ (a) all Eligible Participants.

☒ (b) only Eligible Participants who are Nonhighly Compensated Employees.

(2) Qualified Nonelective Contributions will be contributed and allocated to each Eligible Participant in an amount equal to (select one):

☐ (a) _____ % (no more than 15%) of the Compensation of each Eligible Participant eligible to share in the allocation.

☒ (b) Such an amount determined by the Employer, which is needed to meet either the ADP Test or ACP Test.

(3) At the discretion of the Employer, as needed and taken into account as Elective Deferrals included in the ADP Test on behalf of (select one):

☐ (a) all Eligible Participants.

☒ (b) only those Eligible Participants who are Nonhighly Compensated Employees.

F. ELECTIVE DEFERRALS USED IN ACP TEST (select one):

☒ (1) At the discretion of the Employer, Elective Deferrals may be used to satisfy the ACP Test.

☐ (2) Elective Deferrals may not be used to satisfy the ACP Test.

G. MAKING AND MODIFYING A 401(k) ELECTION

An Eligible Employee shall be entitled to increase, decrease or resume his or her Elective Deferral percentage with the following frequency during the Plan Year (select one):

☐ (1) annually.

☐ (2) semi-annually.

☒ (3) quarterly.

☐ (4) monthly

☐ (5) other (specify): _____.

Any such increase, decrease or resumption shall be effective as of the first payroll period coincident with or next following the first day of each period set forth above. A Participant may completely discontinue making Elective Deferrals at any time effective for the payroll period after written notice is provided to the Administrator.

ARTICLE IV. PROFIT-SHARING CONTRIBUTIONS

AND ACCOUNT ALLOCATION

A. PROFIT-SHARING CONTRIBUTIONS

If selected below, the following contributions for each Plan Year will be made:

Contributions to Employer Contributions Accounts (select one):

- ☐ (a) Such an amount, if any, as determined by the Employer.
☐ (b) _____ % of each Participant's Compensation.

B. ALLOCATION OF CONTRIBUTIONS TO EMPLOYER CONTRIBUTIONS ACCOUNTS (select one):

☐ (1) Non-Integrated Allocation

The Employer Contributions Account of each Participant eligible to share in the allocation for a Plan Year shall be credited with a portion of the contribution, plus any forfeitures if forfeitures are reallocated to Participants, equal to the ratio that the Participant's Compensation for the Plan Year bears to the Compensation for that Plan Year of all Participants entitled to share in the contribution.

☐ (2) Integrated Allocation

Contributions to Employer Contributions Accounts with respect to a Plan Year, plus any forfeitures if forfeitures are reallocated to Participants, shall be allocated to the Employer Contributions Account of each eligible Participant as follows:

(a) First, in the ratio that each such eligible Participant's Compensation for the Plan Year bears to the Compensation for that Plan Year of all eligible Participants but not in excess of 3% of each Participant's Compensation.

(b) Second, any remaining contributions and forfeitures will be allocated in the ratio that each eligible Participant's Compensation for the Plan Year in excess of the Integration Level bears to all such Participants' excess Compensation for the Plan Year but not in excess of 3%.

(c) Third, any remaining contributions and forfeitures will be allocated in the ratio that the sum of each Participant's Compensation and Compensation in excess of the Integration Level bears to the sum of all Participants' Compensation and Compensation in excess of the Integration Level, but not in excess of the Maximum Profit-Sharing Disparity Rate (defined below).

(d) Fourth, any remaining contributions or forfeitures will be allocated in the ratio that each Participant's Compensation for that year bears to all Participants' Compensation for that year.

The Maximum Profit-Sharing Disparity Rate is equal to the lesser of:

(a) 2.7% or

(b) The applicable percentage determined in accordance with the following table:

IF THE INTEGRATION LEVEL IS (AS A % OF THE TAXABLE WAGE BASE ("TWB")).	THE APPLICABLE PERCENTAGE IS:
20% (or \$10,000 if greater) or less of the TWB	2.7%
More than 20% (but not less than \$10,001) but not more than 80% of the TWB	1.3%
More than 80% but not less than 100% of the TWB	2.4%
100% of the TWB	2.7%

C. PARTICIPANTS ELIGIBLE FOR EMPLOYER CONTRITION ALLOCATION

The fo1lowing Participants shall be eligible for an allocation to their Employer Contributions Account (select all those applicable):

- ☐ (1) Any Participant who was employed during the Plan Year.
- ☐ (2) In the case of a Plan using the hourly record method for determining Vesting Service, any Participant who was credited with a Year of Service during the Plan Year.
- ☐ (3) Any Participant who was employed on the last day of the Plan Year.
- ☐ (4) Any Participant who was on a leave of absence on the last day of the Plan Year.
- ☐ (5) Any Participant who during the Plan Year died or became Disabled while an Employee or terminated employment after attaining Normal Retirement Age.
- ☐ (6) Any Participant who was credited with at least 501 Hours of Service whether or not employed on the last day of the Plan Year.
- ☐ (7) Any Participant who was credited with at least 1,000 Hours of Service and was employed on the last day of the Plan Year.

ARTICLE V. THRIFT CONTRIBUTIONS

THIS ARTICLE IS NOT APPLICABLE

A. EMPLOYEE THRIFT CONTRIBUTIONS

If selected below, Employee Thrift Contributions, which are required for Matching Thrift Contributions, may be made by a Participant in an amount equal to (select one):

- ☐ (1) A dollar amount or a percentage of the Participant's Compensation which may not be less than % nor may not exceed % of his or her Compensation. ---- --
- ☐ (2) An amount not less than % of and not more than % of each Participant's Compensation. --- ---

B. MAKING AND MODIFYING AN EMPLOYEE THRIFT CONTRIBUTION ELECTION

A Participant shall be entitled to increase, decrease or resume his or her Employee Thrift Contribution percentage with the following frequency during the Plan Year (select one):

- ☐ (1) annually
☐ (2) semi-annually
☐ (3) quarterly
☐ (4) monthly
☐ (5) other (specify) _____

Any such increase, decrease or resumption shall be effective as of the first payroll period coincident with or next following the first day of each period set forth above. A Participant may completely discontinue making Employee Thrift Contributions at any time effective for the payroll period after written notice is provided to the Administrator.

C. THRIFT MATCHING CONTRIBUTIONS

If selected below, the Employer will make Matching Thrift Contributions for each Plan Year (select one):

- ☐ (1) Discretionary Formula:

A discretionary Matching Thrift Contribution equal to such a dollar amount or percentage as determined by the Employer, which shall be allocated (select one):

- ☐ (a) based on the ratio of each Participant's Employee Thrift Contribution for the Plan Year to the total Employee Thrift Contributions of all Participants for the Plan Year. If inserted, Matching Thrift Contributions shall be subject to a maximum amount of \$ _____ for each Participant or _____ % of each Participant's Compensation.

- ☐ (b) in an amount not to exceed _____ % of each Participant's first _____ % of Compensation contributed as Employee Thrift Contributions for the Plan Year. If any Matching Thrift Contribution remains, it is allocated to each such Participant in an amount not to exceed _____ % of the next _____ % of each Participant's Compensation contributed as Employee Thrift Contributions for the Plan Year.

Any remaining Matching Thrift Contribution shall be allocated to each such Participant in the ratio that such Participant's Employee Thrift Contributions for the Plan Year bears to the total Employee Thrift Contributions of all such Participants for the Plan Year. If inserted, Matching Thrift Contributions shall be subject to a maximum amount of \$ _____ for each Participant or _____ % of each Participant's Compensation.

☐ (2) Nondiscretionary Formula:

A nondiscretionary Matching Thrift Contribution for each Plan Year equal to (select one):

- ☐ (a) _____ % of each Participant's Compensation contributed as
Employee Thrift Contributions. If inserted, Matching Thrift
Contributions shall be subject to a maximum amount of
\$ _____ for each Participant or _____ % of each Participant's
Compensation.
- ☐ (b) _____ % of the first _____ % of the Participant's Compensation
contributed as Employee Thrift Contributions and _____ % of the
next _____ % of the Participant's Compensation contributed as
Employee Thrift Contributions. If inserted, Matching Thrift
Contributions shall be subject to a maximum amount of \$ _____
for each Participant or _____ % of each Participant's
Compensation.

D. QUALIFIED MATCHING CONTRIBUTIONS

If selected below, the Employer may make Qualified Matching Contributions
for each Plan Year (select all those applicable):

- (1) In its discretion, the Employer may make Qualified Matching
Contributions on behalf of (select one):
- ☐ (a) all Participants who make Employee Thrift Contributions.
- ☐ (b) only those Participants who are Nonhighly Compensated
Employees and who make Employee Thrift Contributions.
- (2) Qualified Matching Contributions will be contributed and allocated
to each Participant in an amount equal to:
- ☐ (a) _____ % of the Participant's Employee Thrift Contributions.

If inserted, Qualified Matching Contributions shall not
exceed _____ % of the Participant's Compensation.

- ☐ (b) such an amount, determined by the Employer, which is
needed to meet the ACP Test.

ARTICLE VI. PARTICIPANT CONTRIBUTIONS

PARTICIPANT VOLUNTARY NONDEDUCTIBLE CONTRIBUTIONS

Participant Voluntary Nondeductible Contributions are (select one):

- ☐ (a) permitted.
- ☒ (b) not permitted.

— — — — —

(Select one):

PROFIT-SHARING CONTRIBUTIONS

100% after 7 years of Vesting Service.

(2) Top Heavy Plan

MATCHING 401(k)
AND/OR MATCHING
THRIFT
CONTRIBUTIONS
- - - - -

PROFIT-SHARING
CONTRIBUTIONS
- - - - -

Vesting Schedule (Select one):

- ☐ ☐ (a) 100% vesting immediately upon participation.
- ☐ ☐ (b) 100% after ____ (not more than 3) years of Vesting Service.
- ☒ ☒ (c) Graded vesting schedule:
- | | |
|-----|-----------------------------------------------------------|
| 0% | 0% after 1 year of Vesting Service; |
| -- | -- |
| 20% | 20% (not less than 20%) after 2 years of Vesting Service. |
| -- | -- |
| 40% | 40% (not less than 40%) after 3 years of Vesting Service. |
| -- | -- |
| 60% | 60% (not less than 60%) after 4 years of Vesting Service. |
| -- | -- |
| 80% | 80% (not less than 80%) after 5 years of Vesting Service. |
| -- | -- |
| | 100% after 6 years of Vesting Service. |

Top Heavy Ratio:

- (a) If the adopting Employer maintains or has ever maintained a qualified defined benefit plan, for purposes of establishing present value to compute the top-heavy ratio, any benefit shall be discounted only for mortality and interest based on the following:

Interest Rate: 8 %

Mortality Table: UP' 84

- (b) For purposes of computing the top-heavy ratio, the valuation date shall be the last business day of each Plan Year.

B. ALLOCATION OF FORFEITURES

Forfeitures shall be (select one from each applicable column):

MATCHING 401(k)
AND/OR MATCHING
THRIFT
CONTRIBUTIONS

PROFIT-SHARING
CONTRIBUTIONS

- | | |
|-------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <input checked="" type="checkbox"/> | <input type="checkbox"/> (1) used to reduce Employer contributions for succeeding Plan Year. |
| <input type="checkbox"/> | <input type="checkbox"/> (2) allocated in the succeeding Plan Year in the ratio which the Compensation of each Participant for the Plan Year bears to the total Compensation of all Participants entitled to share in the Contributions. If the Plan is integrated with Social Security, forfeitures shall be allocated in accordance with the formula elected by the Employer. |

C. VESTING SERVICE

For purposes of determining Years of Service for Vesting Service [select (1) or (2) and/or (3)]:

- ☒ (1) All Years of Service shall be included.
- ☐ (2) Years of Service before the Participant attained age 18 shall be excluded.
- ☐ (3) Service with the Employer prior to the effective date of the Plan shall be excluded.

ARTICLE VIII. DEFERRAL OF BENEFIT DISTRIBUTIONS,
IN-SERVICE WITHDRAWALS AND LOANS

A. DEFERRAL OF BENEFIT DISTRIBUTIONS

401(k) AND/ OR THRIFT -----	PROFIT- SHARING -----
-----------------------------------	-----------------------------

☐ ☐ If this item is checked, a Participant's vested benefit in his or her Employer Accounts shall be payable as soon as practicable after the earlier of: (1) the date the Participant terminates Employment due to Disability or (2) the end of the Plan Year in which a terminated Participant attains Early Retirement Age, if applicable, or Normal Retirement Age.

B. IN-SERVICE DISTRIBUTIONS

☒ (1) In-service distributions may be made from any of the Participant's vested Accounts, at any time upon or after the occurrence of the following events (select all applicable):

- ☒ (a) a Participant's attainment of age 59-1/2.
☒ (b) due to hardships as defined in Section 5.9 of the Plan.

☐ (2) In-service distributions are not permitted.

C. LOANS ARE:

401(k) AND/ PROFIT-
OR THRIFT SHARING

- ☒ ☐ (1) permitted.
☐ ☐ (2) not permitted.

ARTICLE IX. GROUP TRUST

☐ If this item is checked, the Employer elects to establish a Group Trust consisting of such Plan assets as shall from time to time be transferred to the Trustee pursuant to Article X of the Plan. The Trust Fund shall be a Group Trust consisting of assets of this Plan plus assets of the following plans of the Employer or of an Affiliate:

ARTICLE X. MISCELLANEOUS

A. IDENTIFICATION OF SPONSOR

The address and telephone number of the Sponsor's authorized representative is 800 Scudders Mill Road, Plainsboro, New Jersey 08536; (609) 282-2272. This

authorized representative can answer inquiries regarding the adoption of the Plan, the intended meaning of any Plan provisions, and the effect of the opinion letter.

The Sponsor will inform the adopting Employer of any amendments made to the Plan or the discontinuance or abandonment of the Plan.

B. PLAN OF REGISTRATION

1. Initial Registration

This Plan must be registered with the Sponsor, Merrill Lynch, Pierce, Fenner & Smith Incorporated, in order to be considered a Prototype Plan by the Sponsor. Registration is required so that the Sponsor is able to provide the Administrator with documents, forms and announcements relating to the administration of the Plan and with Plan amendments and other documents, all of which relate to administering the Plan in accordance with applicable law and maintaining compliance of the Plan with the law.

The Employer must complete and sign the Adoption Agreement. Upon receipt of the Adoption Agreement, the Plan will be registered as a Prototype Plan of Merrill Lynch, Pierce, Fenner & Smith Incorporated. The Adoption Agreement will be countersigned by an authorized representative and a copy of the countersigned Adoption Agreement will be returned to the Employer.

2. Registration Renewal

Annual registration renewal is required in order for the Employer to continue to receive any and all necessary updating documents. There is an annual registration renewal fee in the amount set forth with the initial registration material. The adopting Employer authorizes Merrill Lynch, Pierce, Fenner & Smith Incorporated, to debit the account established for the Plan for payment of agreed upon annual fee; provided, however, if the assets of an account are invested solely in Participant-Directed Assets, a notice for this annual fee will be sent to the Employer annually. The Sponsor reserves the right to change this fee from time to time and will provide written notice in advance of any change.

C. PROTOTYPE REPLACEMENT PLAN

This Adoption Agreement is a replacement prototype plan for the (1) Merrill Lynch Special Prototype Defined Contribution Plan and Trust - 401(k) Plan #03-004 and (2) Merrill Lynch Asset Management, Inc., Special Prototype Defined Contribution Plan and Trust - 401 (k) Plan Adoption Agreement #03-004.

D. RELIANCE

The adopting Employer may not rely on the opinion letter issued by the National Office of the Internal Revenue Service as evidence that this Plan is qualified under Code Section 401. In order to obtain reliance, the Employer must apply to the appropriate date Key District Director of the Internal Revenue Service for a determination letter with respect to the Plan.

Dated: 1/3 , 1994

EMPLOYER
By: /s/ R. Douglas Armstrong

To be executed by the sole proprietor, an
authorized partner or corporate officer, as
appropriate.

R. DOUGLAS ARMSTRONG

Print Name

PRESIDENT and CEO

Title, if a corporate officer

SPONSOR ACCEPTANCE

Subject to the terms and conditions of the Prototype Plan and this Adoption Agreement, this Adoption Agreement is accepted by Merrill Lynch, Pierce, Fenner & Smith Incorporated as the Prototype Sponsor.

Authorized Signature: /s/ Rebecca Freberg

MERRILL LYNCH TRUST COMPANY IS NOT A TRUSTEE

ACCEPTANCE BY TRUSTEE(S)

A. This Trustee Acceptance is to be completed only if the Employer appoints one or more Trustees and does not appoint a Merrill Lynch Trust Company as Trustee.

The undersigned hereby accept all of the terms, conditions, and obligations of appointment as Trustee under the Plan. If the Employer has elected a Group Trust in this Adoption Agreement, the undersigned Trustee(s) shall be the Trustee(s) of the Group Trust.

as TRUSTEE

/s/ R. DOUGLAS R. ARMSTRONG

R. DOUGLAS ARMSTRONG

(Signature)

(print or type name)

as TRUSTEE

/s/ TODD E. SIMPSON

TODD E. SIMPSON

(Signature)

(print or type name)

as TRUSTEE

(Signature)

(print or type name)

as TRUSTEE

(Signature)

(print or type name)

Dated: _____, 19
----- --

MERRILL LYNCH TRUST COMPANY AS TRUSTEE

This Trustee Acceptance and designation of Investment Committee are to be completed only when a Merrill Lynch Trust Company is appointed as Trustee.

The undersigned hereby accept all of the terms, conditions, and obligations of appointment as Trustee under the Plan, If the Employer has elected a Group Trust in this Adoption Agreement, the undersigned Trustee(s) shall be the Trustee(s) of the Group Trust.

SEAL

MERRILL LYNCH TRUST COMPANY

Dated: _____, 19
----- --

By: _____

DESIGNATION OF INVESTMENT COMMITTEE

The Investment Committee for the Plan is (print or type name):

MERRILL LYNCH TRUST COMPANY IS ONE OF THE TRUSTEES

This Trustee Acceptance is to be completed only if, in addition to a Merrill Lynch Trust Company as Trustee, the Employer appoints an additional Trustee of a second trust fund.

The undersigned hereby accept all of the terms, conditions, and obligations of appointment as Trustee under the Plan. If the Employer has elected a Group Trust in this Adoption Agreement, the undersigned Trustee(s) shall be the Trustee(s) of the Group Trust.

as TRUSTEE

(Signature) (print or type name)

Dated: _____, 19

SEAL MERRILL LYNCH TRUST COMPANY

Dated: _____, 19 By: _____

DESIGNATION OF INVESTMENT COMMITTEE

The Investment Committee for the Plan is (print or type name):

AASTROM BIOSCIENCES, INC.
AMENDED AND RESTATED
1992 INCENTIVE AND
NON-QUALIFIED STOCK OPTION PLAN
(AS AMENDED EFFECTIVE OCTOBER 30, 1996)

Section 1. Purpose.

The purpose of the 1992 Incentive and Non-qualified Stock Option Plan (the "Plan") of Aastrom Biosciences, Inc. (the "Company") is to encourage stock ownership by directors, officers, employees of and consultants to the Company and its Affiliates and others who directly or indirectly provide goods or services to the Company and its Affiliates by issuing options to purchase shares of the Company's stock ("Options," and individually an "Option"), enabling such persons to acquire or increase their proprietary interest in the Company and thereby encouraging them to remain in the employ or remain directors of or consultants to the Company and its Affiliates or continue providing goods or services to the Company and its Affiliates. The term "Affiliates" as used herein shall include any parent corporation or subsidiary corporation as defined in Sections 424(e) and (f) respectively of the Internal Revenue Code of 1986, as amended (the "Code"). The Options issued pursuant to the Plan are intended to constitute either incentive stock options within the meaning of Section 422 of the Code, or non-qualified stock options, at the discretion of the Option Committee (as hereinafter defined) of the board of directors of the Company (the "Board of Directors") at the time of grant. The type of Options granted will be specified in the letter of grant to the person who is granted the Options (the "Optionee"). The terms of this Plan shall be incorporated in the grant letter.

Section 2. Administration.

The Plan will be administered by the Board of Directors or a committee of two or more members of the Board or Directors (such member or the Board of Directors acting as Plan administrators shall be referred to herein as the "Option Committee"). If the Company or an Affiliate is a "publicly held corporation" within the meaning of Section 162(m) of the Code, the Board may establish a Committee of "outside directors" within the meaning of Section 162(m) to approve the grant of any Option which might reasonably be anticipated to result in the payment of employee remuneration that would otherwise exceed the limit on employee remuneration deductible for income tax purposes pursuant to Section 162(m).

The interpretation and construction by the Option Committee of any provision of the Plan will be final. Anything herein to the contrary notwithstanding, no member of the Board of Directors or the Option Committee will be liable for any action or determination made in good faith with respect to the Plan or any Option granted under it.

Section 3. Eligibility.

Directors, officers and employees of the Company and its Affiliates who are expected to make significant contributions to the long term success of the Company are eligible to receive incentive stock options under the Plan, as may be determined from time to time by the Option Committee. Directors, officers and employees of and consultants to the Company and its Affiliates, and others who directly or indirectly provide goods or services to the Company and its Affiliates, are eligible to receive non-qualified options under the Plan, as may be determined from time to time by the Option Committee. A director, officer, employee, consultant or other person who is granted an Option is an Optionee (which term also includes the Optionee's legal representative under Section 5(g) hereof). An Optionee may be granted more than one Option.

For purposes of the foregoing paragraph, "employees" shall include prospective employees to whom Options are granted in connection with written offers of employment with the Company or one of its Affiliates, and "consultants" shall include prospective consultants to whom Options are granted in connection with written offers of engagement with the Company or one of its Affiliates.

Any person who is not an employee on the date of Option grant may only be granted a non-qualified stock option. A director who is not an employee or officer of or consultant to the Company or its Affiliates, or who does not directly or indirectly provide goods or services to the Company or its Affiliates, shall not be eligible to receive non-qualified stock options.

Notwithstanding the foregoing, no director of the Company who is not also an employee of the Company may be granted an Option at any time that any class of equity security of the Company is registered pursuant to Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act").

Section 4. Stock.

The stock subject to an Option will be shares of the Company's authorized but unissued or reacquired Common Stock, no par value (the "Shares"). Options shall not be issued with respect to more than One Million

Nine Hundred Thousand (1,900,000) Shares, after giving effect to the two-for-three reverse stock split approved by the Board of Directors on April 30, 1996, and subject to further adjustment as provided in Section 5(i) hereof. If an outstanding Option for any reason expires or is terminated or canceled or Shares acquired, subject to repurchase, upon the exercise of an Option are repurchased by the Company, the Shares allocable to the unexercised portion of such Option, or such repurchased Shares, shall again be available for issuance under the Plan.

Section 5. Terms and Conditions of Options.

Each Option granted pursuant to the Plan will be authorized by the Option Committee and will be evidenced by a notice (the "Option Notice") in such form as the Option Committee may from time to time determine. Each Option Notice will include the information required in subparagraphs (a), (b) and (c) of this Section 5 and will be in conformity with and will incorporate by reference all other terms and conditions of the Plan, including the following terms and conditions:

(a) Number of Shares. The number of Shares subject to the Option will be stated in the Option Notice.

(b) Exercise Price. In the case of incentive stock options, the price per Share payable on the exercise of the Option will be stated in the Option Notice and will be not less than 100% of the fair market value per share of the outstanding shares of Common Stock of the Company on the date the Option is granted, without regard to any restriction other than a restriction which will never lapse. In the case of a non-qualified stock option, the price per Share payable upon exercise of the Option shall be stated in the Option Notice and will be not less than 85% of the fair market value per share of the outstanding shares of Common Stock of the Company on the date the Option is granted, without regard to any restriction other than a restriction which will never lapse. Unless the Company's Common Stock is quoted on the National Association of Securities Dealers Automated Quotation System ("NASDAQ") or listed on a recognized securities exchange, the fair market value, for purposes of complying with the foregoing sentence with respect to incentive stock options, shall be as determined by the Option Committee in its sole discretion. If the Company's Common Stock is either quoted on NASDAQ or listed on a recognized securities exchange, the fair market value shall be the representative closing price of the stock as obtained from NASDAQ or such recognized securities exchange on the date of the grant of the Option, or if there is no such quotation on the date of the grant of the Option on the preceding business day.

(c) Form of Option. The Option Notice will state whether the Option granted is an incentive stock option or a non-qualified stock

option, and will constitute a binding determination as to the form of Option granted. At the discretion of the Option Committee, the Option Notice may require the Optionee to execute a Stock Transfer Restriction and Buy-Out Agreement, or such other agreements as the Option Committee considers appropriate.

(d) Payment. The price payable on the exercise of the Option in whole or in part will be equal to the Option price multiplied by the number of Shares as to which the Option is exercisable, and shall be paid in full upon exercise of any Option, either (i) in cash, (ii) at the discretion of the Option Committee either at the time the Option is granted or exercised, by delivering to the Company Shares having a fair market value, as of the close of business on the day preceding such delivery, equal to the aggregate exercise price of the Shares being purchased on exercise of the Options, (iii) by a combination of such cash and shares, or (iv) any other form of legal consideration that may be acceptable to the Option Committee. In the case of any deferred payment arrangement, interest shall be payable at least annually at the minimum applicable federal rate under Section 1274(d) of the Code to avoid imputed interest to the Company under the Code.

Anything to the contrary herein notwithstanding, all payments required to be made by the Company hereunder to an Optionee, his legal representative, his heir or devisee, shall be subject to the withholding of such amounts as the Company may determine that it is required to withhold pursuant to any applicable federal, state or local law or regulation. To the extent provided in the terms of the Option, and to the extent allowed under the Exchange Act, the Optionee may satisfy any federal, state or local tax withholding obligation relating to the exercise of such Option by one or more of the following: (1) tender of a cash payment; (2) authorization of the Company to withhold Shares otherwise to be issued pursuant to the Option of a value not in excess of the withholding tax obligation; or (3) delivering to the Company unencumbered Shares owned by the Optionee of a value not in excess of the withholding tax obligation.

(e) Notwithstanding any other provision of this Plan:

(i) No Option shall be granted under this Plan more than ten (10) years after April 30, 1996. Notwithstanding the foregoing, if the maximum number of Shares issuable pursuant to the Plan as provided in Section 4 has been increased at any time (other than pursuant to Section 5(i)), all Options shall be granted, if at all, no later than the last day preceding the tenth (10th) anniversary of the earlier of (a) the date on which the latest such increase in the maximum number of Shares issuable under the Plan was approved by the stockholders of the Company or (b) the date such amendment was adopted by the Board of Directors.

(ii) No incentive stock option granted under this Plan shall be exercisable later than ten (10) years from the date of grant.

(iii) No Option granted to any Optionee shall be treated as an incentive stock option, to the extent such Option would cause the aggregate fair market value (determined as of the date of grant of each such Option) of the Shares with respect to which incentive stock options are exercisable by such Optionee for the first time during any calendar year to exceed \$100,000. For purposes of determining whether an incentive stock option would cause the aggregate fair market value of the Shares to exceed the \$100,000 limitation, such incentive stock options shall be taken into account in the order granted. For purposes of this subsection, incentive stock options include all incentive stock options under all plans of the Company (or one of its Affiliates) that are incentive stock option plans within the meaning of Section 422 of the Code. If the Code is amended to provide for a different limitation from that set forth in this subsection, such different limitation shall be deemed incorporated herein effective as of the date and with respect to such Options as required or permitted by such amendment to the Code.

(iv) Options granted pursuant to this Plan may be exercised in any order elected by the Optionee whether or not the Optionee holds any unexercised Options under this Plan or any other Plan of the Company.

(v) Notwithstanding any provision herein to the contrary, no incentive stock option shall be granted under this Plan to any person who, at the time of the grant of such Option, owns stock possessing more than 10% of the total combined voting power of all classes of the stock of the Company or any affiliate, unless the option price at the time the Option is granted is at least 110 percent (110%) of the fair market value of the stock, and subject to the condition that the Option expires five years from the Option grant date.

(vi) No Option granted under this Plan may be transferred except by will or by the laws of descent and distribution.

(f) Term and Exercise of Options.

(i) Subject to the provisions of Section 5(e)(i), (ii) and (v) hereof, Options granted hereunder may be exercisable in whole or in part at such time or times as the Option Committee shall designate when granting such Options. However, no Option granted to a prospective employee or prospective consultant may become exercisable prior to the date on which such person commences service with the Company or one of its Affiliates.

(ii) Unless sooner terminated as provided in this Plan, each Option shall expire no later than ten years from the date of grant and shall be void and unexercisable thereafter. An Option may be exercised only by the Optionee and may not be exercised by any other person except as provided in Section 5(g) hereof.

(g) Termination of Options Granted to Employees and Directors.

(i) Except as provided herein and unless otherwise specified in the Option Notice, Options shall terminate when the Optionee ceases to be employed by the Company or ceases to be a director of the Company.

(ii) Unless otherwise specified in the Option Notice, upon the death of an Optionee while in the employ of the Company or while a director of the Company, Options held by such Optionee which are exercisable on the date of his or her death shall be exercisable by his or her executor(s) or administrator(s) for a period of eighteen (18) months following the date of such Optionee's death.

(iii) Unless otherwise specified in the Option Notice, upon termination of an Optionee's employment with the Company (or if the Optionee is a director only, upon termination of the Optionee's term of office, or if the Optionee is both an employee and a director, upon termination of both) for any reason other than "Cause," as defined in Section 5(g)(v), or for retirement or permanent disability as set forth in Section 5(g)(iv) with respect to non-qualified stock options, Options exercisable by such Optionee on the date of termination of employment shall be exercisable by the Optionee (or in the case of the Optionee's death subsequent to termination of employment, by the Optionee's executor(s) or administrator(s)) for a period of three (3) months from the date of such Optionee's termination of employment.

(iv) Solely with respect to non-qualified stock options, unless otherwise specified in the Option Notice, upon termination of an Optionee's employment with the Company (or if the Optionee is a director only, upon termination of the Optionee's term of office, or if the Optionee is an employee and a director, upon termination of both) for reasons of retirement or permanent disability, non-qualified stock options exercisable by the Optionee on the date of termination of employment shall be exercisable by such Optionee (or in the case of the Optionee's death subsequent to termination of employment, by the Optionee's executor(s) or administrator(s)) for a period of one (1) year from the date of such Optionee's termination of employment; provided, however, that if such

Optionee shall commence any employment during this one (1) year period with a competitor of the Company (including, but not limited to, full or part-time employment or independent consulting work), as determined solely in the judgment of the Board of Directors, all Options held by such Optionee which have not yet been exercised shall terminate immediately upon commencement thereof.

(v) Unless otherwise specified in the Option Notice, upon the termination of an Optionee's employment (or if the Optionee is a director only, upon termination of the Optionee's term of office, or if the Optionee is both an employee and a director, upon termination of both) for "Cause," as defined in this Section 5(g)(v), all Options held by such Optionee shall terminate concurrently with receipt by the Optionee of oral or written notice that his or her employment has been terminated. For the purposes of this Plan, termination for "Cause" shall include termination by reason of being convicted of any felony or committing willful and gross negligence or willful and gross misconduct in carrying out duties properly assigned to such Optionee by the Company.

(vi) The Option Notice may provide that the Options issued thereunder may be exercised for one year following the "disability" of the Optionee as such term is defined in Section 22(c)(3) of the Code.

(vii) In the case of a leave of absence taken by an Optionee, the Company shall have the unilateral right to (1) determine whether such leave of absence shall be treated as a termination of employment, and (2) suspend or otherwise delay the time or times at which the Shares subject to the Option would otherwise vest.

(viii) Options granted to employees and directors of the Company and its Affiliates may be terminated at any time by agreement between the Company and the Optionee.

(h) Termination of Options Granted to Non-Employees.

(i) With respect to Options granted to persons who are not employees or directors of the Company or its Affiliates, the Option Notice shall state the conditions, if any, under which the Options shall terminate.

(ii) Options granted to persons who are not employees or directors of the Company or its Affiliates may be terminated at any time by agreement between the Company and the Optionee.

(i) Recapitalization.

(i) Subject to any required action by the stockholders, if any, the number of Shares as to which Options may be granted under this Plan and the number of Shares subject to outstanding Options and the Option prices thereto will be adjusted proportionately for any increase or decrease in the number of outstanding shares of Common Stock of the Company resulting from stock splits and reverse stock splits, but not for stock dividends. The number of Shares will be adjusted to the nearest whole share. Any stock dividend resulting in an increase of five percent (5%) or more in the outstanding Common Stock shall be deemed a stock split.

(ii) If the Company is a party to any merger in which the Company is not the surviving entity, any consolidation or dissolution (other than the merger or consolidation of the Company with one or more of its wholly-owned subsidiaries), the Company, in the discretion of the Option Committee and to the extent permitted by law, (1) will cause any successor corporation to assume the Options outstanding hereunder or substitute similar options to those outstanding hereunder, or (2) will continue such Options in full force and effect. In the event that any successor to the Company in a merger, consolidation or dissolution will not assume the Options or substitute similar Options then, with respect to Options held by Optionees then performing services for the Company, the time for exercising such Options will be accelerated and the Options will be terminated if not exercised prior to the merger, consolidation or dissolution.

(iii) Except as expressly provided in this Section 5(i), the Optionee will have no rights by reason of (1) any subdivision or consolidation of shares of stock of any class of the Company; (2) payment of any stock dividend by the Company; (3) any other increase or decrease in the number of shares of stock of any class of the Company; or (4) by reason of any dissolution, liquidation, merger, consolidation or spin-off of assets or stock of another corporation.

(iv) The grant or existence of any Option shall not affect in any way the right or power of the Company to make adjustments, reclassifications, reorganizations, or changes of its capital or business structure, or to merge, consolidate, dissolve, liquidate, sell or transfer all or any part of its stock or assets.

(j) Rights as a Stockholder. The Optionee will have no rights as a stockholder of the Company with respect to any Shares subject to an Option until such Option has been exercised and a certificate with respect to the Shares purchased upon exercise has been issued to him or

her. No adjustment will be made for dividends (ordinary or extraordinary, whether in cash, securities or other property), distributions or other rights for which the record date is prior to the date the Shares so purchased have been issued. Throughout the term of any Option issued hereunder, the Company shall make available to each Optionee, not less than 120 days after the close of each fiscal year of the Company, upon request by the Optionee, any financial or other information contained in the annual report to the shareholders of the Company as provided in the Company's by-laws.

(k) Modification, Extension and Renewal of Option. Subject to the terms and conditions of the Plan, the Option Committee may modify, extend or renew an Option, or accept the surrender of an Option (to the extent not theretofore exercised), provided that no incentive stock option may be modified, extended or renewed if such action would cause it to cease to be an "incentive stock option" under the Code. Notwithstanding the foregoing, no modification of an Option which adversely affects the Optionee shall be made without the consent of the Optionee.

(l) Purchase for Investment. The issuance of Shares on exercise of the Option will be conditioned on obtaining appropriate representations and warranties of the Optionee that the purchase of Shares thereunder will be for investment, and not with a view to the public resale or distribution thereof, unless the Shares subject to the Option are registered under the Securities Act of 1933, as amended (the "Act"), and comply with any other law, regulation or rule applicable thereto. Unless the Shares are registered under the Act, the Optionee shall acknowledge that the Shares purchased on exercise of the Option are not registered under the Act and may not be sold or otherwise transferred unless the Shares have been registered under the Act in connection with the sale or other transfer, or that counsel satisfactory to the Company is of the opinion that the sale or other transfer is exempt from registration under the Act, and unless said sale or transfer is in compliance with any other applicable law, including all applicable state securities laws.

(m) No Rights to Employment. Officers or employees granted Options under this Plan shall not have any right to continue in the employment of the Company or its Affiliates by reason of the existence of such Options and consultants granted Options under this Plan shall not have any right to continue as consultants to the Company or its Affiliates by reason of the existence of such options. Persons who directly or indirectly provide goods or services to the Company or its Affiliates shall not have any right to continue providing such goods and services by reason of the existence of such Options. An Optionee who is not an employee of the Company or its Affiliates shall have no right to become an employee, or to obtain any benefit of employment, by reason of having been granted

Options under this Plan. An Optionee whose employment is terminated shall have no rights against the Company by reason of the termination of such Option whether the termination of the employment be with or without "Cause," as defined in Section 5(g)(iv).

(n) Other Provisions. The Option Notice may contain such other provisions as the Option Committee in its discretion deems advisable and which are not inconsistent with the provisions of this Plan, including, without limitation, restrictions upon the exercise of the Option.

Section 6. Amendment of the Plan.

Insofar as permitted by law and the Plan, the Option Committee may from time to time suspend or discontinue the Plan or revise or amend it in any respect whatsoever with respect to any Shares at the time not subject to an Option; provided, however, that without approval of the stockholders, no such revision or amendment may change the aggregate number of Shares for which Options may be granted hereunder, change the designation of the class of employees eligible to receive Options or decrease the price at which Options may be granted.

Any other provision of this Section 6 notwithstanding, the Option Committee or the Board of Directors specifically is authorized to adopt any amendment to this Plan deemed by the Board of Directors to be necessary or advisable to assure that the incentive stock options or the non-qualified stock options available under the Plan continue to be treated as such, respectively, under the law.

Section 7. Application of Funds.

The proceeds received by the Company from the sale of Shares pursuant to the exercise of Options will be used for general corporate purposes.

Section 8. No Obligation to Exercise Option.

The granting of an Option will impose no obligation upon the Optionee to exercise such Option.

Section 9. Restrictions on Sale of Shares. Optionee may not dispose of any Shares received under the Plan within one hundred and eighty (180) days of the date on which the Company's initial S-1 Registration Statement for registration of the Company's common stock under the Securities Act of 1933, as amended, is declared effective.

Section 10. Indemnification. In addition to such other rights of indemnification as they may have as members of the Board of Directors or officers or employees of the Company or one of its Affiliates, members of the Board of Directors and any officers or employees of the Company or any one of its Affiliates to whom authority to act for the Board of Directors is delegated shall be indemnified by the Company against all reasonable expenses, including attorneys' fees, actually and necessarily incurred in connection with the defense of any action, suit or proceeding, or in connection with any appeal therein, to which they or any of them may be a party by reason of any action taken or failure to act under or in connection with the Plan, or any right granted hereunder, and against all amounts paid by them in settlement thereof (provided such settlement is approved by independent legal counsel selected by the Company) or paid by them in satisfaction of a judgment in any such action, suit or proceeding, except in relation to matters as to which it shall be adjudged in such action, suit or proceeding that such person is liable for gross negligence, bad faith or intentional misconduct in duties; provided, however, that within sixty (60) days after the institution of such action, suit or proceeding, such person shall offer to the Company, in writing, the opportunity at its own expense to handle and defend the same.

Section 11. Approval of Stockholders.

This Plan shall become effective on the date that it is adopted by the Board of Directors; provided, however, that it shall become null and void if it is not approved by a majority of the holders of the Company's Common Stock within one year (365 days) of its adoption by the Board of Directors. The Option Committee may grant Options hereunder prior to approval of the Plan or any material amendments thereto by the holders of a majority of the Company's Common Stock; provided, however, that no Option so granted shall be exercisable within 365 days of the date of the adoption or material amendment of the Plan, and all Options so granted shall terminate and become null and void if the Plan is not approved by a majority of the holders of the Company's Common Stock within 365 days of its adoption or material amendment.

AASTROM BIOSCIENCES, INC.
1992 EMPLOYEE INCENTIVE
STOCK OPTION AGREEMENT

AASTROM BIOSCIENCES, INC., a Michigan corporation (the "Company"), hereby grants to _____ ("Optionee"), an option to purchase a total of _____ shares (the "Shares") of common stock of the Company, at the price determined as provided herein, and in all respects subject to the terms, definitions and provisions of the Company's 1992 Incentive and Non-Qualified Stock Option Plan (the "Plan") incorporated herein by reference. Terms which are defined in the Plan shall have the same meanings when used herein.

1. Nature of the Option. This Option is an incentive stock option within the meaning of Section 422 of the Internal Revenue Code of 1986, as amended.

2. Exercise Price. The option price shall be _____ for each Share (the "Exercise Price"), which is not less than the fair market value of each Share on the date hereof. The Option Price shall be adjusted proportionately for increases or decreases in the number of outstanding Shares resulting from stock splits.

3. Exercise of Option. Subject to Section 6 hereof, this Option shall be exercisable during its term as follows:

(a) Right to Exercise. This Option shall be exercisable with respect to _____ Shares on _____ and shall be exercisable with respect to an additional _____ Shares on the first day of every third month thereafter, as long as Optionee remains an employee or director of the Company.

(b) Method of Exercise. This Option shall be exercisable by written notice in the form of Exhibit A attached hereto. Such written notice shall be signed by Optionee and shall be delivered in person, by certified mail, or by such other means as the Company may permit to the Secretary of the Company. The written notice shall be accompanied by payment of the aggregate Exercise Price.

No Shares will be issued pursuant to the exercise of this Option unless such issuance and such exercise shall comply with all relevant provisions of law and the requirements of any stock exchange upon which the Shares may then be listed.

(c) Number of Shares Exercisable. Each exercise of this Option in part shall reduce, pro tanto, the total number of Shares that may thereafter be purchased under such Option.

4. Optionee's Representations. If the shares which may be purchased pursuant to the exercise of this Option have not been registered under the Securities Act of 1933, as amended (the "Securities Act"), at the time this Option is exercised, Optionee shall, concurrently with the exercise of all or any portion of this Option, deliver to the Company his Investment Representation Statement in the form attached hereto as Exhibit B.

5. Method of Payment. Payment of the Exercise Price, may be in any of the following forms, or a combination thereof, in the discretion of the Company:

(a) cash or check in the full amount of the aggregate Exercise Price;
or

(b) surrender to the Company of other shares of Common Stock of the Company having a fair market value on the date of surrender equal to the aggregate Exercise Price of the Shares as to which this Option is being exercised. If the Company's Common Stock is then quoted on the National Association of Securities Dealers Automated Quotation System ("Nasdaq") or listed on a recognized securities exchange, the fair market value of the shares shall be the representative closing price of the stock as obtained from Nasdaq or such recognized securities exchange on the date of the exercise of the Option, or if there is no such quotation on the date of the exercise, on the last trading day prior to the date of exercise. If the Company's Common Stock is not quoted on Nasdaq or listed on a recognized securities exchange, the fair market value of such shares shall be as determined by the Board of Directors in its sole discretion; or

(c) promissory note, bearing a reasonable rate of interest, requiring at least annual payments of accrued interest, maturing in not more than four (4) years, secured by the shares purchased, and being a full recourse obligation of the Optionee. Such recourse promissory note shall be in a form satisfactory to the Company, and the Company may require the Optionee to deposit any shares securing the promissory note with an agent designated by the Company under the terms and conditions of escrow and security agreements approved by the Company. It shall be at the sole and absolute discretion of the Company's Board of Directors as to whether or not the Optionee is allowed to exercise this Option by a

promissory note payment, and the Optionee shall have no right to do so unless the Board of Directors expressly exercises its discretion to allow the use of a promissory note. Any such approval by the Board of Directors shall not constitute a precedent for any subsequent exercise of this Option by the Optionee.

(d) through "Cashless Exercise." A "Cashless Exercise" means the assignment in a form acceptable to the Company of the proceeds of a sale or loan with respect to some or all of the Shares of Common Stock acquired upon the exercise of the Option pursuant to a program or procedure approved by the Company (including, without limitation, through an exercise complying with the provisions of Regulation T as promulgated from time to time by the Board of Governors of the Federal Reserve System). The Company reserves, at any and all times, the right, in the Company's sole and absolute discretion, to decline to approve or terminate any such program or procedure.

6. Restrictions on Exercise. This Option may not be exercised if the issuance of such Shares upon such exercise or the method of payment of consideration for such Shares would constitute a violation of any applicable federal or state securities or other law or regulation, including any rule under Part 207 of Title 12 of the Code of Federal Regulations ("Regulation G") as promulgated by the Federal Reserve Board. As a condition to the exercise of this Option, the Company may require the Optionee to make any representation and warranty to the Company as may be required by any applicable law or regulation.

7. Termination of Options.

(a) Except as provided herein, this Option shall terminate at such time as Optionee ceases to be employed by the Company or ceases to be a director of the Company.

(b) Upon the death of Optionee while in the employ of the Company or while a director of the Company, Options held by Optionee which are exercisable on the date of his or her death shall be exercisable by his or her executor(s) or administrator(s) for a period of eighteen (18) months following the date of Optionee's death.

(c) Upon termination of Optionee's employment with the Company (or if Optionee is a director only, upon termination of the Optionee's term of office, or if the Optionee is both an employee and a director, upon termination of both) for any reason other than death,

disability or "Cause," as defined in Section 7(d), Options exercisable by Optionee on the date of termination of employment shall be exercisable by Optionee (or in the case of the Optionee's death subsequent to termination of employment, by the Optionee's executor(s) or administrator(s)) for a period of three (3) months from the date of Optionee's termination of employment.

(d) Upon the termination of Optionee's employment (or if Optionee is a director only, upon termination of Optionee's term of office, or if Optionee is both an employee and a director, upon termination of both) for "Cause," as defined in this Section 7(d), all Options held by Optionee shall terminate concurrently with receipt by the Optionee of oral or written notice that his or her employment has been terminated. Termination for "Cause" shall include termination by reason of being convicted of any felony or committing willful and gross negligence or willful and gross misconduct in carrying out duties properly assigned to Optionee by the Company.

(e) Upon termination of Optionee's employment due to the "disability" of Optionee as such term is defined in Section 22(c)(3) of the Code an Option exercisable by Optionee on the date of termination shall be exercisable by Optionee (or Optionee's legal guardian or representative) for a period of one (1) year from the date of Optionee's termination of employment.

(f) Notwithstanding the provisions of subsections (b), (c) and (e) above, if a sale within the applicable time periods set forth in subsections (b), (c) and (e) of this Section 7 of shares acquired upon the exercise of the Option would subject the Optionee to suit under Section 16(b) of the Exchange Act, the Option shall remain exercisable until the earliest to occur of (i) the tenth (10th) day following the date on which a sale of such shares by the Optionee would no longer be subject to such suit, (ii) the one hundred and ninetieth (190th) day after the Optionee's termination of employment or service, or (iii) the Option term date determined pursuant to Section 8. The Company makes no representation as to the tax consequences of any such delayed exercise. The Optionee should consult with the Optionee's own tax advisor as to the tax consequences to the Optionee of any such delayed exercise.

8. Non-Transferability of Option. This Option may not be sold, pledged, assigned, hypothecated, transferred or disposed of in any manner during the lifetime of Optionee other than by will or the laws of descent and distribution, and may be exercised during the lifetime of the Optionee

only by him or her. The terms of this Option shall be binding upon the executors, administrators, heirs and successors of the Optionee.

9. Term of Option. This Option may not be exercised more than ten (10) years from the date of grant of this Option, and may be exercised during such term only in accordance with the terms of the Plan and this Option.

10. Early Disposition of Stock. Optionee hereby agrees that if he disposes of any Shares received under this Option within one (1) year after such Shares were transferred to him, or within two (2) years of the grant of this Option, he will notify the Company in writing within 30 days after the date of any such disposition.

11. Acknowledgment. The Optionee acknowledges receipt of a copy of the Plan, which is annexed hereto as Exhibit C. The Optionee represents that he has read the terms and provisions of the Plan and accepts this Option subject to all of the terms and provisions thereof. The Optionee hereby agrees to accept as binding, conclusive and final all decisions or interpretations of the Committee upon any questions arising under the Plan.

12. Entire Agreement. This Agreement, together with the exhibits attached hereto, represents the entire agreement between the parties.

13. Governing Law. This Agreement shall be construed in accordance with the laws of the State of Michigan.

14. Amendment. This Agreement may only be amended by a writing signed by each of the parties hereto.

DATE OF GRANT: _____

AASTROM BIOSCIENCES, INC.

By: _____
R. Douglas Armstrong, Ph.D.
Its: President and CEO

Agreed to this ____ day of

_____, 19__

Optionee

EXHIBIT A

NOTICE OF EXERCISE

[Date]

AASTROM Biosciences, Inc.
Domino's Farms, Lobby L
P.O. Box 376
Ann Arbor, MI 48106
Attn.: Corporate Secretary

Dear Madam or Sir:

I hereby notify AASTROM Biosciences, Inc. of my intent to exercise
_____ Options granted to me pursuant to a Stock Option Agreement dated
_____ at an exercise price of \$_____ per share. I have enclosed a
check for \$_____.

I hereby agree that if I dispose of any Shares received upon exercise
of the Option within one (1) year after this date of exercise, or within two (2)
years after the Date of Grant of this Option, I will notify the Company in
writing within 30 days after the date of any such disposition.

[Signature of Optionee]

[Print Name of Optionee]

EXHIBIT B

INVESTMENT REPRESENTATION STATEMENT

PURCHASER: []

COMPANY: Aastrom Biosciences, Inc.

SECURITY: COMMON STOCK

AMOUNT: [] SHARES

DATE: []

In connection with the purchase of the above-listed Securities, I, the Purchaser, represent to the Company, the following:

(a) I am aware of the Company's business affairs and financial condition, and have acquired all such information about the Company as I deem necessary and appropriate to enable me to reach an informed and knowledgeable decision to acquire the Securities. I am purchasing these Securities for my own account for investment and not with a view to, or for the resale in connection with, any "distribution" thereof for purposes for the Securities Act of 1933, as amended ("Securities Act").

(b) I understand that the Securities have not been registered under the Securities Act in reliance upon a specific exemption therefrom, which exemption depends upon, among other things, the bona fide nature of my investment intent as expressed herein.

(c) I further understand that the Securities may not be sold publicly and must be held indefinitely unless they are subsequently registered under the Securities Act or unless an exemption from registration is available. I am able, without impairing my financial condition, to hold the Securities for an indefinite period of time and to suffer a complete loss of my investment. I understand that the Company is under no obligation to register the Securities. In addition, I understand that the certificate evidencing the Securities will be imprinted with a legend which prohibits the transfer of the Securities unless they are registered or such registration is not required in the opinion of counsel for the Company.

(d) I am familiar with the provisions of Rule 144, promulgated under the Securities Act, which, in substance, permits limited public resale of "restricted securities" acquired, directly or indirectly, from the issuer thereof (or from an affiliate of such issuer), in a non-public offering subject to the satisfaction of certain conditions, including, among other things: (1) the availability of certain public information about the Company; (2) the resale occurring not less than two years after the party has purchased, and made full payment for, within the meaning of Rule 144, the securities to be sold; and (3) in the case of an affiliate, or of a non-affiliate who has held the securities less than three years, the sale being made through a broker in an unsolicited "broker's transaction" or in transactions directly with a market maker (as said term is defined under the Securities Exchange Act of 1934) and the amount of securities being sold during any three month period not exceeding the specified limitations stated therein, if applicable.

(e) I further understand that at the time I wish to sell the Securities there may be no public market upon which to make such a sale, and that, even if such a public market then exists, the Company may not be satisfying the current public information requirements of Rule 144, and that, in such event, I would be precluded from selling the Securities under Rule 144 even if the two-year minimum holding period had been satisfied. I understand that the Company is not currently required to file reports pursuant to the Securities Exchange Act of 1934, as amended, and is under no obligation to make Rule 144 available.

(f) I further understand that, in the event all of the applicable requirements of Rule 144 are not satisfied, registration under the Securities Act, compliance with Regulation A, or some other registration exemption will be required; and that, notwithstanding the fact that Rule 144 is not exclusive, the Staff of the Securities and Exchange Commission has expressed its opinion that persons proposing to sell private placement securities other than in a registered offering and otherwise than pursuant to Rule 144 will have a substantial burden of proof in establishing that an exemption from registration is available for such offers or sales, and that such persons and their respective brokers who participate in such transactions do so at their own risk.

Signature of Purchaser:

Name:

Date: _____

AASTROM BIOSCIENCES, INC.
1992 EMPLOYEE NON-QUALIFIED
STOCK OPTION AGREEMENT

AASTROM BIOSCIENCES, INC., a Michigan corporation (the "Company"), hereby grants to _____ ("Optionee"), an option to purchase a total of _____ shares (the "Shares") of common stock of the Company, at the price determined as provided herein, and in all respects subject to the terms, definitions and provisions of the Company's 1992 Incentive and Non-Qualified Stock Option Plan (the "Plan") incorporated herein by reference. Terms which are defined in the Plan shall have the same meanings when used herein.

1. Nature of the Option. This Option is a non-qualified stock option and is not intended to qualify for any special tax benefits to the Optionee.

2. Exercise Price. The option price shall be \$_____ for each Share (the "Exercise Price"), which is not less than the fair market value of each Share on the date hereof. The Option Price shall be adjusted proportionately for increases or decreases in the number of outstanding Shares resulting from stock splits.

3. Exercise of Option. Subject to Section 6 hereof, this Option shall be exercisable during its term as follows:

(a) Right to Exercise. This Option shall be exercisable with respect to _____ Shares on _____ and shall be exercisable with respect to an additional _____ Shares on the first day of every third month thereafter, as long as Optionee remains an employee, director or consultant of the Company.

(b) Method of Exercise. This Option shall be exercisable by written notice in the form of Exhibit A attached hereto. Such written notice shall be signed by Optionee and shall be delivered in person, by certified mail, or by such other means as the Company may permit to the Secretary of the Company. The written notice shall be accompanied by payment of the aggregate Exercise Price.

No Shares will be issued pursuant to the exercise of this Option unless such issuance and such exercise shall comply with all relevant

provisions of law and the requirements of any stock exchange upon which the Shares may then be listed.

(c) Number of Shares Exercisable. Each exercise of this Option in part shall reduce, pro tanto, the total number of Shares that may thereafter be purchased under such Option.

4. Optionee's Representations. If the Shares which may be purchased pursuant to the exercise of this Option have not been registered under the Securities Act of 1933, as amended (the "Securities Act"), at the time this Option is exercised, Optionee shall, concurrently with the exercise of all or any portion of this Option, deliver to the Company his Investment Representation Statement in the form attached hereto as Exhibit B.

5. Method of Payment. Payment of the Exercise Price, may be in any of the following forms, or a combination thereof, in the discretion of the Company:

(a) cash or check in the full amount of the aggregate Exercise Price;

or

(b) surrender to the Company of other shares of Common Stock of the Company having a fair market value on the date of surrender equal to the aggregate Exercise Price of the Shares as to which this Option is being exercised. If the Company's Common Stock is then quoted on the National Association of Securities Dealers Automated Quotation System ("Nasdaq") or listed on a recognized securities exchange, the fair market value of the shares shall be the representative closing price of the stock as obtained from the Nasdaq or such recognized securities exchange on the date of the exercise of the Option, or if there is no such quotation on the date of the exercise, on the last trading day prior to the date of exercise. If the Company's Common Stock is not quoted on Nasdaq or listed on a recognized securities exchange, the fair market value of such shares shall be as determined by the Board of Directors in its sole discretion; or

(c) promissory note, bearing a reasonable rate of interest, requiring at least annual payments of accrued interest, maturing in not more than four (4) years, secured by the shares purchased, and being a full recourse obligation of the Optionee. Such recourse promissory note shall be in a form satisfactory to the Company, and the Company may require the Optionee to deposit any shares securing the promissory note

with an agent designated by the Company under the terms and conditions of escrow and security agreements approved by the Company. It shall be at the sole and absolute discretion of the Company's Board of Directors as to whether or not the Optionee is allowed to exercise this Option by a promissory note payment, and the Optionee shall have no right to do so unless the Board of Directors expressly exercises its discretion to allow the use of a promissory note. Any such approval by the Board of Directors shall not constitute a precedent for any subsequent exercise of this Option by the Optionee.

(d) through "Cashless Exercise". A "Cashless Exercise" means the assignment in a form acceptable to the Company of the proceeds of a sale or loan with respect to some or all of the Shares of Common Stock acquired upon the exercise of the Option pursuant to a program or procedure approved by the Company (including, without limitation, through an exercise complying with the provisions of Regulation T as promulgated from time to time by the Board of Governors of the Federal Reserve System). The Company reserves, at any and all times, the right, in the Company's sole and absolute discretion, to decline to approve or terminate any such program or procedure.

6. Restrictions on Exercise. This Option may not be exercised if the issuance of such Shares upon such exercise or the method of payment of consideration for such Shares would constitute a violation of any applicable federal or state securities or other law or regulation, including any rule under Part 207 of Title 12 of the Code of Federal Regulations ("Regulation G") as promulgated by the Federal Reserve Board. As a condition to the exercise of this Option, the Company may require the Optionee to make any representation and warranty to the Company as may be required by any applicable law or regulation.

7. Termination of Options.

(a) Except as provided herein, this Option shall terminate at such time as Optionee ceases to be employed by the Company or ceases to be a director of or consultant to the Company.

(b) Upon the death of Optionee while in the employ of the Company or while a director of or consultant to the Company, Options held by Optionee which are exercisable on the date of his or her death shall be exercisable by his or her executor(s) or administrator(s) for a period of eighteen (18) months following the date of Optionee's death.

(c) Upon termination of Optionee's employment with or service as a consultant to the Company (or if Optionee is a director only, upon termination of the Optionee's term of office, or if the Optionee is both an employee and a director, upon termination of both) for any reason other than death, disability or "Cause," as defined in Section 7(d), Options exercisable by Optionee on the date of termination of employment or service shall be exercisable by Optionee (or in the case of the Optionee's death subsequent to termination of employment, by the Optionee's executor(s) or administrator(s)) for a period of three (3) months from the date of Optionee's termination of employment or service.

(d) Upon the termination of Optionee's employment or service as a consultant (or if Optionee is a director only, upon termination of Optionee's term of office, or if Optionee is both an employee and a director, upon termination of both) for "Cause," as defined in this Section 7(d), all Options held by Optionee shall terminate concurrently with receipt by the Optionee of oral or written notice that his or her employment or service has been terminated. Termination for "Cause" shall include termination by reason of being convicted of any felony or committing willful and gross negligence or willful and gross misconduct in carrying out duties properly assigned to Optionee by the Company.

(e) Upon termination of Optionee's employment or service as a consultant due to the "disability" of Optionee as such term is defined in Section 22(c)(3) of the Code an Option exercisable by Optionee on the date of termination shall be exercisable by Optionee (or Optionee's legal guardian or representative) for a period of one (1) year from the date of Optionee's termination of employment or service.

(f) Notwithstanding the provisions of subsections (b), (c) and (e) above, if a sale within the applicable time periods set forth in subsections (b), (c) and (e) of this Section 7 of shares acquired upon the exercise of the Option would subject the Optionee to suit under Section 16(b) of the Exchange Act, the Option shall remain exercisable until the earliest to occur of (i) the tenth (10th) day following the date on which a sale of such shares by the Optionee would no longer be subject to such suit, (ii) the one hundred and ninetieth (190th) day after the Optionee's termination of employment or service, or (iii) the Option term date determined pursuant to Section 8. The Company makes no representation as to the tax consequences of any such delayed exercise. The Optionee should consult with the Optionee's own tax advisor as to the tax consequences to the Optionee of any such delayed exercise.

8. Non-Transferability of Option. This Option may not be sold, pledged, assigned, hypothecated, transferred or disposed of in any manner during the lifetime of Optionee other than by will or the laws of descent and distribution, and may be exercised during the lifetime of the Optionee only by him or her. The terms of this Option shall be binding upon the executors, administrators, heirs and successors of the Optionee.

9. Term of Option. This Option may not be exercised more than ten (10) years from the date of grant of this Option, and may be exercised during such term only in accordance with the terms of the Plan and this Option.

10. Early Disposition of Stock. Optionee hereby agrees that if he disposes of any Shares received under this Option within one (1) year after such Shares were transferred to him, he will notify the Company in writing within 30 days after the date of any such disposition.

11. Acknowledgment. The Optionee acknowledges receipt of a copy of the Plan, which is annexed hereto as Exhibit C. The Optionee represents that he has read the terms and provisions of the Plan and accepts this Option subject to all of the terms and provisions thereof. The Optionee hereby agrees to accept as binding, conclusive and final all decisions or interpretations of the Committee upon any questions arising under the Plan.

12. Entire Agreement. This Agreement, together with the exhibits attached hereto, represents the entire agreement between the parties.

13. Governing Law. This Agreement shall be construed in accordance with the laws of the State of Michigan.

14. Amendment. This Agreement may only be amended by a writing signed by each of the parties hereto.

DATE OF GRANT: _____

AASTROM BIOSCIENCES, INC.

By: _____

R. Douglas Armstrong, Ph.D.
Its: President and CEO

Agreed to this ____ day of
_____, 19__.

Optionee

EXHIBIT A

NOTICE OF EXERCISE

[Date]

AASTROM Biosciences, Inc.
Domino's Farms, Lobby L
P.O. Box 376
Ann Arbor, MI 48106
Attn.: Corporate Secretary

Dear Madam or Sir:

I hereby notify AASTROM Biosciences, Inc. of my intent to exercise
_____ Options granted to me pursuant to a Stock Option Agreement dated
_____ at an exercise price of \$_____ per share. I have enclosed a
check for \$_____.

[Signature of Optionee]

[Print Name of Optionee]

EXHIBIT B

INVESTMENT REPRESENTATION STATEMENT

PURCHASER: []

COMPANY: Aastrom Biosciences, Inc.

SECURITY: COMMON STOCK

AMOUNT: [] SHARES

DATE: []

In connection with the purchase of the above-listed Securities, I, the Purchaser, represent to the Company, the following:

(a) I am aware of the Company's business affairs and financial condition, and have acquired all such information about the Company as I deem necessary and appropriate to enable me to reach an informed and knowledgeable decision to acquire the Securities. I am purchasing these Securities for my own account for investment and not with a view to, or for the resale in connection with, any "distribution" thereof for purposes for the Securities Act of 1933, as amended ("Securities Act").

(b) I understand that the Securities have not been registered under the Securities Act in reliance upon a specific exemption therefrom, which exemption depends upon, among other things, the bona fide nature of my investment intent as expressed herein.

(c) I further understand that the Securities may not be sold publicly and must be held indefinitely unless they are subsequently registered under the Securities Act or unless an exemption from registration is available. I am able, without impairing my financial condition, to hold the Securities for an indefinite period of time and to suffer a complete loss of my investment. I understand that the Company is under no obligation to register the Securities. In addition, I understand that the certificate evidencing the Securities will be imprinted with a legend which prohibits the transfer of the Securities unless they are registered or such registration is not required in the opinion of counsel for the Company.

(d) I am familiar with the provisions of Rule 144, promulgated under the Securities Act, which, in substance, permits limited public resale of "restricted securities" acquired, directly or indirectly, from the issuer thereof (or

from an affiliate of such issuer), in a non-public offering subject to the satisfaction of certain conditions, including, among other things: (1) the availability of certain public information about the Company; (2) the resale occurring not less than two years after the party has purchased, and made full payment for, within the meaning of Rule 144, the securities to be sold; and (3) in the case of an affiliate, or of a non-affiliate who has held the securities less than three years, the sale being made through a broker in an unsolicited "broker's transaction" or in transactions directly with a market maker (as said term is defined under the Securities Exchange Act of 1934) and the amount of securities being sold during any three month period not exceeding the specified limitations stated therein, if applicable.

(e) I further understand that at the time I wish to sell the Securities there may be no public market upon which to make such a sale, and that, even if such a public market then exists, the Company may not be satisfying the current public information requirements of Rule 144, and that, in such event, I would be precluded from selling the Securities under Rule 144 even if the two-year minimum holding period had been satisfied. I understand that the Company is not currently required to file reports pursuant to the Securities Exchange Act of 1934, as amended, and is under no obligation to make Rule 144 available.

(f) I further understand that, in the event all of the applicable requirements of Rule 144 are not satisfied, registration under the Securities Act, compliance with Regulation A, or some other registration exemption will be required; and that, notwithstanding the fact that Rule 144 is not exclusive, the Staff of the Securities and Exchange Commission has expressed its opinion that persons proposing to sell private placement securities other than in a registered offering and otherwise than pursuant to Rule 144 will have a substantial burden of proof in establishing that an exemption from registration is available for such offers or sales, and that such persons and their respective brokers who participate in such transactions do so at their own risk.

Signature of Purchaser:

Name:

Date: _____

AASTROM BIOSCIENCES, INC.

1996 OUTSIDE DIRECTORS STOCK OPTION PLAN

1. ESTABLISHMENT, PURPOSE AND TERM OF PLAN.

1.1 ESTABLISHMENT. The Aastrom Biosciences, Inc. 1996 Outside Directors Stock Option Plan (the "Plan") is hereby established effective as of the effective date of the initial registration by the Company of its Stock under Section 12 of the Exchange Act (the "Effective Date").

1.2 PURPOSE. The purpose of the Plan is to advance the interests of the Participating Company Group and its stockholders by providing an incentive to attract and retain highly qualified persons to serve as Outside Directors of the Company and by creating additional incentive for Outside Directors to promote the growth and profitability of the Participating Company Group.

1.3 TERM OF PLAN. The Plan shall continue in effect until the earlier of its termination by the Board or the date on which all of the shares of Stock available for issuance under the Plan have been issued and all restrictions on such shares under the terms of the Plan and the agreements evidencing Options granted under the Plan have lapsed.

2. DEFINITIONS AND CONSTRUCTION.

2.1 DEFINITIONS. Whenever used herein, the following terms shall have their respective meanings set forth below:

(a) "BOARD" means the Board of Directors of the Company. If one or more Committees have been appointed by the Board to administer the Plan, "Board" also means such Committee(s).

(b) "CODE" means the Internal Revenue Code of 1986, as amended, and any applicable regulations promulgated thereunder.

(c) "COMMITTEE" means a committee of the Board duly appointed to administer the Plan and having such powers as shall be specified by the Board. Unless the powers of the Committee have been specifically limited, the Committee shall have all of the powers of the Board granted herein, including, without limitation, the power to amend or terminate the Plan at any time, subject to the terms of the Plan and any applicable limitations imposed by law.

(d) "COMPANY" means Aastrom Biosciences, Inc., a Michigan corporation, or any successor corporation thereto.

(e) "CONSULTANT" means any person, including an advisor, engaged by a Participating Company to render services other than as an Employee or a Director.

(f) "DIRECTOR" means a member of the Board or the board of directors of any other Participating Company.

(g) "EMPLOYEE" means any person treated as an employee (including an officer or a Director who is also treated as an employee) in the records of a Participating Company; provided, however, that neither service as a Director nor payment of a director's fee shall be sufficient to constitute employment for purposes of the Plan .

(h) "EXCHANGE ACT" means the Securities Exchange Act of 1934, as amended.

(i) "FAIR MARKET VALUE" means, as of any date, if there is then a public market for the Stock, the closing price of the Stock (or the mean of the closing bid and asked prices of the Stock if the Stock is so reported instead) as reported on the National Association of Securities Dealers Automated Quotation ("NASDAQ") System, the NASDAQ National Market System or such other national or regional securities exchange or market system constituting the primary market for the Stock. If the relevant date does not fall on a day on which the Stock is trading on NASDAQ, the NASDAQ National Market System or other national or regional securities exchange or market system, the date on which the Fair Market Value shall be established shall be the last day on which the Stock was so traded prior to the relevant date. If there is then no public market for the Stock, the Fair Market Value on any relevant date shall be as determined by the Board without regard to any restriction other than a restriction which, by its terms, will never lapse.

(j) "OPTION" means a right to purchase Stock (subject to adjustment as provided in Section 4.2) pursuant to the terms and conditions of the Plan.

(k) "OPTIONEE" means a person who has been granted one or more Options.

(l) "OPTION AGREEMENT" means a written agreement between the Company and an Optionee setting forth the terms, conditions and restrictions of the Option granted to the Optionee.

(m) "OUTSIDE DIRECTOR" means a Director of the Company who is not an Employee.

(n) "PARENT CORPORATION" means any present or future "parent corporation" of the Company, as defined in Section 424(e) of the Code.

(o) "PARTICIPATING COMPANY" means the Company or any Parent Corporation or Subsidiary Corporation.

(p) "PARTICIPATING COMPANY GROUP" means, at any point in time, all corporations collectively which are then Participating Companies.

(q) "RULE 16b-3" means Rule 16b-3 as promulgated under the Exchange Act, as amended from time to time, or any successor rule or regulation.

(r) "SERVICE" means the Optionee's service with the Participating Company Group, whether in the capacity of an Employee, a Director or a Consultant. The Optionee's Service shall not be deemed to have terminated merely because of a change in the capacity in which the Optionee renders Service to the Participating Company Group or a change in the Participating Company for which the Optionee renders such Service, provided that there is no interruption or termination of the Optionee's Service. The Optionee's Service shall be deemed to have terminated either upon an actual termination of Service or upon the corporation for which the Optionee performs Service ceasing to be a Participating Company.

(s) "STOCK" means the common stock, no par value, of the Company, as adjusted from time to time in accordance with Section 4.2.

(t) "SUBSIDIARY CORPORATION" means any present or future "subsidiary corporation" of the Company, as defined in Section 424(f) of the Code.

2.2 CONSTRUCTION. Captions and titles contained herein are for convenience only and shall not affect the meaning or interpretation of any provision of the Plan. Except when otherwise indicated by the context, the singular shall include the plural, the plural shall include the singular, and use of the term "or" shall include the conjunctive as well as the disjunctive.

3. ADMINISTRATION. -----

3.1 ADMINISTRATION BY THE BOARD. The Plan shall be administered by the Board, including any duly appointed Committee of the Board. All questions of interpretation of the Plan or of any Option shall be determined by the Board, and such determinations shall be final and binding upon all persons having an interest in the Plan or such Option. Any officer of a Participating Company shall have the authority to act on behalf of the Company with respect to any matter, right, obligation, determination or election which is the responsibility of or which is

allocated to the Company herein, provided the officer has apparent authority with respect to such matter, right, obligation, determination or election.

3.2 LIMITATIONS ON AUTHORITY OF THE BOARD. Notwithstanding any other provision herein to the contrary, the Board shall have no authority, discretion, or power to select the Outside Directors who will receive Options, to set the exercise price of the Options, to determine the number of shares of Stock to be subject to an Option or the time at which an Option shall be granted, to establish the duration of an Option, or to alter any other terms or conditions specified in the Plan, except in the sense of administering the Plan subject to the provisions of the Plan.

4. SHARES SUBJECT TO PLAN.

4.1 MAXIMUM NUMBER OF SHARES ISSUABLE. Subject to adjustment as provided in Section 4.2, the maximum aggregate number of shares of Stock that may be issued under the Plan shall be one hundred fifty thousand (150,000) (on a post-split basis following the two-for-three reverse stock split of the Stock approved by the Board on April 30, 1996) and shall consist of authorized but unissued shares or reacquired shares of Stock or any combination thereof. If an outstanding Option for any reason expires or is terminated or canceled or shares of Stock acquired, subject to repurchase, upon the exercise of an Option are repurchased by the Company, the shares of Stock allocable to the unexercised portion of such Option, or such repurchased shares of Stock, shall again be available for issuance under the Plan.

4.2 ADJUSTMENTS FOR CHANGES IN CAPITAL STRUCTURE. In the event of any stock dividend, stock split, reverse stock split, recapitalization, combination, reclassification or similar change in the capital structure of the Company, appropriate adjustments shall be made in the number and class of shares subject to the Plan, to the "Initial Option" and "Annual Option" (as defined in Section 6.1), and to any outstanding Options, and in the exercise price of any outstanding Options. If a majority of the shares which are of the same class as the shares that are subject to outstanding Options are exchanged for, converted into, or otherwise become (whether or not pursuant to an "Ownership Change Event" as defined in Section 8.1) shares of another corporation (the "NEW SHARES"), the Board may unilaterally amend the outstanding Options to provide that such Options are exercisable for New Shares. In the event of any such amendment, the number of shares subject to, and the exercise price of, the outstanding Options shall be adjusted in a fair and equitable manner as determined by the Board, in its sole discretion. Notwithstanding the foregoing, any fractional share resulting from an adjustment pursuant to this Section 4.2 shall be rounded down to the nearest whole number, and in no event may the exercise price of any Option be decreased to an amount less than the par value, if any, of the stock subject to the Option.

5. Eligibility and Type of Options.

5.1 PERSONS ELIGIBLE FOR OPTIONS. An Option shall be granted only to a person who, at the time of grant, is an Outside Director.

5.2 OPTIONS AUTHORIZED. Options shall be nonstatutory stock options; that is, options which are not treated as incentive stock options within the meaning of Section 422(b) of the Code.

6. Terms and Conditions of Options. Options shall be evidenced by Option

Agreements specifying the number of shares of Stock covered thereby, in such form as the Board shall from time to time establish. Option Agreements may incorporate all or any of the terms of the Plan by reference and shall comply with and be subject to the following terms and conditions:

6.1 AUTOMATIC GRANT OF OPTIONS. Subject to execution by an Outside Director of the appropriate Option Agreement, Options shall be granted automatically and without further action of the Board, as follows:

(a) INITIAL OPTION. Each person who (i) is an Outside Director on the Effective Date, or (ii) first becomes an Outside Director after the Effective Date shall be granted an Option to purchase five thousand (5,000) shares of Stock on the Effective Date or the date he or she first becomes an Outside Director, respectively (an "Initial Option").

(b) ANNUAL OPTION. Each Outside Director (including any Director of the Company who previously did not qualify as an Outside Director but who subsequently becomes an Outside Director) shall be granted, on the date immediately following the date of each annual meeting of the stockholders of the Company (an "Annual Meeting") following which such person remains an Outside Director, an Option to purchase five thousand (5,000) shares of Stock (an "Annual Option"). Notwithstanding the foregoing, an Outside Director who has not served continuously as a Director of the Company for at least six (6) months as of the date immediately following such Annual Meeting shall not receive an Annual Option on such date.

(c) RIGHT TO DECLINE OPTION. Notwithstanding the foregoing, any person may elect not to receive an Option by delivering written notice of such election to the Board no later than the day prior to the date such Option would otherwise be granted. A person so declining an Option shall receive no payment or other consideration in lieu of such declined Option. A person who has declined an Option may revoke such election by delivering written notice of such revocation to the Board no later than the day prior to the date such Option would be granted pursuant to Section 6.1(a) or (b), as the case may be.

6.2 DISCRETION TO VARY OPTION SIZE. Notwithstanding any provision of the Plan to the contrary, the Board may, in its sole discretion, increase or decrease the number of shares of Stock that would otherwise be subject to one or more Initial Options or Annual Options to be granted pursuant to Section 6.1 if, at the time of such exercise of discretion, the exercise of such discretion would not otherwise preclude any transaction in an equity security of the Company by an officer or Director of a Participating Company from being exempt from Section 16(b) of the Exchange Act pursuant to Rule 16b-3.

6.3 EXERCISE PRICE. The exercise price per share of Stock subject to an Option shall be the Fair Market Value of a share of Stock on the date the Option is granted.

6.4 EXERCISE PERIOD. Each Option shall terminate and cease to be exercisable on the date ten (10) years after the date of grant of the Option unless earlier terminated pursuant to the terms of the Plan or the Option Agreement.

6.5 RIGHT TO EXERCISE OPTIONS.

Except as otherwise provided in the Plan or in the Option Agreement, an Option shall (a) first become exercisable on the date which is one (1) month after the date on which the Option was granted (the "Initial Vesting Date"); and (b) be exercisable on and after the Initial Vesting Date and prior to the termination thereof in an amount equal to the number of shares of Stock initially subject to the Option multiplied by the Vested Ratio as set forth below, less the number of shares previously acquired upon exercise thereof. The Vested Ratio described in the preceding sentence shall be determined as follows:

Vested Ratio	

Prior to Initial Option Vesting Date	0
On Initial Vesting Date, provided the Optionee's Service is continuous from the date of grant of the Option until the Initial Vesting Date	1/12
Plus	

For each full month of of the Optionee's continuous	1/12

Service from the Initial
Vesting Date until the Vested
Ratio equals 1/1, an additional

6.6 PAYMENT OF EXERCISE PRICE.

(a) FORMS OF CONSIDERATION AUTHORIZED. Except as otherwise provided below, payment of the exercise price for the number of shares of Stock being purchased pursuant to any Option shall be made (i) in cash, by check, or cash equivalent, (ii) by tender to the Company of shares of Stock owned by the Optionee having a Fair Market Value not less than the exercise price, (iii) by the assignment of the proceeds of a sale or loan with respect to some or all of the shares being acquired upon the exercise of the Option (including, without limitation, through an exercise complying with the provisions of Regulation T as promulgated from time to time by the Board of Governors of the Federal Reserve System) (a "CASHLESS EXERCISE"), or (iv) by any combination thereof.

(b) TENDER OF STOCK. Notwithstanding the foregoing, an Option may not be exercised by tender to the Company of shares of Stock to the extent such tender of Stock would constitute a violation of the provisions of any law, regulation or agreement restricting the redemption of the Company's stock. Unless otherwise provided by the Board, an Option may not be exercised by tender to the Company of shares of Stock unless such shares either have been owned by the Optionee for more than six (6) months or were not acquired, directly or indirectly, from the Company.

(c) CASHLESS EXERCISE. The Company reserves, at any and all times, the right, in the Company's sole and absolute discretion, to establish, decline to approve or terminate any program or procedures for the exercise of Options by means of a Cashless Exercise.

6.7 TAX WITHHOLDING. The Company shall have the right, but not the obligation, to deduct from the shares of Stock issuable upon the exercise of an Option, or to accept from the Optionee the tender of, a number of whole shares of Stock having a Fair Market Value equal to all or any part of the federal, state, local and foreign taxes, if any, required by law to be withheld by the Participating Company Group with respect to such Option or the shares acquired upon exercise thereof. Alternatively or in addition, in its sole discretion, the Company shall have the right to require the Optionee to make adequate provision for any such tax withholding obligations of the Participating Company Group arising in connection with the Option or the shares acquired upon exercise thereof. The Company shall have no obligation to deliver shares of Stock until the Participating Company Group's tax withholding obligations have been satisfied.

7. STANDARD FORM OF OPTION AGREEMENT.

7.1 INITIAL OPTION. Unless otherwise provided for by the Board at the time an Initial Option is granted, each Initial Option shall comply with and be subject to the terms and conditions set forth in the form of Nonstatutory Stock Option Agreement for Outside Directors (Initial Option) adopted by the Board concurrently with its adoption of the Plan and as amended from time to time.

7.2 ANNUAL OPTION. Unless otherwise provided for by the Board at the time an Annual Option is granted, each Annual Option shall comply with and be subject to the terms and conditions set forth in the form of Nonstatutory Stock Option Agreement for Outside Directors (Annual Option) adopted by the Board concurrently with its adoption of the Plan and as amended from time to time.

7.3 AUTHORITY TO VARY TERMS. Subject to the limitations set forth in Section 3.2, the Board shall have the authority from time to time to vary the terms of any of the standard forms of Option Agreement described in this Section 7 either in connection with the grant or amendment of an individual Option or in connection with the authorization of a new standard form or forms; provided,

however, that the terms and conditions of any such new, revised or amended standard form or forms of Option Agreement are not inconsistent with the terms of the Plan. Such authority shall include, but not by way of limitation, the authority to grant Options which are immediately exercisable subject to the Company's right to repurchase any unvested shares of Stock acquired by the Optionee upon the exercise of an Option in the event such Optionee's Service is terminated for any reason.

8. TRANSFER OF CONTROL.

8.1 DEFINITIONS.

(a) AN "OWNERSHIP CHANGE EVENT" shall be deemed to have occurred if any of the following occurs with respect to the Company:

(i) the direct or indirect sale or exchange in a single or series of related transactions by the stockholders of the Company of more than fifty percent (50%) of the voting stock of the Company;

(ii) a merger or consolidation in which the Company is a party;

(iii) the sale, exchange, or transfer of all or substantially all of the assets of the Company; or

(iv) a liquidation or dissolution of the Company.

(b) A "TRANSFER OF CONTROL" shall mean an Ownership Change Event or a series of related Ownership Change Events (collectively, the "TRANSACTION") wherein the stockholders of the Company immediately before the Transaction do not retain immediately after the Transaction, in substantially the same proportions as their ownership of shares of the Company's voting stock immediately before the Transaction, direct or indirect beneficial ownership of more than fifty percent (50%) of the total combined voting power of the outstanding voting stock of the Company or the corporation or corporations to which the assets of the Company were transferred (the "TRANSFEREE CORPORATION(S)"), as the case may be. For purposes of the preceding sentence, indirect beneficial ownership shall include, without limitation, an interest resulting from ownership of the voting stock of one or more corporations which, as a result of the Transaction, own the Company or the Transferee Corporation(s), as the case may be, either directly or through one or more subsidiary corporations. The Board shall have the right to determine whether multiple sales or exchanges of the voting stock of the Company

or multiple Ownership Change Events are related, and its determination shall be final, binding and conclusive.

8.2 EFFECT OF TRANSFER OF CONTROL ON OPTIONS. In the event of a Transfer of Control, any unexercisable or unvested portion of the outstanding Options shall be immediately exercisable and vested in full as of the date ten (10) days prior to the date of the Transfer of Control. The exercise or vesting of any Option that was permissible solely by reason of this Section 8.2 shall be conditioned upon the consummation of the Transfer of Control. In addition, the surviving, continuing, successor, or purchasing corporation or parent corporation thereof, as the case may be (the "ACQUIRING CORPORATION"), may either assume the Company's rights and obligations under outstanding Options or substitute for outstanding Options substantially equivalent options for the Acquiring Corporation's stock. Any Options which are neither assumed or substituted for by the Acquiring Corporation in connection with the Transfer of Control nor exercised as of the date of the Transfer of Control shall terminate and cease to be outstanding effective as of the date of the Transfer of Control. Notwithstanding the foregoing, shares acquired upon exercise of an Option prior to the Transfer of Control and any consideration received pursuant to the Transfer of Control with respect to such shares shall continue to be subject to all applicable provisions of the Option Agreement evidencing such Option except as otherwise provided in such Option Agreement. Furthermore, notwithstanding the foregoing, if the corporation the stock of which is subject to the outstanding Options immediately prior to an Ownership Change Event described in Section 8.1(a)(i) constituting a Transfer of Control is the surviving or continuing corporation and immediately after such Ownership Change Event less than fifty percent (50%) of the total combined voting power of its voting stock is held by another corporation or by other corporations that are members of an affiliated group within the meaning of Section 1504(a) of the Code without regard to the provisions of Section 1504(b) of the Code, the outstanding Options shall not terminate.

9. NONTRANSFERABILITY OF OPTIONS. During the lifetime of the Optionee,

an Option shall be exercisable only by the Optionee or the Optionee's guardian or legal representative. No Option shall be assignable or transferable by the Optionee, except by will or by the laws of descent and distribution.

10. INDEMNIFICATION. In addition to such other rights of indemnification

as they may have as members of the Board or officers or employees of the Participating Company Group, members of the Board and any officers or employees of the Participating Company Group to whom authority to act for the Board is delegated shall be indemnified by the Company against all reasonable expenses, including attorneys' fees, actually and necessarily incurred in connection with the defense of any action, suit or proceeding, or in connection with any appeal therein, to which they or any of them may be a party by reason of any action taken or failure to act under or in connection with the Plan, or any right granted hereunder, and against all amounts paid by them in settlement thereof (provided such

settlement is approved by independent legal counsel selected by the Company) or paid by them in satisfaction of a judgment in any such action, suit or proceeding, except in relation to matters as to which it shall be adjudged in such action, suit or proceeding that such person is liable for gross negligence, bad faith or intentional misconduct in duties; provided, however, that within sixty (60) days after the institution of such action, suit or proceeding, such person shall offer to the Company, in writing, the opportunity at its own expense to handle and defend the same.

11. TERMINATION OR AMENDMENT OF PLAN. The Board may terminate or amend

the Plan at any time. However, subject to changes in the law or other legal requirements that would permit otherwise, without the approval of the Company's stockholders, there shall be (a) no increase in the total number of shares of Stock that may be issued under the Plan (except by operation of the provisions of Section 4.2), and (b) no other amendment of the Plan that would require approval of the Company's stockholders under any applicable law, regulation or rule. In any event, no termination or amendment of the Plan may adversely affect any then outstanding Option, or any unexercised portion thereof, without the consent of the Optionee, unless such termination or amendment is necessary to comply with any applicable law or government regulation.

IN WITNESS WHEREOF, the undersigned Secretary of the Company certifies that the foregoing AASTROM Biosciences, Inc. 1996 Outside Directors Stock Option Plan was duly adopted by the Board on April 30, 1996.

/s/ Todd E. Simpson

Todd E. Simpson, Secretary

AASTROM BIOSCIENCES, INC.

NONSTATUTORY STOCK OPTION AGREEMENT

FOR OUTSIDE DIRECTORS

(INITIAL OPTION)

THIS NONSTATUTORY STOCK OPTION AGREEMENT FOR OUTSIDE DIRECTORS (INITIAL
OPTION) (the "OPTION AGREEMENT") is made and entered into as of
_____, 199____, by and between Aastrom Biosciences, Inc. and

(the "OPTIONEE").

The Company has granted to the Optionee an option to purchase certain
shares of Stock, upon the terms and conditions set forth in this Option
Agreement (the "OPTION").

1. DEFINITIONS AND CONSTRUCTION.

1.1 DEFINITIONS. Whenever used herein, the
following terms shall have their respective meanings set forth below:

(a) "DATE OF OPTION GRANT" means _____, 199____.

(b) "NUMBER OF OPTION SHARES" means five thousand (5,000)
shares of Stock, as adjusted from time to time pursuant to Section 9.

(c) "EXERCISE PRICE" means \$ _____ per
share of Stock, as adjusted from time to time pursuant to Section 9.

(d) "INITIAL EXERCISE DATE" means the Initial
Vesting Date.

(e) "INITIAL VESTING DATE" means the date
occurring one (1) month after the Date of Option Grant.

(f) "VESTED RATIO" means, on any relevant date, the ratio determined as follows:

	Vested Ratio -----
Prior to Initial Vesting Date	0
On Initial Vesting Date, provided the Optionee's Service is continuous from the Date of Option Grant until the Initial Vesting Date	1/12
PLUS - ----	
For each full month of the Optionee's continuous Service from the Initial Vesting Date until the Vested Ratio equals 1/1, an additional	1/12

(g) "OPTION EXPIRATION DATE" means the date ten (10) years after the Date of Option Grant.

(h) "BOARD" means the Board of Directors of the Company. If one or more Committees have been appointed by the Board to administer the Plan, "Board" shall also mean such Committee(s).

(i) "CODE" means the Internal Revenue Code of 1986, as amended, and any applicable regulations promulgated thereunder.

(j) "COMMITTEE" means a committee of the Board duly appointed to administer the Plan and having such powers as shall be specified by the Board. Unless the powers of the Committee have been specifically limited, the Committee shall have all of the powers of the Board granted in the Plan, including, without limitation, the power to amend or terminate the Plan at any time, subject to the terms of the Plan and any applicable limitations imposed by law.

(k) "COMPANY" means Biosciences, Inc., a Michigan corporation, or any successor corporation thereto.

(l) "CONSULTANT" means Aastrom any person, including an advisor, engaged by a Participating Company to render services other than as an Employee or a Director.

(m) "DIRECTOR" means a member of the Board or of the board of directors of any other Participating Company.

(n) "DISABILITY" means the permanent and total disability of the Optionee within the meaning of Section 22(e)(3) of the Code.

(o) "EMPLOYEE" means any person treated as an employee (including an officer or a Director who is also treated as an employee) in the records of a Participating Company; provided, however, that neither service as a Director nor payment of a director's fee shall be sufficient to constitute employment for purposes of the Plan.

(p) "EXCHANGE ACT" means the Securities Exchange Act of 1934, as amended.

(q) "FAIR MARKET VALUE" means, as of any date, if there is then a public market for the Stock, the closing price of the Stock (or the mean of the closing bid and asked prices of the Stock if the Stock is so reported instead) as reported on the National Association of Securities Dealers Automated Quotation ("NASDAQ") System, the NASDAQ National Market System or such other national or regional securities exchange or market system constituting the primary market for the Stock. If the relevant date does not fall on a day on which the Stock is trading on NASDAQ, the NASDAQ National Market System or other national or regional securities exchange or market system, the date on which the Fair Market Value shall be established shall be the last day on which the Stock was so traded prior to the relevant date. If there is then no public market for the Stock, the Fair Market Value on any relevant date shall be as determined by the Board without regard to any restriction other than a restriction which, by its terms, will never lapse.

(r) "PARENT CORPORATION" means any present or future "parent corporation" of the Company, as defined in Section 424(e) of the Code.

(s) "PARTICIPATING COMPANY" means the Company or any Parent Corporation or Subsidiary Corporation.

(t) "PARTICIPATING COMPANY GROUP" means, at any point in time, all corporations collectively which are then Participating Companies.

(u) "PLAN" means the Aastrom Biosciences, Inc. 1996 Outside Directors Stock Option Plan.

(v) "SECURITIES ACT" means the Securities Act of 1933, as amended.

(w) "SERVICE" means the Optionee's service with the Participating Company Group, whether in the capacity of an Employee, a Director or a Consultant. The Optionee's Service shall not be deemed to have terminated merely because of a change in the capacity in which the Optionee renders Service to the Participating Company Group or a change in the Participating Company for which the Optionee renders such Service, provided that there is no interruption or termination of the Optionee's Service. The Optionee's Service shall be deemed to have terminated either upon an actual termination of Service or upon the corporation for which the Optionee performs Service ceasing to be a Participating Company.

(x) "STOCK" means the common stock, no par value of the Company, as adjusted from time to time in accordance with Section 9.

(y) "SUBSIDIARY CORPORATION" means any present or future "subsidiary corporation" of the Company, as defined in Section 424(f) of the Code.

1.2 CONSTRUCTION. Captions and titles contained herein are for convenience only and shall not affect the meaning or interpretation of any provision of this Option Agreement. Except when otherwise indicated by the context, the singular shall include the plural, the plural shall include the singular, and the term "or" shall include the conjunctive as well as the disjunctive.

2. TAX STATUS OF THE OPTION. This Option is intended to be a

nonstatutory stock option and shall not be treated as an incentive stock option within the meaning of Section 422(b) of the Code.

3. ADMINISTRATION. All questions of interpretation concerning this

Option Agreement shall be determined by the Board, including any duly appointed Committee of the Board. All determinations by the Board shall be final and binding upon all persons having an interest in the Option. Any officer of a Participating Company shall have the authority to act on behalf of the Company with respect to any matter, right, obligation, or election which is the responsibility of or which is allocated to the Company herein, provided the officer has apparent authority with respect to such matter, right, obligation, or election.

4. EXERCISE OF THE OPTION.

4.1 RIGHT TO EXERCISE. Except as otherwise provided herein, the Option shall be exercisable on and after the Initial Exercise Date and prior to the termination of the Option (as provided in Section 6) in an amount not to exceed the Number of Option

Shares multiplied by the Vested Ratio less the number of shares previously acquired upon exercise of the Option. In no event shall the Option be exercisable for more shares than the Number of Option Shares.

4.2 METHOD OF EXERCISE. Exercise of the Option shall be by written notice to the Company which must state the election to exercise the Option, the number of whole shares of Stock for which the Option is being exercised and such other representations and agreements as to the Optionee's investment intent with respect to such shares as may be required pursuant to the provisions of this Option Agreement. The written notice must be signed by the Optionee and must be delivered in person, by certified or registered mail, return receipt requested, by confirmed facsimile transmission, or by such other means as the Company may permit, to the Chief Financial Officer of the Company, or other authorized representative of the Participating Company Group, prior to the termination of the Option as set forth in Section 6, accompanied by full payment of the aggregate Exercise Price for the number of shares of Stock being purchased. The Option shall be deemed to be exercised upon receipt by the Company of such written notice and the aggregate Exercise Price.

4.3 PAYMENT OF EXERCISE PRICE.

(a) FORMS OF CONSIDERATION AUTHORIZED. Except as otherwise provided below, payment of the aggregate Exercise Price for the number of shares of Stock for which the Option is being exercised shall be made (i) in cash, by check, or cash equivalent, (ii) by tender to the Company of whole shares of Stock owned by the Optionee having a Fair Market Value not less than the aggregate Exercise Price, (iii) by means of a Cashless Exercise, as defined in Section 4.3(c), or (iv) by any combination of the foregoing.

(b) TENDER OF STOCK. Notwithstanding the foregoing, the Option may not be exercised by tender to the Company of shares of Stock to the extent such tender of Stock would constitute a violation of the provisions of any law, regulation or agreement restricting the redemption of the Company's stock. The Option may not be exercised by tender to the Company of shares of Stock unless such shares either have been owned by the Optionee for more than six (6) months or were not acquired, directly or indirectly, from the Company.

(c) CASHLESS EXERCISE. A "Cashless Exercise" means the assignment in a form acceptable to the Company of the proceeds of a sale or loan with respect to some or all of the shares of Stock acquired upon the exercise of

the Option pursuant to a program or procedure approved by the Company (including, without limitation, through an exercise complying with the provisions of Regulation T as promulgated from time to time by the Board of Governors of the Federal Reserve System). The Company reserves, at any and all times, the right, in the Company's sole and absolute discretion, to decline to approve or terminate any such program or procedure.

4.4 TAX WITHHOLDING. At the time the Option is exercised, in whole or in part, or at any time thereafter as requested by the Company, the Optionee agrees to make adequate provision for any sums required to satisfy the federal, state, local and foreign tax withholding obligations of the Participating Company Group, if any, which arise in connection with the Option, including, without limitation, obligations arising upon (i) the exercise, in whole or in part, of the Option, (ii) the transfer, in whole or in part, of any shares acquired upon exercise of the Option, or (iii) the lapsing of any restriction with respect to any shares acquired upon exercise of the Option.

4.5 CERTIFICATE REGISTRATION. Except in the event the Exercise Price is paid by means of a Cashless Exercise, the certificate for the shares as to which the Option is exercised shall be registered in the name of the Optionee, or, if applicable, the heirs of the Optionee.

4.6 RESTRICTIONS ON GRANT OF THE OPTION AND ISSUANCE OF SHARES. The grant of the Option and the issuance of shares of Stock upon exercise of the Option shall be subject to compliance with all applicable requirements of federal, state or foreign law with respect to such securities. The Option may not be exercised if the issuance of shares of Stock upon exercise would constitute a violation of any applicable federal, state or foreign securities laws or other law or regulations or the requirements of any stock exchange or market system upon which the Stock may then be listed. In addition, the Option may not be exercised unless (i) a registration statement under the Securities Act shall at the time of exercise of the Option be in effect with respect to the shares issuable upon exercise of the Option or (ii) in the opinion of legal counsel to the Company, the shares issuable upon exercise of the Option may be issued in accordance with the terms of an applicable exemption from the registration requirements of the Securities Act. THE OPTIONEE IS CAUTIONED THAT THE OPTION MAY NOT BE EXERCISED UNLESS THE FOREGOING CONDITIONS ARE SATISFIED. ACCORDINGLY, THE OPTIONEE MAY NOT BE ABLE TO EXERCISE THE OPTION WHEN DESIRED EVEN THOUGH THE OPTION IS VESTED. The inability of the Company to obtain from any regulatory body having jurisdiction the authority, if any, deemed by the Company's legal counsel to be necessary to the lawful issuance and sale of any shares subject to the Option shall relieve the Company of any liability in respect of the failure to issue or sell such shares as to which such requisite authority shall not have been obtained. As a condition to the exercise of the Option, the Company may require the Optionee to satisfy any qualifications

that may be necessary or appropriate, to evidence compliance with any applicable law or regulation and to make any representation or warranty with respect thereto as may be requested by the Company.

4.7 FRACTIONAL SHARES. The Company shall not be required to issue fractional shares upon the exercise of the Option.

5. NONTRANSFERABILITY OF THE OPTION. The Option may be exercised during

the lifetime of the Optionee only by the Optionee or the Optionee's guardian or legal representative and may not be assigned or transferred in any manner except by will or by the laws of descent and distribution. Following the death of the Optionee, the Option, to the extent provided in Section 7, may be exercised by the Optionee's legal representative or by any person empowered to do so under the deceased Optionee's will or under the then applicable laws of descent and distribution.

6. TERMINATION OF THE OPTION. The Option shall terminate and may no

longer be exercised on the first to occur of (a) the Option Expiration Date, (b) the last date for exercising the Option following termination of the Optionee's Service as described in Section 7, or (c) a Transfer of Control to the extent provided in Section 8.

7. EFFECT OF TERMINATION OF SERVICE.

7.1 OPTION EXERCISABILITY.

(a) DISABILITY. If the Optionee's Service with the Participating Company Group is terminated because of the Disability of the Optionee, the Option, to the extent unexercised and exercisable on the date on which the Optionee's Service terminated, may be exercised by the Optionee (or the Optionee's guardian or legal representative) at any time prior to the expiration of twelve (12) months after the date on which the Optionee's Service terminated, but in any event no later than the Option Expiration Date.

(b) DEATH. If the Optionee's Service with the Participating Company Group is terminated because of the death of the Optionee, the Option, to the extent unexercised and exercisable on the date on which the Optionee's Service terminated, may be exercised by the Optionee (or the Optionee's legal representative or other person who acquired the right to exercise the Option by reason of the Optionee's death) at any time prior to the expiration of twelve (12) months after the date on which the Optionee's Service terminated, but in any event no later than the Option Expiration Date. The Optionee's Service shall be deemed to have terminated on account of death if the Optionee dies within three (3) months after the Optionee's termination of Service.

(c) OTHER TERMINATION OF SERVICE. If the Optionee's Service with the Participating Company Group terminates for any reason, except Disability or death, the Option, to the extent unexercised and exercisable by the Optionee on the date on which the Optionee's Service terminated, may be exercised by the Optionee within three (3) months after the date on which the Optionee's Service terminated, but in any event no later than the Option Expiration Date.

7.2 EXTENSION IF EXERCISE PREVENTED BY LAW. Notwithstanding the foregoing, if the exercise of the Option within the applicable time periods set forth in Section 7.1 is prevented by the provisions of Section 4.6, the Option shall remain exercisable until three (3) months after the date the Optionee is notified by the Company that the Option is exercisable, but in any event no later than the Option Expiration Date.

7.3 EXTENSION IF OPTIONEE SUBJECT TO SECTION 16(B). Notwithstanding the foregoing, if a sale, within the applicable time periods set forth in Section 7.1, of shares acquired upon the exercise of the Option would subject the Optionee to suit under Section 16(b) of the Exchange Act, the Option shall remain exercisable until the earliest to occur of (i) the tenth (10th) day following the date on which a sale of such shares by the Optionee would no longer be subject to such suit, (ii) the one hundred and ninetieth (190th) day after the Optionee's termination of Service, or (iii) the Option Expiration Date.

8. OWNERSHIP CHANGE AND TRANSFER OF CONTROL.

8.1 DEFINITIONS.

(a) An "OWNERSHIP CHANGE EVENT" shall be deemed to have occurred if any of the following occurs with respect to the Company:

(i) the direct or indirect sale or exchange in a single or series of related transactions by the stockholders of the Company of more than fifty percent (50%) of the voting stock of the Company;

(ii) a merger or consolidation in which the Company is a party;

(iii) the sale, exchange, or transfer of all or substantially all of the assets of the Company; or

(iv) a liquidation or dissolution of the Company.

(b) A "TRANSFER OF CONTROL" shall mean an Ownership Change Event or a series of related Ownership Change Events (collectively, the "Transaction") wherein the stockholders of the Company immediately before the Transaction do not retain immediately after the Transaction, in substantially the

same proportions as their ownership of shares of the Company's voting stock immediately before the Transaction, direct or indirect beneficial ownership of more than fifty percent (50%) of the total combined voting power of the outstanding voting stock of the Company or the corporation or corporations to which the assets of the Company were transferred (the "Transferee Corporation(s)"), as the case may be. For purposes of the preceding sentence, indirect beneficial ownership shall include, without limitation, an interest resulting from ownership of the voting stock of one or more corporations which, as a result of the Transaction, own the Company or the Transferee Corporation(s), as the case may be, either directly or through one or more subsidiary corporations. The Board shall have the right to determine whether multiple sales or exchanges of the voting stock of the Company or multiple Ownership Change Events are related, and its determination shall be final, binding and conclusive.

8.2 EFFECT OF TRANSFER OF CONTROL ON OPTION. In the event of a Transfer of Control, any unexercised portion of the Option shall be immediately exercisable and vested in full as of the date ten (10) days prior to the date of the Transfer of Control. Any exercise of the Option that was permissible solely by reason of this Section 8.2 shall be conditioned upon the consummation of the Transfer of Control. In addition, the surviving, continuing, successor, or purchasing corporation or parent corporation thereof, as the case may be (the "ACQUIRING CORPORATION"), may either assume the Company's rights and obligations under the Option or substitute for the Option a substantially equivalent option for the Acquiring Corporation's stock. The Option shall terminate and cease to be outstanding effective as of the date of the Transfer of Control to the extent that the Option is neither assumed or substituted for by the Acquiring Corporation in connection with the Transfer of Control nor exercised as of the date of the Transfer of Control. Notwithstanding the foregoing, shares acquired upon exercise of the Option prior to the Transfer of Control and any consideration received pursuant to the Transfer of Control with respect to such shares shall continue to be subject to all applicable provisions of this Option Agreement except as otherwise provided herein. Furthermore, notwithstanding the foregoing, if the corporation the stock of which is subject to the Option immediately prior to an Ownership Change Event described in Section 8.1(a)(i) constituting a Transfer of Control is the surviving or continuing corporation and immediately after such Ownership Change Event less than fifty percent (50%) of the total combined voting power of its voting stock is held by another corporation or by other corporations that are members of an affiliated group within the meaning of Section 1504(a) of the Code without regard to the provisions of Section 1504(b) of the Code, the Option shall not terminate.

9. ADJUSTMENTS FOR CHANGES IN CAPITAL STRUCTURE. In the event of any

stock dividend, stock split, reverse stock split, recapitalization, combination, reclassification, or similar change in the capital structure of the Company, appropriate adjustments shall be made in the number, Exercise Price and class of shares of stock subject to the Option. If a majority of the shares which are of the same class as the shares that are subject to the Option are exchanged for,

converted into, or otherwise become (whether or not pursuant to an Ownership Change Event) shares of another corporation (the "NEW SHARES"), the Board may unilaterally amend the Option to provide that the Option is exercisable for New Shares. In the event of any such amendment, the Number of Option Shares and the Exercise Price shall be adjusted in a fair and equitable manner, as determined by the Board, in its sole discretion. Notwithstanding the foregoing, any fractional share resulting from an adjustment pursuant to this Section 9 shall be rounded down to the nearest whole number, and in no event may the Exercise Price be decreased to an amount less than the par value, if any, of the stock subject to the Option.

10. RIGHTS AS A STOCKHOLDER. The Optionee shall have no rights as a

stockholder with respect to any shares covered by the Option until the date of the issuance of a certificate for the shares for which the Option has been exercised (as evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company). No adjustment shall be made for dividends, distributions or other rights for which the record date is prior to the date such certificate is issued, except as provided in Section 9.

11. LEGENDS. The Company may at any time place legends referencing any

applicable federal, state or foreign securities law restrictions on all certificates representing shares of stock subject to the provisions of this Option Agreement. The Optionee shall, at the request of the Company, promptly present to the Company any and all certificates representing shares acquired pursuant to the Option in the possession of the Optionee in order to carry out the provisions of this Section.

12. BINDING EFFECT. Subject to the restrictions on transfer set forth

herein, this Option Agreement shall inure to the benefit of and be binding upon the parties hereto and their respective heirs, executors, administrators, successors and assigns.

13. TERMINATION OR AMENDMENT. The Board may terminate or amend the Plan

or the Option at any time; provided, however, that no such termination or amendment may adversely affect the Option or any unexercised portion hereof without the consent of the Optionee unless such termination or amendment is necessary to comply with any applicable law, regulation or rule. No amendment or addition to this Option Agreement shall be effective unless in writing.

14. INTEGRATED AGREEMENT. This Option Agreement constitutes the entire

understanding and agreement of the Optionee and the Participating Company Group with respect to the subject matter contained herein, and there are no agreements, understandings, restrictions, representations, or warranties among the Optionee and the Participating Company Group with respect to such subject matter other

than those as set forth or provided for herein. To the extent contemplated herein, the provisions of this Option Agreement shall survive any exercise of the Option and shall remain in full force and effect.

15. APPLICABLE LAW. This Option Agreement shall be governed by the laws -----
of the State of Michigan as such laws are applied to agreements between Michigan residents entered into and to be performed entirely within the State of Michigan.

AASTROM BIOSCIENCES, INC.

By:_____

Title:_____

The Optionee represents that the Optionee is familiar with the terms and provisions of this Option Agreement and hereby accepts the Option subject to all of the terms and provisions thereof. The Optionee hereby agrees to accept as binding, conclusive and final all decisions or interpretations of the Board upon any questions arising under this Option Agreement.

OPTIONEE

Date:_____

AASTROM BIOSCIENCES, INC.

NONSTATUTORY STOCK OPTION AGREEMENT

FOR OUTSIDE DIRECTORS

(ANNUAL OPTION)

THIS NONSTATUTORY STOCK OPTION AGREEMENT FOR OUTSIDE DIRECTORS (ANNUAL OPTION) (the "OPTION AGREEMENT") is made and entered into as of _____, 199__ by and between Aastrom Biosciences, Inc. and _____ (the "OPTIONEE").

The Company has granted to the Optionee an option to purchase certain shares of Stock, upon the terms and conditions set forth in this Option Agreement (the "OPTION").

1. DEFINITIONS AND CONSTRUCTION.

1.1 DEFINITIONS. Whenever used herein, the following terms shall have their respective meanings set forth below:

(a) "DATE OF OPTION GRANT" means _____, 199__.

(b) "NUMBER OF OPTION SHARES" means five thousand (5,000) shares of Stock, as adjusted from time to time pursuant to Section 9.

(c) "EXERCISE PRICE" means \$ _____ per share of Stock, as adjusted from time to time pursuant to Section 9.

(d) "INITIAL EXERCISE DATE" means the Initial Vesting Date.

(e) "INITIAL VESTING DATE" means the date occurring one (1) month after the Date of Option Grant.

(f) "VESTED RATIO" means, on any relevant date, the ratio determined as follows:

	Vested Ratio

Prior to Initial Vesting Date	0
On Initial Vesting Date, provided the Optionee's Service is continuous from the Date of Option Grant until the Initial Vesting Date	1/12
Plus	
- ----	
For each full month of the Optionee's continuous Service from the Initial Vesting Date until the Vested Ratio equals 1/1, an additional	1/12

(g) "OPTION EXPIRATION DATE" means the date ten (10) years after the Date of Option Grant.

(h) "BOARD" means the Board of Directors of the Company. If one or more Committees have been appointed by the Board to administer the Plan, "Board" shall also mean such Committee(s).

(i) "CODE" means the Internal Revenue Code of 1986, as amended, and any applicable regulations promulgated thereunder.

(j) "COMMITTEE" means a committee of the Board duly appointed to administer the Plan and having such powers as shall be specified by the Board. Unless the powers of the Committee have been specifically limited, the Committee shall have all of the powers of the Board granted in the Plan, including, without limitation, the power to amend or terminate the Plan at any time, subject to the terms of the Plan and any applicable limitations imposed by law.

(k) "COMPANY" means Aastrom Biosciences, Inc., a Michigan corporation, or any successor corporation thereto.

(l) "CONSULTANT" means Aastrom any person, including an advisor, engaged by a Participating Company to render services other than as an Employee or a Director.

(m) "DIRECTOR" means a member of the Board or of the board of directors of any other Participating Company.

(n) "DISABILITY" means the permanent and total disability of the Optionee within the meaning of Section 22(e)(3) of the Code.

(o) "EMPLOYEE" means any person treated as an employee (including an officer or a Director who is also treated as an employee) in the records of a Participating Company; provided, however, that neither service as a Director nor payment of a director's fee shall be sufficient to constitute employment for purposes of the Plan.

(p) "EXCHANGE ACT" means the Securities Exchange Act of 1934, as amended.

(q) "FAIR MARKET VALUE" means, as of any date, if there is then a public market for the Stock, the closing price of the Stock (or the mean of the closing bid and asked prices of the Stock if the Stock is so reported instead) as reported on the National Association of Securities Dealers Automated Quotation ("NASDAQ") System, the NASDAQ National Market System or such other national or regional securities exchange or market system constituting the primary market for the Stock. If the relevant date does not fall on a day on which the Stock is trading on NASDAQ, the NASDAQ National Market System or other national or regional securities exchange or market system, the date on which the Fair Market Value shall be established shall be the last day on which the Stock was so traded prior to the relevant date. If there is then no public market for the Stock, the Fair Market Value on any relevant date shall be as determined by the Board without regard to any restriction other than a restriction which, by its terms, will never lapse.

(r) "PARENT CORPORATION" means any present or future "parent corporation" of the Company, as defined in Section 424(e) of the Code.

(s) "PARTICIPATING COMPANY" means the Company or any Parent Corporation or Subsidiary Corporation.

(t) "PARTICIPATING COMPANY GROUP" means, at any point in time, all corporations collectively which are then Participating Companies.

(u) "PLAN" means the Aastrom Biosciences, Inc. 1996 Outside Directors Stock Option Plan.

(v) "SECURITIES ACT" means the Securities Act of 1933, as amended.

(w) "SERVICE" means the Optionee's service with the Participating Company Group, whether in the capacity of an Employee, a Director or a Consultant. The Optionee's Service shall not be deemed to have terminated merely because of a change in the capacity in which the Optionee renders Service to the Participating Company Group or a change in the Participating Company for which the Optionee renders such Service, provided that there is no interruption or termination of the Optionee's Service. The Optionee's Service shall be deemed to have terminated either upon an actual termination of Service or upon the corporation for which the Optionee performs Service ceasing to be a Participating Company.

(x) "STOCK" means the common stock, no par value, of the Company, as adjusted from time to time in accordance with Section 9.

(y) "SUBSIDIARY CORPORATION" means any present or future "subsidiary corporation" of the Company, as defined in Section 424(f) of the Code.

1.2 CONSTRUCTION. Captions and titles contained herein are for convenience only and shall not affect the meaning or interpretation of any provision of this Option Agreement. Except when otherwise indicated by the context, the singular shall include the plural, the plural shall include the singular, and the term "or" shall include the conjunctive as well as the disjunctive.

2. TAX STATUS OF THE OPTION. This Option is intended to be a

nonstatutory stock option and shall not be treated as an incentive stock option within the meaning of Section 422(b) of the Code.

3. ADMINISTRATION. All questions of interpretation concerning this

Option Agreement shall be determined by the Board, including any duly appointed Committee of the Board. All determinations by the Board shall be final and binding upon all persons having an interest in the Option. Any officer of a Participating Company shall have the authority to act on behalf of the Company with respect to any matter, right, obligation, or election which is the responsibility of or which is allocated to the Company herein, provided the officer has apparent authority with respect to such matter, right, obligation, or election.

4. EXERCISE OF THE OPTION.

4.1 RIGHT TO EXERCISE. Except as otherwise provided herein, the Option shall be exercisable on and after the Initial Exercise Date and prior to the termination of the Option (as provided in Section 6) in an amount not to exceed the Number of Option

Shares multiplied by the Vested Ratio less the number of shares previously acquired upon exercise of the Option. In no event shall the Option be exercisable for more shares than the Number of Option Shares.

4.2 METHOD OF EXERCISE. Exercise of the Option shall be by written notice to the Company which must state the election to exercise the Option, the number of whole shares of Stock for which the Option is being exercised and such other representations and agreements as to the Optionee's investment intent with respect to such shares as may be required pursuant to the provisions of this Option Agreement. The written notice must be signed by the Optionee and must be delivered in person, by certified or registered mail, return receipt requested, by confirmed facsimile transmission, or by such other means as the Company may permit, to the Chief Financial Officer of the Company, or other authorized representative of the Participating Company Group, prior to the termination of the Option as set forth in Section 6, accompanied by full payment of the aggregate Exercise Price for the number of shares of Stock being purchased. The Option shall be deemed to be exercised upon receipt by the Company of such written notice and the aggregate Exercise Price.

4.3 PAYMENT OF EXERCISE PRICE.

(a) FORMS OF CONSIDERATION AUTHORIZED. Except as otherwise provided below, payment of the aggregate Exercise Price for the number of shares of Stock for which the Option is being exercised shall be made (i) in cash, by check, or cash equivalent, (ii) by tender to the Company of whole shares of Stock owned by the Optionee having a Fair Market Value not less than the aggregate Exercise Price, (iii) by means of a Cashless Exercise, as defined in Section 4.3(c), or (iv) by any combination of the foregoing.

(b) TENDER OF STOCK. Notwithstanding the foregoing, the Option may not be exercised by tender to the Company of shares of Stock to the extent such tender of Stock would constitute a violation of the provisions of any law, regulation or agreement restricting the redemption of the Company's stock. The Option may not be exercised by tender to the Company of shares of Stock unless such shares either have been owned by the Optionee for more than six (6) months or were not acquired, directly or indirectly, from the Company.

(c) CASHLESS EXERCISE. A "CASHLESS EXERCISE" means the assignment in a form acceptable to the Company of the proceeds of a sale or loan with respect to some or all of the shares of Stock acquired upon the exercise of

the Option pursuant to a program or procedure approved by the Company (including, without limitation, through an exercise complying with the provisions of Regulation T as promulgated from time to time by the Board of Governors of the Federal Reserve System). The Company reserves, at any and all times, the right, in the Company's sole and absolute discretion, to decline to approve or terminate any such program or procedure.

4.4 TAX WITHHOLDING. At the time the Option is exercised, in whole or in part, or at any time thereafter as requested by the Company, the Optionee agrees to make adequate provision for any sums required to satisfy the federal, state, local and foreign tax withholding obligations of the Participating Company Group, if any, which arise in connection with the Option, including, without limitation, obligations arising upon (i) the exercise, in whole or in part, of the Option, (ii) the transfer, in whole or in part, of any shares acquired upon exercise of the Option, or (iii) the lapsing of any restriction with respect to any shares acquired upon exercise of the Option.

4.5 CERTIFICATE REGISTRATION. Except in the event the Exercise Price is paid by means of a Cashless Exercise, the certificate for the shares as to which the Option is exercised shall be registered in the name of the Optionee, or, if applicable, the heirs of the Optionee.

4.6 RESTRICTIONS ON GRANT OF THE OPTION AND ISSUANCE OF SHARES. The grant of the Option and the issuance of shares of Stock upon exercise of the Option shall be subject to compliance with all applicable requirements of federal, state or foreign law with respect to such securities. The Option may not be exercised if the issuance of shares of Stock upon exercise would constitute a violation of any applicable federal, state or foreign securities laws or other law or regulations or the requirements of any stock exchange or market system upon which the Stock may then be listed. In addition, the Option may not be exercised unless (i) a registration statement under the Securities Act shall at the time of exercise of the Option be in effect with respect to the shares issuable upon exercise of the Option or (ii) in the opinion of legal counsel to the Company, the shares issuable upon exercise of the Option may be issued in accordance with the terms of an applicable exemption from the registration requirements of the Securities Act. THE OPTIONEE IS CAUTIONED THAT THE OPTION MAY NOT BE EXERCISED UNLESS THE FOREGOING CONDITIONS ARE SATISFIED. ACCORDINGLY, THE OPTIONEE MAY NOT BE ABLE TO EXERCISE THE OPTION WHEN DESIRED EVEN THOUGH THE OPTION IS VESTED. The inability of the Company to obtain from any regulatory body having jurisdiction the authority, if any, deemed by the Company's legal counsel to be necessary to the lawful issuance and sale of any shares subject to the Option shall relieve the Company of any liability in respect of the failure to issue or sell such shares as to which such requisite authority shall not have been obtained. As a condition to the exercise of the Option, the Company may require the Optionee to satisfy any qualifications

that may be necessary or appropriate, to evidence compliance with any applicable law or regulation and to make any representation or warranty with respect thereto as may be requested by the Company.

4.7 FRACTIONAL SHARES. The Company shall not be required to issue fractional shares upon the exercise of the Option.

5. NONTRANSFERABILITY OF THE OPTION. The Option may be exercised during

the lifetime of the Optionee only by the Optionee or the Optionee's guardian or legal representative and may not be assigned or transferred in any manner except by will or by the laws of descent and distribution. Following the death of the Optionee, the Option, to the extent provided in Section 7, may be exercised by the Optionee's legal representative or by any person empowered to do so under the deceased Optionee's will or under the then applicable laws of descent and distribution.

6. TERMINATION OF THE OPTION. The Option shall terminate and may no

longer be exercised on the first to occur of (a) the Option Expiration Date, (b) the last date for exercising the Option following termination of the Optionee's Service as described in Section 7, or (c) a Transfer of Control to the extent provided in Section 8.

7. EFFECT OF TERMINATION OF SERVICE.

7.1 OPTION EXERCISABILITY.

(a) DISABILITY. If the Optionee's Service with the Participating Company Group is terminated because of the Disability of the Optionee, the Option, to the extent unexercised and exercisable on the date on which the Optionee's Service terminated, may be exercised by the Optionee (or the Optionee's guardian or legal representative) at any time prior to the expiration of twelve (12) months after the date on which the Optionee's Service terminated, but in any event no later than the Option Expiration Date.

(b) DEATH. If the Optionee's Service with the Participating Company Group is terminated because of the death of the Optionee, the Option, to the extent unexercised and exercisable on the date on which the Optionee's Service terminated, may be exercised by the Optionee (or the Optionee's legal representative or other person who acquired the right to exercise the Option by reason of the Optionee's death) at any time prior to the expiration of twelve (12) months after the date on which the Optionee's Service terminated, but in any event no later than the Option Expiration Date. The Optionee's Service shall be deemed to have terminated on account of death if the Optionee dies within three (3) months after the Optionee's termination of Service.

(c) OTHER TERMINATION OF SERVICE. If the Optionee's Service with the Participating Company Group terminates for any reason, except Disability or death, the Option, to the extent unexercised and exercisable by the Optionee on the date on which the Optionee's Service terminated, may be exercised by the Optionee within three (3) months after the date on which the Optionee's Service terminated, but in any event no later than the Option Expiration Date.

7.2 EXTENSION IF EXERCISE PREVENTED BY LAW. Notwithstanding the foregoing, if the exercise of the Option within the applicable time periods set forth in Section 7.1 is prevented by the provisions of Section 4.6, the Option shall remain exercisable until three (3) months after the date the Optionee is notified by the Company that the Option is exercisable, but in any event no later than the Option Expiration Date.

7.3 EXTENSION IF OPTIONEE SUBJECT TO SECTION 16(B). Notwithstanding the foregoing, if a sale, within the applicable time periods set forth in Section 7.1, of shares acquired upon the exercise of the Option would subject the Optionee to suit under Section 16(b) of the Exchange Act, the Option shall remain exercisable until the earliest to occur of (i) the tenth (10th) day following the date on which a sale of such shares by the Optionee would no longer be subject to such suit, (ii) the one hundred and ninetieth (190th) day after the Optionee's termination of Service, or (iii) the Option Expiration Date.

8. OWNERSHIP CHANGE AND TRANSFER OF CONTROL.

8.1 DEFINITIONS.

(a) An "OWNERSHIP CHANGE EVENT" shall be deemed to have occurred if any of the following occurs with respect to the Company:

(i) the direct or indirect sale or exchange in a single or series of related transactions by the stockholders of the Company of more than fifty percent (50%) of the voting stock of the Company;

(ii) a merger or consolidation in which the Company is a party;

(iii) the sale, exchange, or transfer of all or substantially all of the assets of the Company; or

(iv) a liquidation or dissolution of the Company.

(b) A "TRANSFER OF CONTROL" shall mean an Ownership Change Event or a series of related Ownership Change Events (collectively, the "TRANSACTION") wherein the stockholders of the Company immediately before the Transaction do not retain immediately after the Transaction, in substantially the

same proportions as their ownership of shares of the Company's voting stock immediately before the Transaction, direct or indirect beneficial ownership of more than fifty percent (50%) of the total combined voting power of the outstanding voting stock of the Company or the corporation or corporations to which the assets of the Company were transferred (the "TRANSFeree CORPORATION(S)"), as the case may be. For purposes of the preceding sentence, indirect beneficial ownership shall include, without limitation, an interest resulting from ownership of the voting stock of one or more corporations which, as a result of the Transaction, own the Company or the Transferee Corporation(s), as the case may be, either directly or through one or more subsidiary corporations. The Board shall have the right to determine whether multiple sales or exchanges of the voting stock of the Company or multiple Ownership Change Events are related, and its determination shall be final, binding and conclusive.

8.2 EFFECT OF TRANSFER OF CONTROL ON OPTION. In the event of a Transfer of Control, any unexercised portion of the Option shall be immediately exercisable and vested in full as of the date ten (10) days prior to the date of the Transfer of Control. Any exercise of the Option that was permissible solely by reason of this Section 8.2 shall be conditioned upon the consummation of the Transfer of Control. In addition, the surviving, continuing, successor, or purchasing corporation or parent corporation thereof, as the case may be (the "ACQUIRING CORPORATION"), may either assume the Company's rights and obligations under the Option or substitute for the Option a substantially equivalent option for the Acquiring Corporation's stock. The Option shall terminate and cease to be outstanding effective as of the date of the Transfer of Control to the extent that the Option is neither assumed or substituted for by the Acquiring Corporation in connection with the Transfer of Control nor exercised as of the date of the Transfer of Control. Notwithstanding the foregoing, shares acquired upon exercise of the Option prior to the Transfer of Control and any consideration received pursuant to the Transfer of Control with respect to such shares shall continue to be subject to all applicable provisions of this Option Agreement except as otherwise provided herein. Furthermore, notwithstanding the foregoing, if the corporation the stock of which is subject to the Option immediately prior to an Ownership Change Event described in Section 8.1(a)(i) constituting a Transfer of Control is the surviving or continuing corporation and immediately after such Ownership Change Event less than fifty percent (50%) of the total combined voting power of its voting stock is held by another corporation or by other corporations that are members of an affiliated group within the meaning of Section 1504(a) of the Code without regard to the provisions of Section 1504(b) of the Code, the Option shall not terminate.

9. ADJUSTMENTS FOR CHANGES IN CAPITAL STRUCTURE. In the event of any

stock dividend, stock split, reverse stock split, recapitalization, combination, reclassification, or similar change in the capital structure of the Company, appropriate adjustments shall be made in the number, Exercise Price and class of shares of stock subject to the Option. If a majority of the shares which are of the same class as the shares that are subject to the Option are exchanged for,

converted into, or otherwise become (whether or not pursuant to an Ownership Change Event) shares of another corporation (the "NEW SHARES"), the Board may unilaterally amend the Option to provide that the Option is exercisable for New Shares. In the event of any such amendment, the Number of Option Shares and the Exercise Price shall be adjusted in a fair and equitable manner, as determined by the Board, in its sole discretion. Notwithstanding the foregoing, any fractional share resulting from an adjustment pursuant to this Section 9 shall be rounded down to the nearest whole number, and in no event may the Exercise Price be decreased to an amount less than the par value, if any, of the stock subject to the Option.

10. RIGHTS AS A STOCKHOLDER. The Optionee shall have no rights as a

stockholder with respect to any shares covered by the Option until the date of the issuance of a certificate for the shares for which the Option has been exercised (as evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company). No adjustment shall be made for dividends, distributions or other rights for which the record date is prior to the date such certificate is issued, except as provided in Section 9.

11. LEGENDS. The Company may at any time place legends referencing any

applicable federal, state or foreign securities law restrictions on all certificates representing shares of stock subject to the provisions of this Option Agreement. The Optionee shall, at the request of the Company, promptly present to the Company any and all certificates representing shares acquired pursuant to the Option in the possession of the Optionee in order to carry out the provisions of this Section.

12. BINDING EFFECT. Subject to the restrictions on transfer set forth

herein, this Option Agreement shall inure to the benefit of and be binding upon the parties hereto and their respective heirs, executors, administrators, successors and assigns.

13. TERMINATION OR AMENDMENT. The Board may terminate or amend the Plan

or the Option at any time; provided, however, that no such termination or amendment may adversely affect the Option or any unexercised portion hereof without the consent of the Optionee unless such termination or amendment is necessary to comply with any applicable law or government regulation. No amendment or addition to this Option Agreement shall be effective unless in writing.

14. INTEGRATED AGREEMENT. This Option Agreement constitutes the entire

understanding and agreement of the Optionee and the Participating Company Group with respect to the subject matter contained herein, and there are no agreements, understandings, restrictions, representations, or warranties among the Optionee and the Participating Company Group with respect to such subject matter other

than those as set forth or provided for herein. To the extent contemplated herein, the provisions of this Option Agreement shall survive any exercise of the Option and shall remain in full force and effect.

15. APPLICABLE LAW. This Option Agreement shall be governed by the laws

of the State of Michigan as such laws are applied to agreements between Michigan residents entered into and to be performed entirely within the State of Michigan.

AASTROM BIOSCIENCES, INC.

By:_____

Title:_____

The Optionee represents that the Optionee is familiar with the terms and provisions of this Option Agreement and hereby accepts the Option subject to all of the terms and provisions thereof. The Optionee hereby agrees to accept as binding, conclusive and final all decisions or interpretations of the Board upon any questions arising under this Option Agreement.

OPTIONEE

Date:_____

than those as set forth or provided for herein. To the extent contemplated herein, the provisions of this Option Agreement shall survive any exercise of the Option and shall remain in full force and effect.

15. APPLICABLE LAW. This Option Agreement shall be governed by the laws -----
of the State of Michigan as such laws are applied to agreements between Michigan residents entered into and to be performed entirely within the State of Michigan.

AASTROM BIOSCIENCES, INC.

By:_____

Title:_____

The Optionee represents that the Optionee is familiar with the terms and provisions of this Option Agreement and hereby accepts the Option subject to all of the terms and provisions thereof. The Optionee hereby agrees to accept as binding, conclusive and final all decisions or interpretations of the Board upon any questions arising under this Option Agreement.

OPTIONEE

Date:_____

AASTROM BIOSCIENCES, INC.

1996 EMPLOYEE STOCK PURCHASE PLAN

1. ESTABLISHMENT, PURPOSE AND TERM OF PLAN.

1.1 ESTABLISHMENT. The Biosciences, Inc. 1996 Employee Stock Purchase Plan (the "Plan") is hereby established effective as of the effective date of the initial registration by the Company of its Stock under Section 12 of the Exchange Act (the "Effective Date").

1.2 PURPOSE. The purpose of the Plan to provide Eligible Employees of the Participating Company Group with an opportunity to acquire a proprietary interest in the Company through the purchase of Stock. The Company intends that the Plan shall qualify as an "employee stock purchase plan" under Section 423 of the Code (including any amendments or replacements of such section), and the Plan shall be so construed.

1.3 TERM OF PLAN. The Plan shall continue in effect until the earlier of its termination by the Board or the date on which all of the shares of Stock available for issuance under the Plan have been issued.

2. DEFINITIONS AND CONSTRUCTION.

2.1 DEFINITIONS. Any term not expressly defined in the Plan but defined for purposes of Section 423 of the Code shall have the same definition herein. Whenever used herein, the following terms shall have their respective meanings set forth below:

(a) "BOARD" means the Board of Directors of the Company. If one or more Committees have been appointed by the Board to administer the Plan, "Board" also means such Committee(s).

(b) "CODE" means the Internal Revenue Code of 1986, as amended, and any applicable regulations promulgated thereunder.

(c) "COMMITTEE" means a committee of the Board duly appointed to administer the Plan and having such powers as shall be specified by the Board. Unless the powers of the Committee have been specifically limited, the Committee shall have all of the powers of the Board granted herein, including, without limitation, the power to amend or terminate the Plan at any time, subject to the terms of the Plan and any applicable limitations imposed by law.

(d) "COMPANY" means Biosciences, Inc., a Michigan corporation, or any successor corporation thereto.

(e) "COMPENSATION" means, with respect to an Offering Period under the Plan, all amounts paid in cash in the forms of base salary, commissions, overtime, bonuses, annual awards, other incentive payments, shift premiums, and all other compensation paid in cash during such Offering Period before deduction for any contributions to any plan maintained by a Participating Company and described in Section 401(k) or Section 125 of the Code. Compensation shall not include reimbursements of expenses, allowances, long-term disability, workers' compensation or any amount deemed received without the actual transfer of cash or any amounts directly or indirectly paid pursuant to the Plan or any other stock purchase or stock option plan.

(f) "ELIGIBLE EMPLOYEE" means an Employee who meets the requirements set forth in Section 5 for eligibility to participate in the Plan.

(g) "EMPLOYEE" means any person treated as an employee (including an officer or a director who is also treated as an employee) in the records of a Participating Company and for purposes of Section 423 of the Code; provided, however, that neither service as a director nor payment of a director's fee shall be sufficient to constitute employment for purposes of the Plan.

(h) "EXCHANGE ACT" means the Securities Exchange Act of 1934, as amended.

(i) "FAIR MARKET VALUE" means, as of any date, if there is then a public market for the Stock, the closing price of a share of Stock (or the mean of the closing bid and asked prices of a share of Stock if the Stock is so reported instead) as reported on the National Association of Securities Dealers Automated Quotation ("NASDAQ") System, the NASDAQ National Market System or such other national or regional securities exchange or market system constituting the primary market for the Stock. If the relevant date does not fall on a day on which the Stock is trading on NASDAQ, the NASDAQ National Market System or other national or regional securities exchange or market system, the date on which the Fair Market Value shall be established shall be the last day on which the Stock was so traded prior to the relevant date, or such other appropriate day as shall be determined by the Board, in its sole discretion. If there is then no public market for the Stock, the Fair Market Value on any relevant date shall be as determined by the Board without regard to any restriction other than a restriction which, by its terms, will never lapse. Notwithstanding the foregoing, the Fair Market Value per share of Stock on the Effective Date shall be deemed to be the public offering price set forth in the final prospectus filed with the Securities and Exchange Commission in connection with the initial public offering of the Stock.

(j) "OFFERING" means an offering of Stock as provided in

Section 6.

(k) "OFFERING DATE" means, for any Offering Period, the first day of such Offering Period.

(l) "OFFERING PERIOD" means a period determined in accordance with Section 6.1.

(m) "PARENT CORPORATION" means any present or future "parent corporation" of the Company, as defined in Section 424(e) of the Code.

(n) "PARTICIPANT" means an Eligible Employee participating in the Plan.

(o) "PARTICIPATING COMPANY" means the Company or any Parent Corporation or Subsidiary Corporation which the Board determines should be included in the Plan. The Board shall have the sole and absolute discretion to determine from time to time what Parent Corporations or Subsidiary Corporations shall be Participating Companies.

(p) "PARTICIPATING COMPANY GROUP" means, at any point in time, the Company and all other corporations collectively which are then Participating Companies.

(q) "PURCHASE DATE" means, for any Purchase Period, the last day of such Purchase Period.

(r) "PURCHASE PERIOD" means a period determined in accordance with Section 6.2.

(s) "PURCHASE PRICE" means the price at which a share of Stock may be purchased pursuant to the Plan, as determined in accordance with Section 9.

(t) "PURCHASE RIGHT" means an option pursuant to the Plan to purchase such shares of Stock as provided in Section 8 which may or may not be exercised at the end of an Offering Period. Such option arises from the right of a Participant to withdraw such Participant's accumulated payroll deductions (if any) and terminate participation in the Plan or any Offering therein at any time during a Purchase Period.

(u) "STOCK" means the common stock, no par value, of the Company, as adjusted from time to time in accordance with Section 4.2.

(v) "SUBSIDIARY CORPORATION" means any present or future "subsidiary corporation" of the Company, as defined in Section 424(f) of the Code.

2.2 CONSTRUCTION. Captions and titles contained herein are for convenience only and shall not affect the meaning or interpretation of any provision of the Plan. Except when otherwise indicated by the context, the singular shall include the plural, the plural shall include the singular, and use of the term "or" shall include the conjunctive as well as the disjunctive.

3. ADMINISTRATION. The Plan shall be administered by the Board, including -----
any duly appointed Committee of the Board. All questions of interpretation of the Plan or of any Purchase Right shall be determined by the Board and shall be final and binding upon all persons having an interest in the Plan or such Purchase Right. Subject to the provisions of the Plan, the Board shall determine all of the relevant terms and conditions of Purchase Rights granted pursuant to the Plan; provided, however, that all Participants granted Purchase Rights pursuant to the Plan shall have the same rights and privileges within the meaning of Section 423(b)(5) of the Code. All expenses incurred in connection with the administration of the Plan shall be paid by the Company.

4. SHARES SUBJECT TO PLAN.

4.1 MAXIMUM NUMBER OF SHARES ISSUABLE. Subject to adjustment as provided in Section 4.2, the maximum aggregate number of shares of Stock that may be issued under the Plan shall be two hundred fifty thousand (250,000) (on a post-split basis following the two-for-three reverse stock split of the Stock approved by the Board on April 30, 1996) and shall consist of authorized but unissued or reacquired shares of the Stock, or any combination thereof. If an outstanding Purchase Right for any reason expires or is terminated or canceled, the shares of Stock allocable to the unexercised portion of such Purchase Right shall again be available for issuance under the Plan.

4.2 ADJUSTMENTS FOR CHANGES IN CAPITAL STRUCTURE. In the event of any stock dividend, stock split, reverse stock split, recapitalization, combination, reclassification or similar change in the capital structure of the Company, or in the event of any merger (including a merger effected for the purpose of changing the Company's domicile), sale of assets or other reorganization in which the Company is a party, appropriate adjustments shall be made in the number and class of shares subject to the Plan, to the Per Offering Share Limit set forth in Section 8.1 and to each Purchase Right and in the Purchase Price.

5. ELIGIBILITY.

5.1 EMPLOYEES ELIGIBLE TO PARTICIPATE. Any Employee of a Participating Company is eligible to participate in the Plan except the following:

(a) Employees who are customarily employed by the Participating Company Group for twenty (20) hours or less per week;

(b) Employees who are customarily employed by the Participating Company Group for not more than five (5) months in any calendar year; and

(c) Employees who own or hold options to purchase or who, as a result of participation in the Plan, would own or hold options to purchase, stock of the Company or of any Parent Corporation or Subsidiary Corporation possessing five percent (5%) or more of the total combined voting power or value of all classes of stock of such corporation within the meaning of Section 423(b)(3) of the Code.

5.2 LEASED EMPLOYEES EXCLUDED. Notwithstanding anything herein to the contrary, any individual performing services for a Participating Company solely through a leasing agency or employment agency shall not be deemed an "Employee" of such Participating Company.

6. OFFERINGS.

6.1 OFFERING PERIODS. Except as otherwise set forth below, the Plan shall be implemented by sequential Offerings of approximately twenty-four (24) months duration (an "OFFERING PERIOD"); provided, however that the first Offering Period shall commence on the Effective Date and end on August 31, 1998 (the "INITIAL OFFERING PERIOD"). Subsequent Offerings shall commence on the first days of March and September of each year and end on the last days of the second February and August, respectively, occurring thereafter. Notwithstanding the foregoing, the Board may establish a different term for one or more Offerings or different commencing or ending dates for such Offerings; provided, however, that no Offering may exceed a term of twenty-seven (27) months. An Employee who becomes an Eligible Employee after an Offering Period has commenced shall not be eligible to participate in such Offering but may participate in any subsequent Offering provided such Employee is still an Eligible Employee as of the commencement of any such subsequent Offering. Eligible Employees may not participate in more than one Offering at a time. In the event the first or last day of an Offering Period is not a business day, the Company shall specify the business day that will be deemed the first or last day, as the case may be, of the Offering Period.

6.2 PURCHASE PERIODS. Each Offering Period shall consist of four (4) consecutive purchase periods of approximately six (6) months duration (individually, a "PURCHASE PERIOD"). The Purchase Period commencing on the Offering Date of the Initial Offering Period shall end on February 28, 1997. A Purchase Period commencing on the first day of March shall end on the last day of the next following August. A Purchase Period commencing on the first day of September shall end on the last day of the next following February. Notwithstanding the foregoing, the Board may establish a different term for one or more Purchase Periods or different commencing or ending dates for such Purchase

Periods. In the event the first or last day of a Purchase Period is not a business day, the Company shall specify the business day that will be deemed the first or last day, as the case may be, of the Purchase Period.

6.3 GOVERNMENTAL APPROVAL; STOCKHOLDER APPROVAL. Notwithstanding any other provision of the Plan to the contrary, any Purchase Right granted pursuant to the Plan shall be subject to (a) obtaining all necessary governmental approvals or qualifications of the sale or issuance of the Purchase Rights or the shares of Stock and (b) obtaining stockholder approval of the Plan. Notwithstanding the foregoing, stockholder approval shall not be necessary in order to grant any Purchase Right granted in the Plan's Initial Offering Period; provided, however, that the exercise of any such Purchase Right shall be subject to obtaining stockholder approval of the Plan.

7. PARTICIPATION IN THE PLAN.

7.1 INITIAL PARTICIPATION. An Eligible Employee shall become a Participant on the first Offering Date after satisfying the eligibility requirements of Section 5 and delivering to the Company's payroll office or other office designated by the Company not later than the close of business for such office on the last business day before such Offering Date (the "SUBSCRIPTION DATE") a subscription agreement indicating the Employee's election to participate in the Plan and authorizing payroll deductions. An Eligible Employee who does not deliver a subscription agreement to the Company's payroll or other designated office on or before the Subscription Date shall not participate in the Plan for that Offering Period or for any subsequent Offering Period unless such Employee subsequently enrolls in the Plan by filing a subscription agreement with the Company by the Subscription Date for such subsequent Offering Period. The Company may, from time to time, change the Subscription Date as deemed advisable by the Company in its sole discretion for proper administration of the Plan.

7.2 CONTINUED PARTICIPATION. A Participant shall automatically participate in the Offering Period commencing immediately after the final Purchase Date of each Offering Period in which the Participant participates until such time as such Participant (a) ceases to be an Eligible Employee, (b) withdraws from the Plan pursuant to Section 14.2 or (c) terminates employment as provided in Section 15. If a Participant automatically may participate in a subsequent Offering Period pursuant to this Section 7.2, then the Participant is not required to file any additional subscription agreement for such subsequent Offering Period in order to continue participation in the Plan. However, a Participant may file a subscription agreement with respect to a subsequent Offering Period if the Participant desires to change any of the Participant's elections contained in the Participant's then effective subscription agreement.

8. RIGHT TO PURCHASE SHARES.

8.1 PURCHASE RIGHT. Except as set forth below, during an Offering Period each Participant in such Offering Period shall have a Purchase Right consisting of the right to purchase that number of whole shares of Stock arrived at by dividing Fifty Thousand Dollars (\$50,000) by the Fair Market Value of a share of Stock on the Offering Date of such Offering Period; provided, however, that such number shall not exceed five thousand (5,000) shares (the "Per Offering Share Limit"). Shares of Stock may only be purchased through a Participant's payroll deductions pursuant to Section 10.

8.2 PRO RATA ADJUSTMENT OF PURCHASE RIGHT. Notwithstanding the foregoing, if the Board shall establish an Offering Period of less than twenty-three and one-half (23 1/2) months or more than twenty-four and one-half (24 1/2) months in duration, (a) the dollar amount in Section 8.1 shall be determined by multiplying \$2,083.33 by the number of months in the Offering Period and rounding to the nearest whole dollar, and (b) the Per Offering Share Limit shall be determined by multiplying 208.33 shares by the number of months in the Offering Period and rounding to the nearest whole share. For purposes of the preceding sentence, fractional months shall be rounded to the nearest whole month.

9. PURCHASE PRICE. The Purchase Price at which each share of Stock may be

acquired in a given Offering Period pursuant to the exercise of all or any portion of a Purchase Right granted under the Plan shall be set by the Board; provided, however, that the Purchase Price shall not be less than eighty-five percent (85%) of the lesser of (a) the Fair Market Value of a share of Stock on the Offering Date of the Offering Period, or (b) the Fair Market Value of a share of Stock on the Purchase Date of the Offering Period. Unless otherwise provided by the Board prior to the commencement of an Offering Period, the Purchase Price for that Offering Period shall be eighty-five percent (85%) of the lesser of (a) the Fair Market Value of a share of Stock on the Offering Date of the Offering Period, or (b) the Fair Market Value of a share of Stock on the Purchase Date of the Offering Period.

10. ACCUMULATION OF PURCHASE PRICE THROUGH PAYROLL DEDUCTION. Shares of

Stock which are acquired pursuant to the exercise of all or any portion of a Purchase Right for an Offering Period may be paid for only by means of payroll deductions from the Participant's Compensation accumulated during the Offering Period. Except as set forth below, the amount of Compensation to be deducted from a Participant's Compensation during each pay period shall be determined by the Participant's subscription agreement.

10.1 COMMENCEMENT OF PAYROLL DEDUCTIONS. Payroll deductions shall commence on the first payday following the Offering Date and shall continue to the end of the Offering Period unless sooner altered or terminated as provided in the Plan.

10.2 LIMITATIONS ON PAYROLL DEDUCTIONS. The amount of payroll deductions with respect to the Plan for any Participant during any pay period shall be in one percent (1%) increments not to exceed ten percent (10%) of the Participant's Compensation for such pay period. Notwithstanding the foregoing, the Board may change the limits on payroll deductions effective as of a future Offering Date, as determined by the Board. Amounts deducted from Compensation shall be reduced by any amounts contributed by the Participant and applied to the purchase of Company stock pursuant to any other employee stock purchase plan qualifying under Section 423 of the Code.

10.3 ELECTION TO DECREASE OR STOP PAYROLL DEDUCTIONS. During an Offering Period, a Participant may elect to decrease the amount deducted or stop deductions from his or her Compensation by filing an amended subscription agreement with the Company on or before the "Change Notice Date." The "CHANGE NOTICE DATE" shall initially be the seventh (7th) day prior to the end of the first pay period for which such election is to be effective; however, the Company may change such Change Notice Date from time to time. A Participant may not elect to increase the amount deducted from the Participant's Compensation during an Offering Period.

10.4 PARTICIPANT ACCOUNTS. Individual Plan accounts shall be maintained for each Participant. All payroll deductions from a Participant's Compensation shall be credited to such account and shall be deposited with the general funds of the Company. All payroll deductions received or held by the Company may be used by the Company for any corporate purpose.

10.5 NO INTEREST PAID. Interest shall not be paid on sums deducted from a Participant's Compensation pursuant to the Plan.

10.6 COMPANY ESTABLISHED PROCEDURES. The Company may, from time to time, establish or change (a) a minimum required payroll deduction amount for participation in an Offering, (b) limitations on the frequency or number of changes in the rate of payroll deduction during an Offering, (c) an exchange ratio applicable to amounts withheld in a currency other than U.S. dollars, (d) payroll deduction in excess of or less than the amount designated by a Participant in order to adjust for delays or mistakes in the Company's processing of subscription agreements, (e) the date(s) and manner by which the Fair Market Value of a share of Stock is determined for purposes of administration of the Plan, or (f) such other limitations or procedures as deemed advisable by the Company in the Company's sole discretion which are consistent with the Plan and in accordance with the requirements of Section 423 of the Code.

11. PURCHASE OF SHARES. -----

11.1 EXERCISE OF PURCHASE RIGHT. On each Purchase Date of an Offering Period, each Participant who has not withdrawn from the Offering or

whose participation in the Offering has not terminated on or before such Purchase Date shall automatically acquire pursuant to the exercise of the Participant's Purchase Right the number of whole shares of Stock arrived at by dividing the total amount of the Participant's accumulated payroll deductions for the Purchase Period by the Purchase Price; provided, however, in no event shall the number of shares purchased by the Participant during an Offering Period exceed the number of shares subject to the Participant's Purchase Right. No shares of Stock shall be purchased on a Purchase Date on behalf of a Participant whose participation in the Offering or the Plan has terminated on or before such Purchase Date.

11.2 RETURN OF CASH BALANCE. Any cash balance remaining in the Participant's Plan account shall be refunded to the Participant as soon as practicable after the Purchase Date. In the event the cash to be returned to a Participant pursuant to the preceding sentence is an amount less than the amount necessary to purchase a whole share of Stock, the Company may establish procedures whereby such cash is maintained in the Participant's Plan account and applied toward the purchase of shares of Stock in the subsequent Purchase Period or Offering Period.

11.3 TAX WITHHOLDING. At the time a Participant's Purchase Right is exercised, in whole or in part, or at the time a Participant disposes of some or all of the shares of Stock he or she acquires under the Plan, the Participant shall make adequate provision for the foreign, federal, state and local tax withholding obligations of the Participating Company Group, if any, which arise upon exercise of the Purchase Right or upon such disposition of shares, respectively. The Participating Company Group may, but shall not be obligated to, withhold from the Participant's compensation the amount necessary to meet such withholding obligations.

11.4 EXPIRATION OF PURCHASE RIGHT. Any portion of a Participant's Purchase Right remaining unexercised after the end of the Offering Period to which such Purchase Right relates shall expire immediately upon the end of such Offering Period.

12. MARKET STAND-OFF PERIOD. No Participant shall, for a period of 180 ----- days following the Purchase Date upon which a share of Stock is acquired, directly or indirectly sell, offer to sell, contract to sell (including, without limitation, any short sale), grant any option to purchase or otherwise transfer or dispose (other than to donees who agree to be similarly bound) of such share of Stock. The restriction on transfer of this Section 12 shall terminate immediately upon a Transfer of Control, as defined in Section 16.

13. LIMITATIONS ON PURCHASE OF SHARES; RIGHTS AS A STOCKHOLDER.

13.1 FAIR MARKET VALUE LIMITATION. Notwithstanding any other provision of the Plan, no Participant shall be entitled to purchase shares of Stock

under the Plan (or any other employee stock purchase plan which is intended to meet the requirements of Section 423 of the Code sponsored by the Company or a Parent Corporation or Subsidiary Corporation at a rate which exceeds \$25,000 in Fair Market Value, which Fair Market Value is determined for shares purchased during a given Offering Period as of the Offering Date for such Offering Period (or such other limit as may be imposed by the Code), for each calendar year in which the Participant participates in the Plan (or any other employee stock purchase plan described in this sentence).

13.2 PRO RATA ALLOCATION. In the event the number of shares of Stock which might be purchased by all Participants in the Plan exceeds the number of shares of Stock available in the Plan, the Company shall make a pro rata allocation of the remaining shares in as uniform a manner as shall be practicable and as the Company shall determine to be equitable.

13.3 RIGHTS AS A STOCKHOLDER AND EMPLOYEE. A Participant shall have no rights as a stockholder by virtue of the Participant's participation in the Plan until the date of the issuance of a stock certificate for the shares of Stock being purchased pursuant to the exercise of the Participant's Purchase Right. No adjustment shall be made for cash dividends or distributions or other rights for which the record date is prior to the date such stock certificate is issued. Nothing herein shall confer upon a Participant any right to continue in the employ of the Participating Company Group or interfere in any way with any right of the Participating Company Group to terminate the Participant's employment at any time.

14. WITHDRAWAL.

14.1 WITHDRAWAL FROM AN OFFERING. A Participant may withdraw from an Offering by signing and delivering to the Company's payroll or other designated office a written notice of withdrawal on a form provided by the Company for such purpose. Such withdrawal may be elected at any time prior to the end of an Offering Period; provided, however, if a Participant withdraws after the Purchase Date for a Purchase Period of an Offering, the withdrawal shall not affect shares of Stock acquired by the Participant in such Purchase Period. Unless otherwise indicated, withdrawal from an Offering shall not result in a withdrawal from the Plan or any succeeding Offering therein. By withdrawing from an Offering effective as of the close of a given Purchase Date, a Participant may have shares of Stock purchased on such Purchase Date and immediately commence participation in the new Offering commencing immediately after such Purchase Date. A Participant is prohibited from again participating in an Offering at any time following withdrawal from such Offering. The Company may impose, from time to time, a requirement that the notice of withdrawal be on file with the Company's payroll office or other designated office for a reasonable period prior to the effectiveness of the Participant's withdrawal from an Offering.

14.2 WITHDRAWAL FROM THE PLAN. A Participant may withdraw from the Plan by signing and delivering to the Company's payroll office or other designated office a written notice of withdrawal on a form provided by the Company for such purpose. Withdrawals made after a Purchase Date shall not affect shares of Stock acquired by the Participant on such Purchase Date. In the event a Participant voluntarily elects to withdraw from the Plan, the Participant may not resume participation in the Plan during the same Offering Period, but may participate in any subsequent Offering under the Plan by again satisfying the requirements of Sections 5 and 7.1. The Company may impose, from time to time, a requirement that the notice of withdrawal be on file with the Company's payroll office or other designated office for a reasonable period prior to the effectiveness of the Participant's withdrawal from the Plan.

14.3 RETURN OF PAYROLL DEDUCTIONS. Upon a Participant's withdrawal from an Offering or the Plan pursuant to Sections 14.1 or 14.2, respectively, the Participant's accumulated payroll deductions which have not been applied toward the purchase of shares of Stock shall be returned as soon as practicable after the withdrawal, without the payment of any interest, to the Participant, and the Participant's interest in the Offering or the Plan, as applicable, shall terminate. Such accumulated payroll deductions may not be applied to any other Offering under the Plan.

14.4 AUTOMATIC WITHDRAWAL FROM AN OFFERING. If the Fair Market Value of a share of Stock on a Purchase Date of an Offering (other than the final Purchase Date of such Offering) is less than the Fair Market Value of a share of Stock on the Offering Date for such Offering, then every Participant shall automatically (a) be withdrawn from such Offering at the close of such Purchase Date and after the acquisition of shares of Stock for such Purchase Period and (b) be enrolled in the Offering commencing on the first business day subsequent to such Purchase Period. A Participant may elect not to be automatically withdrawn from an Offering Period pursuant to this Section 14.4 by delivering to the Company not later than the close of business on the last day before the Purchase Date a written notice indicating such election.

15. TERMINATION OF EMPLOYMENT OR ELIGIBILITY. Termination of a

Participant's employment with a Participating Company for any reason, including retirement, disability or death or the failure of a Participant to remain an Eligible Employee, shall terminate the Participant's participation in the Plan immediately. In such event, the payroll deductions credited to the Participant's Plan account since the last Purchase Date shall, as soon as practicable, be returned to the Participant or, in the case of the Participant's death, to the Participant's legal representative, and all of the Participant's rights under the Plan shall terminate. Interest shall not be paid on sums returned to a Participant pursuant to this Section 15. A Participant whose participation has been so terminated may again become eligible to participate in the Plan by again satisfying the requirements of Sections 5 and 7.1.

16. TRANSFER OF CONTROL.

16.1 DEFINITIONS.

(a) An "OWNERSHIP CHANGE EVENT" shall be deemed to have occurred if any of the following occurs with respect to the Company: (i) the direct or indirect sale or exchange in a single or series of related transactions by the stockholders of the Company of more than fifty percent (50%) of the voting stock of the Company; (ii) a merger or consolidation in which the Company a party; (iii) the sale, exchange, or transfer of all or substantially all of the assets of the Company; or (iv) a liquidation or dissolution of the Company.

(b) A "TRANSFER OF CONTROL" shall mean an Ownership Change Event or a series of related Ownership Change Events (collectively, the "TRANSACTION") wherein the stockholders of the Company immediately before the Transaction do not retain immediately after the Transaction, in substantially the same proportions as their ownership of shares of the Company's voting stock immediately before the Transaction, direct or indirect beneficial ownership of more than fifty percent (50%) of the total combined voting power of the outstanding voting stock of the Company or the corporation or corporations to which the assets of the Company were transferred (the "TRANSFEREE CORPORATION(S)"), as the case may be. For purposes of the preceding sentence, indirect beneficial ownership shall include, without limitation, an interest resulting from ownership of the voting stock of one or more corporations which, as a result of the Transaction, own the Company or the Transferee Corporation(s), as the case may be, either directly or through one or more subsidiary corporations. The Board shall have the right to determine whether multiple sales or exchanges of the voting stock of the Company or multiple Ownership Change Events are related, and its determination shall be final, binding and conclusive.

16.2 EFFECT OF TRANSFER OF CONTROL ON PURCHASE RIGHTS. In the event of a Transfer of Control, the surviving, continuing, successor, or purchasing corporation or parent corporation thereof, as the case may be (the "ACQUIRING

CORPORATION"), may assume the Company's rights and obligations under the Plan or substitute substantially equivalent Purchase Rights for stock of the Acquiring Corporation. If the Acquiring Corporation elects not to assume or substitute for the outstanding Purchase Rights, the Board may, in its sole discretion and notwithstanding any other provision herein to the contrary, adjust the Purchase Date of the then current Purchase Period to a date on or before the date of the Transfer of Control, but shall not adjust the number of shares of Stock subject to any Purchase Right. All Purchase Rights which are neither assumed or substituted for by the Acquiring Corporation in connection with the Transfer of Control nor exercised as of the date of the Transfer of Control shall terminate and cease to be outstanding effective as of the date of the Transfer of Control. Notwithstanding the foregoing, if the corporation the stock of which is subject to the outstanding Purchase Rights immediately prior to an Ownership Change Event described in Section 16.1(a)(i) constituting a Transfer of Control is the surviving or continuing corporation and immediately after such Ownership Change Event less than fifty percent (50%) of the total combined voting power of its voting stock is held by another corporation or by other corporations that are members of an affiliated group within the meaning of section 1504(a) of the Code without regard to the provisions of section 1504(b) of the Code, the outstanding Purchase Rights shall not terminate unless the Board otherwise provides in its sole discretion.

17. NONTRANSFERABILITY OF PURCHASE RIGHTS. A Purchase Right may not be

transferred in any manner otherwise than by will or the laws of descent and distribution and shall be exercisable during the lifetime of the Participant only by the Participant. The Company, in its absolute discretion, may impose such restrictions on the transferability of the shares purchasable upon the exercise of a Purchase Right as it deems appropriate and any such restriction shall be set forth in the respective subscription agreement and may be referred to on the certificates evidencing such shares.

18. REPORTS. Each Participant who exercised all or part of his or her

Purchase Right for a Purchase Period shall receive, as soon as practicable after the Purchase Date of such Purchase Period, a report of such Participant's Plan account setting forth the total payroll deductions accumulated, the number of shares of Stock purchased, the Purchase Price for such shares, the date of purchase and the remaining cash balance to be refunded or retained in the Participant's Plan account pursuant to Section 11.2, if any. Each Participant shall be provided information concerning the Company equivalent to that information generally made available to the Company's common stockholders.

19. RESTRICTION ON ISSUANCE OF SHARES. The issuance of shares under the

Plan shall be subject to compliance with all applicable requirements of foreign, federal or state law with respect to such securities. A Purchase Right may not be exercised if the issuance of shares upon such exercise would constitute a violation of any applicable foreign, federal or state securities laws or other law or regulations. In addition, no Purchase Right may be exercised unless (a)
a

registration statement under the Securities Act of 1933, as amended, shall at the time of exercise of the Purchase Right be in effect with respect to the shares issuable upon exercise of the Purchase Right, or (b) in the opinion of legal counsel to the Company, the shares issuable upon exercise of the Purchase Right may be issued in accordance with the terms of an applicable exemption from the registration requirements of said Act. The inability of the Company to obtain from any regulatory body having jurisdiction the authority, if any, deemed by the Company's legal counsel to be necessary to the lawful issuance and sale of any shares under the Plan shall relieve the Company of any liability in respect of the failure to issue or sell such shares as to which such requisite authority shall not have been obtained. As a condition to the exercise of a Purchase Right, the Company may require the Participant to satisfy any qualifications that may be necessary or appropriate, to evidence compliance with any applicable law or regulation, and to make any representation or warranty with respect thereto as may be requested by the Company.

20. LEGENDS. The Company may at any time place legends or other

identifying symbols referencing any applicable foreign, federal or state securities law restrictions or any provision convenient in the administration of the Plan on some or all of the certificates representing shares of Stock issued under the Plan. The Participant shall, at the request of the Company, promptly present to the Company any and all certificates representing shares acquired pursuant to a Purchase Right in the possession of the Participant in order to carry out the provisions of this Section. Unless otherwise specified by the Company, legends placed on such certificates may include but shall not be limited to the following:

"THE SHARES EVIDENCED BY THIS CERTIFICATE WERE ISSUED BY THE CORPORATION TO THE REGISTERED HOLDER UPON THE PURCHASE OF SHARES UNDER AN EMPLOYEE STOCK PURCHASE PLAN AS DEFINED IN SECTION 423 OF THE INTERNAL REVENUE CODE OF 1986, AS AMENDED. THE TRANSFER AGENT FOR THE SHARES EVIDENCED HEREBY SHALL NOTIFY THE CORPORATION IMMEDIATELY OF ANY TRANSFER OF THE SHARES BY THE REGISTERED HOLDER HEREOF MADE ON OR BEFORE _____, 19___. THE REGISTERED HOLDER SHALL HOLD ALL SHARES PURCHASED UNDER THE PLAN IN THE REGISTERED HOLDER'S NAME (AND NOT IN THE NAME OF ANY NOMINEE) PRIOR TO THIS DATE."

"THE SHARES EVIDENCED BY THIS CERTIFICATE WERE ISSUED BY THE CORPORATION TO THE REGISTERED HOLDER UPON THE PURCHASE OF SHARES UNDER AN EMPLOYEE STOCK PURCHASE PLAN, PURSUANT TO WHICH THE SHARES MAY NOT BE SOLD, TRANSFERRED, OR DISPOSED OF (OTHER THAN TO DONEES WHO AGREE TO BE SIMILARLY BOUND) UNTIL _____, 19__."

21. NOTIFICATION OF SALE OF SHARES. The Company may require the

Participant to give the Company prompt notice of any disposition of shares

acquired by exercise of a Purchase Right within two years from the date of granting such Purchase Right or one year from the date of exercise of such Purchase Right. The Company may require that until such time as a Participant disposes of shares acquired upon exercise of a Purchase Right, the Participant shall hold all such shares in the Participant's name (and not in the name of any nominee) until the lapse of the time periods with respect to such Purchase Right referred to in the preceding sentence. The Company may direct that the certificates evidencing shares acquired by exercise of a Purchase Right refer to such requirement to give prompt notice of disposition.

22. AMENDMENT OR TERMINATION OF THE PLAN. The Board may at any time amend

or terminate the Plan, except that (a) such termination shall not affect Purchase Rights previously granted under the Plan, except as permitted under the Plan, and (b) no amendment may adversely affect a Purchase Right previously granted under the Plan (except to the extent permitted by the Plan or as may be necessary to qualify the Plan as an employee stock purchase plan pursuant to Section 423 of the Code or to obtain qualification or registration of the shares of Stock under applicable foreign, federal or state securities laws). In addition, an amendment to the Plan must be approved by the stockholders of the Company within twelve (12) months of the adoption of such amendment if such amendment would authorize the sale of more shares than are authorized for issuance under the Plan or would change the definition of the corporations that may be designated by the Board as Participating Companies.

IN WITNESS WHEREOF, the undersigned Secretary of the Company certifies that the foregoing AASTROM Biosciences, Inc. 1996 Employee Stock Purchase Plan was duly adopted by the Board of Directors of the Company on April 30, 1996.

/s/ Todd E. Simpson

Todd E. Simpson, Secretary

AASTROM BIOSCIENCES, INC.
1996 EMPLOYEE STOCK PURCHASE PLAN
SUBSCRIPTION AGREEMENT

☐ Original Application

☐ Change in Percentage of Payroll Deductions

I hereby elect to participate in the 1996 Employee Stock Purchase Plan (the "Plan") of AASTROM Biosciences, Inc. (the "COMPANY") and subscribe to purchase shares of the Company's common stock as determined in accordance with the terms of the Plan.

I hereby authorize payroll deductions in the amount of _____ percent (in 1% increments not to exceed 10%) of my "COMPENSATION" (as defined in the Plan) from each paycheck throughout the "OFFERING PERIOD" (as defined in the Plan) in accordance with the terms of the Plan. I understand that these payroll deductions will be accumulated for the purchase of shares of common stock of the Company at the applicable purchase price determined in accordance with the Plan. I further understand that, except as otherwise set forth in the Plan, shares will be purchased for me automatically on the last day of each Purchase Period unless I withdraw from the Plan or from the Offering by giving written notice to the Company or unless I terminate employment.

I further understand that I will automatically participate in each subsequent Offering which commences immediately after the last day of an Offering in which I am participating under the Plan until such time as I file with the Company a notice of withdrawal from the Plan on such form as may be established from time to time by the Company or I terminate employment.

Shares purchased for me under the Plan should be issued in the name set forth below. (I understand that shares may be issued either in my name alone or together with my spouse as community property or in joint tenancy.)

NAME: _____

ADDRESS: _____

MY SOCIAL SECURITY NUMBER: _____

I hereby authorize withholding from my compensation in order to satisfy the foreign, federal, state and local tax withholding obligations, if any, which may arise upon my purchase of shares under the Plan and/or upon my disposition of shares I acquired under the Plan. I hereby agree that until I dispose of the shares, unless otherwise permitted by the Company, I will hold all shares I acquire under the Plan in the name entered above (and not in the name of any nominee) for at least two (2) years from the first day of the Offering Period in which, and at least one (1) year from the Purchase Date on which, I acquired such shares. I further agree that I will promptly notify the Chief Financial Officer of the Company in writing of any transfer of such shares prior to the end of the periods referred to in the preceding sentence.

I am familiar with the provisions of the Plan and hereby agree to participate in the Plan subject to all of the provisions thereof. I understand that any shares purchased under the Plan are subject to a 180-day "market stand-off" period, as provided in the Plan. I understand that the Board of Directors of the Company reserves the right to amend the Plan and my right to purchase stock under the Plan as may be necessary to qualify the Plan as an employee stock purchase plan as defined in section 423 of the Internal Revenue Code of 1986, as amended, or to obtain qualification or registration of the Company's common stock to be issued out of the Plan under applicable foreign, federal and state securities laws. I understand that the effectiveness of this subscription agreement is dependent upon my eligibility to participate in the Plan.

Date: _____ Signature: _____

Name Printed: _____

AASTROM BIOSCIENCES, INC.
1996 EMPLOYEE STOCK PURCHASE PLAN
NOTICE OF WITHDRAWAL

I hereby elect to withdraw from the current offering (the "CURRENT OFFERING") of the common stock of AASTROM Biosciences, Inc. (the "COMPANY") under the Company's 1996 Employee Stock Purchase Plan (the "PLAN").

MAKE ONE ELECTION UNDER SECTION A AND ONE ELECTION UNDER SECTION B:

A. Current Offering. As to my participation in the current purchase period

(the "Current Purchase Period") of the Current Offering under the Plan, I elect as follows (check one):

_____ 1. I elect to terminate my participation in the Current Purchase Period immediately.

I hereby request that all payroll deductions credited to my account under the Plan (if any) not previously used to purchase shares under the Plan shall not be used to purchase shares on the last day of the

Current Purchase Period. Instead, I request that all such amounts be paid to me as soon as practicable. I understand that this election immediately terminates my interest in the Current Offering.

_____ 2. I elect to terminate my participation in the Current Offering following my purchase of shares on the last day of the Current Purchase Period.

I hereby request that all payroll deductions credited to my account under the Plan (if any) not previously used to purchase shares under the Plan shall be used to purchase shares on the last day of the Current Purchase Period. I understand that this election will terminate my interest in the Current Offering immediately following such purchase. I request that any cash balance remaining in my account under the Plan after my purchase of shares be returned to me as soon as practicable.

I understand that if no election is made as to participation in the Current Offering under the Plan, I will be deemed to have elected to participate in the Current Offering.

B. Future Offerings. As to my participation in future offerings of common

stock under the Plan, I elect as follows (check one):

_____ 1. I elect to participate in future offerings under the Plan.

I understand that by making this election I will participate in the next offering under the Plan commencing subsequent to the Current Offering, and in each subsequent offering commencing immediately after the last day of an offering in which I participate, until such time as I elect to withdraw from the Plan or from any such subsequent offering.

_____ 2. I elect not to participate in future offerings under the Plan.

I understand that by making this election I terminate my interest in the Plan and that no further payroll deductions will be made unless I elect in accordance with the Plan to become a participant in another offering under the Plan.

I understand that if no election is made as to participation in future offerings under the Plan, I will be deemed to have elected to participate in such future offerings.

Date: _____ Signature: _____

Name Printed: _____

Employment Agreement

This Employment Agreement (the "Agreement") is entered into as of _____ 1996, by and between AASTROM BIOSCIENCES, INC., a Michigan corporation ("Employer") and [name] ("Employee").

NOW, THEREFORE, the parties agree as follows:

1. EMPLOYMENT Employer hereby engages Employee, and Employee hereby accepts such engagement, upon the terms and conditions set forth herein.

2. DUTIES Employee is engaged as an [position]. Employee shall perform faithfully and diligently the duties customarily performed by persons in the position for which employee is engaged, together with such other reasonable and appropriate duties as Employer shall designate from time to time. Employee shall devote Employee's full business time and efforts to the rendition of such services and to the performance of such duties. As a full-time employee of Employer, Employee shall not be entitled to provide consulting services or other business or scientific services to any other party, without the prior written consent of Employer.

3. COMPENSATION

3.1 BASE SALARY During the term of this Agreement, as compensation for the proper and satisfactory performance of all duties to be performed by Employee hereunder, Employer shall pay Employee at an annual salary rate of [salary written] Dollars (\$[salary]), payable in arrears in equal bi-weekly installments, less required deductions for state and federal withholding tax, Social Security and all other employee taxes and payroll deductions. The base salary shall be subject to review and adjustment on an annual basis.

4. TERM

4.1 COMMENCEMENT The employment relationship pursuant to this Agreement shall commence [start_date].

4.2 TERMINATION AT WILL Although Employer and Employee anticipate a long and mutually rewarding employment relationship, either party may terminate this Agreement, without cause, upon fourteen (14) days' prior written notice delivered to the other. It is expressly understood and agreed that the employment relationship is "at will", and with no agreement for employment for any specified term, and with no agreement for employment for so long as Employee performs satisfactorily. Provided, however, before Employer exercises this right of termination at will, Employer shall first either (i) discuss with Employee the needs of Employer and why Employee no longer meets those needs, or (ii) discuss with Employee any concerns or dissatisfactions which Employer has with Employee's performance, and give to Employee a reasonable

opportunity to remedy those concerns or dissatisfactions, to the reasonable satisfaction of Employer.

4.3 TERMINATION FOR CAUSE Either party may terminate this employment relationship immediately upon notice to the other party in the event of any good cause, such as a default, dishonesty, neglect of duties, failure to perform by the other party, or death or disability of Employee.

4.4 PAYMENT OF COMPENSATION UPON TERMINATION Upon termination for cause, Employee shall be entitled to the compensation set forth as "base salary" herein, prorated to the effective date of such termination as full compensation for any and all claims of Employee under this Agreement.

5. FRINGE BENEFITS

5.1 CUSTOMARY FRINGE BENEFITS Employee shall be entitled to such fringe benefits as Employer customarily makes available to employees of Employer engaged in the same or similar position as Employee ("Fringe Benefits"). Such Fringe Benefits may include vacation leave, sick leave, and health insurance coverage. Employer reserves the right to change the Fringe Benefits on a prospective basis, at any time, effective upon delivery of written notice to Employee.

5.2 ACCUMULATION Employee shall not earn and accumulate unused vacation in excess of Fifteen (15) days. Employee shall not earn and accumulate sick leave or other Fringe Benefits in excess of an unused amount equal to twice the amount earned for one year. Further, Employee shall not be entitled to receive payments in lieu of said Fringe Benefits, other than for unused vacation leave earned and accumulated at the time the employment relationship terminates.

6. INVENTIONS, TRADE SECRETS AND CONFIDENTIALITY

6.1 DEFINITIONS

6.1.1 Invention Defined. As used herein "Invention" means inventions, discoveries, concepts, and ideas, whether patentable or copyrightable or not, including but not limited to processes, methods, formulas, techniques, materials, devices, designs, programs (including computer programs), computer graphics, apparatus, products, as well as improvements thereof or know-how related thereto, relating to any present or anticipated business or activities of Employer.

6.1.2 Trade Secret Defined. As used herein "Trade Secret" means, without limitation, any document or information relating to Employer's products, processes or services, including documents and information relating to Inventions, and to the research, development, engineering or manufacture of Inventions, and to Employer's purchasing, customer or supplier lists, which documents or information have been disclosed to Employee or known to

Employee as a consequence of or through Employee's employment by Employer (including documents, information or Inventions conceived, originated, discovered or developed by Employee), which is not generally known in the relevant trade or industry.

6.2 INVENTIONS

6.2.1 Disclosure. Employee shall disclose promptly to Employer each Invention, whether or not reduced to practice, which is conceived or learned by Employee (either alone or jointly with others) during the term of his employment with Employer. Employee shall disclose in confidence to Employer all patent applications filed by or on behalf of Employee during the term of his employment and for a period of three (3) years thereafter. Any disclosure of an Invention, or any patent application, made within one (1) year after termination of employment shall be presumed to relate to an Invention made during Employee's term of Employment with Employer, unless Employee clearly proves otherwise.

6.2.2 Employer Property; Assignment. Employee acknowledges and agrees that all Inventions which are discovered, conceived, developed, made, produced or prepared by Employee (alone or in conjunction with others) during the duration of Employee's employment with Employer shall be the sole property of Employer. Said property rights of Employer include without limitation all domestic and foreign patent rights, rights of registration or other protection under the patent and copyright laws, and all other rights pertaining to the Inventions. Employee further agrees that all services, products and Inventions that directly or indirectly result from engagement with Company shall be deemed "works for hire" as that term is defined in Title 17 of the United States Codes, and accordingly all rights associated therewith shall vest in the Company. Notwithstanding the foregoing, Employee hereby assigns to Employer all of Employee's right, title and interest in any such services, products and Inventions, in the event any such services, products and Inventions shall be determined not to constitute "works for hire."

6.2.3 Exclusion Notice. The Assignment by Employee of Inventions under this Agreement does not apply to any Inventions which are owned or controlled by Employee prior to the commencement of employment of Employee by Employer (all of which are set forth on Exhibit "A" hereto). Additionally, Employee is not required to assign an idea or invention where the invention or idea meets all of the following criteria; namely if the invention

or idea: (i) was created or conceived without the use of any of Employer's equipment, supplies, facilities, or trade secret information, and (ii) was developed entirely on Employee's own time, and (iii) does not relate to the business of Employer, and (iv) does not relate to Employer's actual or demonstrably anticipated research or development, and (v) does not result from any work performed by Employee for Employer.

6.2.4 Patents and Copyrights; Attorney-in Fact. Both before and after termination of this Agreement (and with reasonable compensation paid by Employer to Employee after termination), Employee

agrees to assist the Employer to apply for, obtain and enforce patents on, and to apply for, obtain and enforce copyright protection and registration of, the Inventions described in Section 6.2.2 in any and all countries. To that end, Employee shall (at Employer's request) without limitation, testify in any proceeding, and execute any documents and assignments determined to be necessary or convenient for use in applying for, obtaining, registering and enforcing patent or copyright protection involving any of the Inventions. Employee hereby irrevocably appoints Employer, and its duly authorized officers and agents, as Employee's agent and attorney-in-fact, to act for and in behalf of Employee in filing all patent applications, applications for copyright protection and registration, amendments, renewals, and all other appropriate documents in any way related to the Inventions described in Section 6.2.2.

6.3 TRADE SECRETS

6.3.1 Acknowledgement of Proprietary Interest. Employee recognizes the proprietary interest of Employer in any Trade Secrets of Employer. Employee acknowledges and agrees that any and all Trade Secrets of Employer, whether developed by Employee alone or in conjunction with others or otherwise, shall be and are the property of Employer.

6.3.2 Covenant Not to Divulge Trade Secrets. Employee acknowledges and agrees that Employer is entitled to prevent the disclosure of Trade Secrets of Employer. As a portion of the consideration for the employment of Employee and for the compensation being paid to Employee by Employer, Employee agrees at all times during the term of the employment by Employer and thereafter to hold in strictest confidence, and not to use, disclose or allow to be disclosed to any person, firm, or corporation, Trade Secrets of Employer, including Trade Secrets developed by Employee, other than disclosures to persons engaged by Employer to further the business of Employer, and other than use in the pursuit of the business of Employer.

6.3.3 Confidential Information of Others. Employee represents and warrants that if Employee has any confidential information belonging to others, Employee will not use or disclose to Employer any such information or documents. Employee represents that his employment with Employer will not require him to violate any obligation to or confidence with any other party.

6.4 NO ADVERSE USE Employee will not at any time use Employer's Trade Secrets or Inventions in any manner which may directly or indirectly have an adverse effect upon Employer's business, nor will Employee perform any acts which would tend to reduce Employer's proprietary value in Employer's Trade Secrets or Inventions.

6.5 RETURN OF MATERIALS AT TERMINATION In the event of any termination of Employee's employment, Employee will promptly deliver to Employer all materials, property, documents, data, and other information belonging to Employer or pertaining to Trade Secrets or Inventions. Employee

shall not take any materials, property, documents or other information, or any reproduction or excerpt thereof, belonging to Employer or containing or pertaining to any Trade Secrets or Inventions.

6.6 REMEDIES UPON BREACH In the event of any breach by Employee of the provision in this Section 6, Employer shall be entitled, if it so elects, to institute and prosecute proceedings in any court of competent jurisdiction, either in law or in equity, to enjoin Employee from violating any of the terms of this Section 6, to enforce the specific performance by Employee of any of the terms of this Section 6, and to obtain damages for any of them, but nothing herein contained shall be construed to prevent such remedy or combination of remedies as Employer may elect to invoke. The failure of Employer to promptly institute legal action upon any breach of this Section 6 shall not constitute a waiver of that or any other breach hereof.

7. COVENANT NOT TO COMPETE Employee agrees that, during Employee's employment, Employee will not directly or indirectly compete with Employer in any way, and that Employee will not act as an officer, director, employee, consultant, shareholder, lender or agent of any other entity which is engaged in any business of the same nature as, or in competition with, the business in which Employer is now engaged, or in which Employer becomes engaged during the term of Employee's employment, or which is involved in science or technology which is similar to Employer's science or technology.

8. GENERAL PROVISIONS

8.1 ATTORNEYS' FEES In the event of any dispute or breach arising with respect to this Agreement, the party prevailing in any negotiations or proceedings for the resolution or enforcement thereof shall be entitled to recover from the losing party reasonable expenses, attorneys' fees and costs incurred therein.

8.2 AMENDMENTS No amendment or modification of the terms or conditions of this Agreement shall be valid unless in writing and signed by both parties hereto. There shall be no implied-in-fact contracts modifying the terms of this Agreement.

8.3 ENTIRE AGREEMENT This Agreement constitutes the entire agreement between the parties with respect to the employment of Employee. This Agreement supersedes all prior agreements, understandings, negotiations and representation with respect to the employment relationship.

8.4 SUCCESSORS AND ASSIGNS The Rights and obligations of Employer under this Agreement shall inure to the benefit of and shall be binding upon the successors and assigns of Employer. Employee shall not be entitled to assign any of Employee's rights or obligations under this Agreement.

8.5 WAIVER Either party's failure to enforce any provision of this Agreement shall not in any way be construed as a waiver of any such

provision, or prevent that party thereafter from enforcing each and every other provision of this Agreement.

8.6 SEVERABLE PROVISIONS The provisions of this Agreement are severable, and if any or more provisions may be determined to be judicially unenforceable, in whole or in part, the remaining provisions shall nevertheless be binding and enforceable.

9. EMPLOYEE'S REPRESENTATIONS Employee represents and warrants that Employee (i) is free to enter into this Agreement and to perform each of the terms and covenants contained herein, (ii) is not restricted or prohibited, contractually or otherwise, from entering into and performing this Agreement, and (iii) will not be in violation or breach of any other agreement by reason of Employee's execution and performance of this Agreement.

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date set forth above.

EMPLOYER:

AASTROM BIOSCIENCES, INC.

By: _____
R. Douglas Armstrong, Ph.D.
President and Chief Executive Officer

EMPLOYEE:

Address: _____

Exhibit A

List of Prior Inventions
(Section 6.2.3)

None, other than the following:

- [illegible]

=====

STOCK PURCHASE AGREEMENT

Between

COBE LABORATORIES, INC.

and

AASTROM BIOSCIENCES, INC.

Dated as of October 22, 1993

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DISCLOSURE SCHEDULE

STOCK PURCHASE AGREEMENT dated as of October __, 1993 between
AASTROM BIOSCIENCES, INC., a Michigan corporation (the "Company"), and COBE

LABORATORIES, INC., a Colorado corporation (the "Purchaser").

W I T N E S S E T H:
- - - - -

WHEREAS, the Company desires to authorize, issue, and sell to the
Purchaser, and the Purchaser desires to purchase from the Company, the Shares
(as hereinafter defined).

NOW, THEREFORE, in consideration of the premises and the mutual covenants
and agreements hereinafter set forth, the parties hereto agree as follows:

ARTICLE I

DEFINITIONS

SECTION 1.01. Definitions. As used in this Agreement, the following terms

shall have the following meanings:

"Action" means any claim, action, suit, arbitration, inquiry, proceeding or

investigation by or before any federal, state or local or any foreign
government, governmental, regulatory or administrative authority, agency or
commission or any court, tribunal or judicial or arbitral body.

"Affiliate" means, with respect to any specified Person, any other Person

that directly, or indirectly through one or more intermediaries, controls, is
controlled by, or is under common control with, such specified Person.

"Agreement" or "this Agreement" means this Stock Purchase Agreement dated

as of October __, 1993 between the Company and the Purchaser (including the
--
Exhibits hereto and the Disclosure Schedule) and all amendments made in
accordance with the provisions of Section 6.02.

"Applicable Percentage" has the meaning specified in Section 5.04(d).

"Applicable Preemptive Price" means (a) if the Issuance is or was a Public

Offering, the quotient of (i) the aggregate price to the public of the New
Voting Securities sold by the Company in such Public Offering, less underwriting
discounts and commissions, divided by (ii) the number of New Voting Securities
sold by the Company in such Public Offering; (b) if the Issuance is or was a
Private Placement, the Private Placement Price paid to the Company by Persons
other than the Purchaser in such Private Placement; (c) if the Issuance is or
was a Non-Cash Transaction and the New Voting Securities to be issued are
publicly traded prior to such Issuance, the Market Price on the date of the
Post-Determination Subscription Notice; (d) if the Issuance is or was a Non-Cash
Transaction not described in (c) above in which

a monetary value of the New Voting Securities is established, such value; and (e) otherwise, the greater of (i) the Compounded Private Placement Price or (ii) \$8 per share of Common Stock. For purposes of calculating the Applicable Preemptive Price, the price of shares of Non-Coupon Preferred Stock shall be calculated based upon the number of shares of Common Stock into which such shares of Non-Coupon Preferred Stock are convertible at the time of such calculation.

"Articles" means the Restated Articles of Incorporation attached as Exhibit 2.02(b)(iv) hereto establishing and designating the Preferred Stock.

"Board" means the Board of Directors of the Company.

"Business Combination" has the meaning specified in Section 5.07.

"Business Combination Notice" has the meaning specified in Section 5.07.

"Business Day" means any day that is not a Saturday, a Sunday or other day on which banks are required or authorized by law to be closed in Denver, Colorado or Ann Arbor, Michigan.

"By-Laws" means the Restated By-Laws of the Company, as amended through the date hereof.

"Chapter 7B" means Chapter 7B (known as the "Stacey, Bennett and Randall Shareholder Equity Act") of the MBCA.

"Closing" means the completion of the transactions specified herein relating to the purchase and sale of the Shares as contemplated by Section 2.02 hereof.

"Code" means the Internal Revenue Code of 1986, as amended, together with the rules and regulations promulgated thereunder.

"Common Stock" means the common shares of the Company, no par value.

"Company" has the meaning specified in the recitals to this Agreement.

"Company Benefit Plans" has the meaning specified in Section 3.11(a).

"Company Option" has the meaning specified in Section 5.05(a).

"Company's Accountants" means Coopers & Lybrand, independent accountants of the Company.

"Compounded Private Placement Price" means the Private Placement Price for the last Private Placement preceding the date on which the Compounded Private Placement Price is calculated, plus interest on such Private Placement Price compounded annually at a rate of 15

percent from the date of the closing of such preceding Private Placement to the date of calculation.

"Confidential Information" means all confidential or secret data, reports,

interpretations, forecasts, records, marketing, sales and other commercial data or reports, trade secrets information, know-how, methods, procedures, designs, technology, inventions, ideas, specifications, plans, patent applications and related correspondence, or other information that the parties hereto provide to each other in connection with the transactions contemplated by this Agreement, together with analyses, compilations, studies or other documents, whether prepared by their respective agents or attorneys, which contain or otherwise reflect such information; provided, however, that the following will not

constitute Confidential Information for purposes of this Agreement:

- (a) information which was in one of such parties' possession prior to its receipt from the other of such parties;
- (b) information which is obtained by one of such parties from a third person who, insofar as is known to such party, is not prohibited from transmitting the information to such party by a contractual, legal or fiduciary obligation to the other of such parties; and
- (c) information which is or becomes publicly available through no fault of either of such parties.

"Control" (including the terms "controlled by" and "under common

control with"), with respect to the relationship between or among two or more

Persons, means the possession, directly or indirectly or as trustee or executor, of the power to direct or cause the direction of the affairs or management of a Person, whether through the ownership of voting securities, as trustee or executor, by contract or otherwise, including, without limitation, the ownership, directly or indirectly, of securities having the power to elect a majority of the board of directors or similar body governing the affairs of such Person.

"Conversion Determination Date" has the meaning specified in Section

5.04(a).

"Disclosure Schedule" means the Disclosure Schedule attached hereto,

dated as of the date hereof, delivered and forming a part of this Agreement.

"Distribution Agreement" means the Distribution Agreement, dated as of

the date hereof, between the Company and an Affiliate of the Purchaser, substantially in the form of Exhibit 2.02(b)(viii) hereto, as it may be amended from time to time in accordance with its terms.

"Encumbrance" means any security interest, pledge, mortgage, lien,

charge, encumbrance, adverse claim, preferential arrangement or restriction of any kind, including, without limitation, any restriction on the use, voting, transfer, receipt of income or other exercise of any attributes of ownership.

"Environmental Laws" means any federal, state, local or foreign law,

regulation, agency interpretation, policy, order, decree, judgment, or judicial opinion relating to (A) the manufacture, transport, use, treatment, storage, recycling, disposal, release or threatened release of Hazardous Substances or (B) relating to the preservation, restoration, or protection of natural resources or health.

"Environmental Permits" means any permit, license, approval,

identification number or other authorization involving Hazardous Substances or required under any Environmental Law.

"Equity Securities" means shares of Common Stock and any other

securities convertible into, or exchangeable for, shares of Common Stock or giving the holder the right to acquire shares of Common Stock.

"ERISA" means the Employee Retirement Income Security Act of 1974, as

amended, together with the rules and regulations promulgated thereunder.

"ERISA Affiliate" means any trade or business (whether or not

incorporated) that is part of the same controlled group as, or under common control with, the Company within the meaning of Section 414(b)(c)(m) or (o) of the Code.

"Exchange Act" means the Securities and Exchange Act of 1934, as

amended, together with the rules and regulations promulgated thereunder.

"Exclusivity Period" has the meaning specified in Section 5.07.

"Financial Statements" has the meaning specified in Section 3.09.

"Fully Diluted Outstanding Common Stock" means all of the outstanding

Common Stock, all shares of Common Stock that can be acquired by any Person upon conversion of the Shares and all shares of Common Stock that can be acquired upon conversion or exchange of any other convertible or exchangeable securities of the Company or pursuant to outstanding options, warrants or other securities or arrangements having a conversion, exchange or exercise price that is less than or equal to the Option Price and excluding the shares of Common Stock subject to the Option and any shares of Common Stock held in the treasury of the Company.

"GAAP" means U.S. generally accepted accounting principles and

practices in effect from time to time applied consistently throughout the periods involved.

"Hazardous Substances" means any matter containing substances which

are: (A) listed, classified or regulated pursuant to any Environmental Law, including, without limitation, the Comprehensive Environmental Response, Compensation, and Liability Act of 1980, 42 U.S.C. (S) 9601 et seq.; the

Resource Conservation and Recovery Act, 42 U.S.C. (S) 6901 et seq.; the Federal

Water Pollution Control Act, 33 U.S.C. (S) 1251 et seq.; the Toxic Substances

Control Act, 15 U.S.C. (S) 2601 et seq.; and the Clean Air Act, 42 U.S.C.

(S) 7401 et seq.; each as

amended; (B) any petroleum products or by-products, asbestos-containing material, polychlorinated biphenyls, radioactive materials or radon gas; or (C) any other matter to which exposure is prohibited, limited or regulated by any government authority or Environmental Law.

"HSR Act" means the Hart-Scott-Rodino Antitrust Improvements Act of -----
1976, as amended, and the rules and regulations promulgated thereunder.

"Initial Public Offering" means the initial offering to the public by -----
the Company of shares of Common Stock registered under the Securities Act.

"Intellectual Property" means (a) inventions, whether or not -----
patentable, whether or not reduced to practice, and whether or not yet made the subject of a pending patent application or applications, (b) ideas and conceptions of potentially patentable subject matter, including, without limitation, any patent disclosures, whether or not reduced to practice and whether or not yet made the subject of a pending patent application or applications, (c) national (including the United States) and multinational statutory invention registrations, patents, patent registrations and patent applications (including all reissues, divisions, continuations, continuations-in-part, extensions and reexaminations) and all rights therein provided by international treaties or conventions and all improvements to the inventions disclosed in each such registration, patent or application, (d) trademarks, service marks, trade dress, logos, trade names and corporate names, whether or not registered, including all common law rights, and registrations and applications for registration thereof, including, but not limited to, all marks registered in the United States Patent and Trademark Office, the Trademark Offices of the States and Territories of the United States of America, and the Trademark Offices of other nations throughout the world, and all rights therein provided by international treaties or conventions, (e) copyrights (registered or otherwise) and registrations and applications for registration thereof, and all rights therein provided by international treaties or conventions, (f) computer software, including, without limitation, source code, operating systems and specifications, data, data bases, files, documentation and other materials related thereto, data and documentation, (g) trade secrets and confidential, technical and business information (including ideas, formulas, compositions, inventions, and conceptions of inventions whether patentable or unpatentable and whether or not reduced to practice), (h) whether or not confidential, technology (including know-how and show-how), manufacturing and production processes and techniques, research and development information, drawings, specifications, designs, plans, proposals, technical data, copyrightable works, financial, marketing and business data, pricing and cost information, business and marketing plans and customer and supplier lists and information, (i) copies and tangible embodiments of all the foregoing, in whatever form or medium, (j) all rights to obtain and rights to apply for patents, and to register trademarks and copyrights, and (k) all rights to sue or recover and retain damages and costs and attorneys' fees for present and past infringement of any of the foregoing.

"Interim Financial Statements" has the meaning specified in Section -----
3.09.

"IRS" means the United States Internal Revenue Service.

"Issuance" means a Post-Conversion Issuance or a Pre-Conversion

Issuance.

"Leased Real Property" means the real property leased by the Company,

together with, to the extent leased by the Company, all buildings and other structures, facilities or improvements presently or hereafter located thereon, all fixtures, systems, equipment and items of personal property of the Company attached or appurtenant thereto and all easements, licenses, rights and appurtenances relating to the foregoing.

"Liabilities" means any and all debts, liabilities and obligations,

whether accrued or fixed, absolute or contingent, mature or unmatured or determined or determinable, including, without limitation, those arising under any law, rule, regulation, or order by a governmental authority and those arising under any contract, agreement, commitment or undertaking.

"Licensed Intellectual Property" means all Intellectual Property

licensed or sublicensed to the Company from a third party.

"Market Price" of a security means the average of the daily closing

prices of such security for the 30 consecutive trading days immediately preceding the day as of which "Market Price" is being determined. The closing price for each day shall be the last sale price regular way or, in case no such sale takes place on such day, the average of the closing bid and asked prices regular way, in either case on the New York Stock Exchange, or, if such securities are not listed or admitted to trading on the New York Stock Exchange, on the principal national securities exchange on which such securities are listed or admitted to trading, or if such securities are not so listed or admitted to trading but are listed in NASDAQ'S National Market System, the closing price of such security regular way as reported by the National Market System, or if the securities are not so listed or admitted to trading, the last reported bid price as furnished by the National Association of Securities Dealers, Inc. through NASDAQ or through a similar organization if NASDAQ is no longer reporting such information.

"Material Adverse Effect" means any circumstance, change, event,

transaction, loss, failure, effect on the business of the Company or other occurrence that is, or could be, materially adverse to the business, operations, properties (including intangible properties), condition (financial or otherwise), assets, Liabilities, results of operations or prospects of the Company.

"MBCA" means the Michigan Business Corporation Act, effective

January 1, 1973, as amended.

"New Voting Securities" means any shares of Common Stock (or other

securities representing the common equity of the Company), any securities that are convertible into or exchangeable for or otherwise give the holder the right to acquire shares of Common Stock (or such other securities) or other Voting Securities that are issued by the Company after the date hereof, other than shares of Common Stock issued upon conversion of the Shares and Permitted Employee Stock.

"Non-Cash Transaction" means any Issuance other than a Public Offering

or a

Private Placement.

"Non-Coupon Preferred Stock" means the Shares and any other preferred

stock of the Company that carries no fixed dividend and is convertible by the
holder into shares of Common Stock.

"Observation Period" has the meaning specified in Section 5.09(a).

"Option" has the meaning specified in Section 5.03(a).

"Option Closing" has the meaning specified in Section 5.03(c).

"Option Closing Date" has the meaning specified in Section 5.03(c).

"Option Notice Date" has the meaning specified in Section 5.03(c).

"Option Period" has the meaning specified in Section 5.03(b).

"Option Price" means a price per Option Share equal to 120% of the

Market Price on the Option Notice Date.

"Option Shares" means the number of newly issued shares of Common

Stock which, immediately following the issuance thereof, will be equal to 30
percent of the Fully Diluted Outstanding Common Stock, and "Option Share" means

one of the Option Shares.

"Out of the Money Price" means a conversion, exchange or exercise

price that is equal to or greater than the Option Price.

"Out of the Money Option Stock" means any Common Stock issued or to be

issued by the Company upon conversion or exchange of any convertible or
exchangeable securities of the Company or pursuant to the exercise of any
outstanding options, warrants or other securities having an Out of the Money
Option Price.

"Owned Intellectual Property" means all Intellectual Property, other

than the Licensed Intellectual Property, in and to which the Company holds, or
has a right to hold, any right, title and interest.

"Permitted Encumbrances" means such of the following as to which no

enforcement, collection, execution, levy or foreclosure proceeding shall have
been commenced: (a) liens for taxes, assessments and governmental charges or
levies not yet due and payable; (b) Encumbrances imposed by law, such as
materialmen's, mechanics', carriers', workmen's and repairmen's liens and other
similar liens arising in the ordinary course of business; and (c) pledges or
deposits to secure obligations under workers' compensation laws or similar
legislation or to secure public or statutory obligations.

"Permitted Employee Stock" means (a) shares of Common Stock or options

to

purchase Common Stock issued to employees of the Company after the Initial Public Offering, (b) all shares issuable to employees or consultants of the Company pursuant to options issued by the Company prior to the date hereof, (c) all options and shares issuable pursuant to the Stock Option Plans, up to the sum of (i) the aggregate number of shares authorized in the Stock Option Plans as of the date hereof and (ii) up to an additional 300,000 shares of Common Stock issuable pursuant to options granted after the date hereof, and (d) an additional number of shares of Common Stock (or options therefor) equal to not more than 25% of the additional shares (of Common Stock or of Non-Coupon Preferred Stock) issued by the Company from and after the date hereof (including the Shares) until one day prior to the date of the Initial Public Offering.

"Person" means an individual, corporation, partnership, association, -----
trust, joint venture, unincorporated organization, other entity or group (as defined in Section 13(d)(3) of the Exchange Act).

"Post-Determination Issuance" has the meaning specified in Section -----
5.04(a).

"Post-Determination Issuance Notice" has the meaning specified in -----
Section 5.04(a).

"Post-Determination Preemptive Right" has the meaning specified in -----
Section 5.04(b).

"Post-Determination Subscription Notice" has the meaning specified in -----
Section 5.04(a).

"Post-Option Issuance" has the meaning specified in Section 5.03(g).

"Post-Option Issuance Notice" has the meaning specified in Section -----
5.03(g).

"Post-Option Purchase Right" has the meaning specified in Section -----
5.03(g).

"Pre-Determination Issuance" has the meaning specified in Section -----
5.04(d).

"Pre-Determination Preemptive Rights" has the meaning specified in -----
Section 5.04(d).

"Preferred Stock" means the shares of Series C convertible preferred -----
stock of the Company to be issued pursuant to this Agreement.

"Private Placement" means an Issuance for cash other than a Public -----
Offering.

"Private Placement Price" means the quotient of (i) the aggregate -----
price paid to the Company in a Private Placement less the sales agency and placement fees of such Private Placement borne by the Company, divided by (ii) the number of securities sold by the Company in such Private Placement. For purposes of calculating the Private Placement Price, the price of shares of Non-Coupon Preferred Stock shall be calculated based upon the number of shares

of Common Stock into which such shares of Non-Coupon Preferred Stock are convertible at the time of such calculation.

"Public Offering" means a public offering of New Voting Securities

registered on a registration statement under the Securities Act.

"Purchase Price" has the meaning specified in Section 2.01.

"Purchaser" has the meaning specified in the recitals to this

Agreement.

"Purchaser Designees" has the meaning specified in Section 5.09(b).

"Purchaser Observer" has the meaning specified in Section 5.09(a).

"Put Notice" has the meaning specified in Section 5.05(b).

"Qualifying IPO" has the meaning specified in Section 5.05(a).

"Qualifying Private Placement" has the meaning specified in Section

5.05(a).

"Registration Rights" means the registration rights of the Purchaser

as set forth in Exhibit 5.02 hereto.

"Reserve Amount" has the meaning specified in Section 5.11.

"Restated Articles of Incorporation" means the Restated Articles of

Incorporation of the Company, as amended through the date hereof.

"Securities Act" means the Securities Act of 1933, as amended,

together with the rules and regulations promulgated thereunder.

"Series A Preferred Stock" means the Series A preferred stock of the

Company.

"Series B Preferred Stock" means the Series B preferred stock of the

Company.

"Shares" has the meaning specified in Section 2.01.

"Stock Option Plans" means the Company's 1992 Stock Option Plan, the

1989 Stock Option Plan and the Ancillary Stock Option Plan.

"Subsidiaries" means any and all corporations, partnerships, joint

ventures, associations and other entities controlled by the Company directly or indirectly through one or more intermediaries.

"Total Voting Power" means the combined voting power of all the Voting

Securities.

"Voting Securities" means any shares of any class of capital stock of

the Company entitled to vote generally in the election of directors.

ARTICLE II

PURCHASE AND SALE OF SHARES; CLOSING -----

SECTION 2.01. Authorization, Purchase and Sale of Shares. Upon the

terms set forth herein, at the Closing, the Company shall authorize, issue and
sell to the Purchaser, and the Purchaser shall purchase from the Company, 10,000
shares of Preferred Stock (the "Shares") for a purchase price of \$10,000,000

(the "Purchase Price"). The Company hereby acknowledges receipt of \$1,000,000

received from the Purchaser by the Company prior to the date hereof, which
\$1,000,000 shall be a credit against the Purchase Price.

SECTION 2.02. Closing. (a) The Closing of the purchase and sale

shall take place simultaneously with the execution of this Agreement at the
offices of the Company in Ann Arbor, Michigan.

(b) At the Closing, the Company shall deliver or cause to be
delivered to the Purchaser: (i) stock certificates evidencing the Shares
registered in the name of the Purchaser; (ii) a legal opinion from Pepper,
Hamilton & Scheetz, Michigan, legal counsel to the Company substantially in the
form of Exhibit 2.02(b)(ii) hereto; (iii) a receipt for the Purchase Price;
(iv) a copy of the Restated Articles of Incorporation certified by the
Corporations and Securities Bureau of the Department of Commerce of the State of
Michigan and a copy of the By-Laws certified by the Secretary of the Company;
(v) a certificate from the Corporations and Securities Bureau of the Department
of Commerce, certifying as to the good standing of the Company under the laws of
such state; (vi) evidence reasonably satisfactory to the Purchaser of the
adoption by the Board of the Company of actions duly approving this Agreement,
the Distribution Agreement and the transactions contemplated hereby and thereby;
(vii) agreements executed by H & Q Life Science Technology Fund I, H & Q London
Ventures, Brentwood Associates V, L.P., Wind Point II, L.P. and State Treasurer
of State of Michigan, as custodian for certain pension funds, which shareholders
of the Company hold in excess of 80% of the Voting Securities of the Company, in
the form of Exhibit 2.02(b)(vii) hereto agreeing (A) to vote shares held by such
shareholder against any proposal to amend the By-Laws or the Restated Articles
of Incorporation so as to make Chapter 7B of the MBCA applicable to acquisitions
of shares of Common Stock or Voting Securities and (B) to vote in favor of the
Purchaser Designees as directors; and (viii) a copy of the Distribution
Agreement, duly executed by the Company.

(c) At the Closing, the Purchaser shall deliver to the Company:
(i) the Purchase Price, by wire transfer, to an account or accounts designated
by the Company at least five Business Days prior to the Closing Date; (ii) a
receipt for the Shares; and (iii) a copy of the Distribution Agreement duly
executed by the Purchaser.

ARTICLE III

REPRESENTATIONS AND WARRANTIES OF THE COMPANY

The Company represents and warrants to the Purchaser that:

SECTION 3.01. Organization, Authority and Qualification of the

Company; No Subsidiaries. The Company is a corporation duly organized, validly

existing and in good standing under the laws of the State of Michigan and has all necessary power and authority to own, operate or lease the properties and assets now owned, operated or leased by it and to carry on the business of the Company as it has been and is currently conducted. The Company is duly licensed or qualified to do business and is in good standing in Michigan which is the only jurisdiction in which the properties owned or leased by it or the operation of its business makes such licensing or qualification necessary or desirable. The Company has no Subsidiaries.

SECTION 3.02. Restated Articles of Incorporation and By-Laws. The

Company has heretofore furnished to the Purchaser a complete and correct copy of the Restated Articles of Incorporation and the By-Laws, each as amended to date, each of which is in full force and effect. The Company is not in violation of any of the provisions of the Restated Articles of Incorporation or By-Laws.

SECTION 3.03. Capitalization. (a) The authorized capital stock of

the Company consists of (x) 5,540,000 shares of Preferred Stock, consisting of 2,500,000 issued and outstanding shares of Series A Preferred Stock, 3,030,000 issued and outstanding shares of Series B Preferred Stock and the Shares, none of which is issued, outstanding or reserved for issuance, except pursuant to this Agreement, and (y) 15,000,000 shares of Common Stock, of which (i) 1,736,219 shares of Common Stock are issued and outstanding, all of which are validly issued, fully paid and nonassessable (except as noted in Section 3.03(a) of the Disclosure Schedule), (ii) 5,530,000 shares of Common Stock are reserved for issuance upon conversion of the Series A and Series B Preferred Stock, (iii) no shares of Common Stock are held in the treasury of the Company and (iv) an aggregate of 1,573,940 shares of Common Stock are reserved for issuance pursuant to the Company's Stock Option Plans. None of the issued and outstanding shares of Common Stock was issued in violation of any preemptive rights.

(b) Except as set forth in Section 3.03(b) of the Disclosure Schedule, there are no options, warrants or other rights, agreements, arrangements or commitments of any character to which the Company or, to the knowledge of the Company, any of its stockholders is a party or obligating the Company or any of its stockholders to issue or to sell any shares of capital stock of, or other equity interests in, the Company. There are no outstanding contractual obligations of the Company to repurchase, redeem or otherwise acquire any of the capital stock of the Company or to provide funds to or make any investment (in the form of a loan, capital contribution or otherwise) in any other Person.

(c) Except as set forth in Section 3.03(c) of the Disclosure Schedule, the Company is not party to any agreement granting registration rights to any Person with respect to any equity or debt securities of the Company.

SECTION 3.04. Authority. The Company has all necessary corporate

power and authority to execute and deliver this Agreement and the Distribution Agreement and to perform its obligations and to consummate the transactions contemplated hereunder and thereunder. The execution, delivery and performance of this Agreement and the Distribution Agreement by the Company have been duly and validly authorized by all necessary corporate action and no other corporate proceedings on the part of the Company are necessary to authorize this Agreement or the Distribution Agreement or to consummate the transactions contemplated by this Agreement or the Distribution Agreement. This Agreement and the Distribution Agreement have been duly and validly executed and delivered by the Company and, assuming the due authorization, execution and delivery hereof by the Purchaser and payment for the Shares as contemplated by this Agreement, constitute the legal, valid and binding obligation of the Company enforceable against the Company in accordance with their terms.

SECTION 3.05. No Conflict. The execution and delivery of this

Agreement and the Distribution Agreement by the Company do not, and the performance of this Agreement and the Distribution Agreement by the Company will not, (i) conflict with or violate the Restated Articles of Incorporation or By-Laws, (ii) conflict with or violate any law, rule, regulation, order, judgment or decree applicable to the Company or by which its properties are bound or affected, or (iii) result in any breach of or constitute a default (or an event which with notice or lapse of time or both would become a default) under, or give to others any rights of termination, amendment, acceleration or cancellation of, or result in the creation of an Encumbrance on any of the properties or assets of the Company pursuant to any note, bond, mortgage, indenture, contract, agreement, lease, license, permit, insurance policy or other instrument or obligation to which the Company is a party, or by which the Company or its properties are bound or affected.

SECTION 3.06. Common Stock; Preferred Stock. All Shares and all

shares of Common Stock subject to issuance as contemplated by this Agreement (including, without limitation, the Common Stock issuable upon conversion of the Shares and pursuant to Article V of this Agreement), upon such issuance against payment therefor in accordance herewith or upon conversion of the Shares, as the case may be, shall (i) be duly authorized, validly issued, fully paid and nonassessable and (ii) be free and clear of all Encumbrances of any kind whatsoever (including, without limitation, any preemptive rights of any other stockholder of the Company). Upon issuance in accordance with the Articles and herewith, all such shares of Common Stock shall have accorded to them full voting rights. Upon issuance in accordance herewith, the Shares will have the rights, including, without limitation, the voting rights, set forth in the Articles.

SECTION 3.07. Compliance with Laws. Except as set forth in Schedule

3.07 of the Disclosure Schedule and as would not have a Material Adverse Effect, to the best knowledge of the Company, the Company is not in conflict with, or violation of, any law, rule, regulation, order, judgment or decree applicable to the Company or by which the Company or any of its properties are bound or affected.

SECTION 3.08. Governmental Consents and Approvals. The execution,

delivery and performance of this Agreement by the Company do not and will not require any consent,

approval, authorization or other order of, action by, filing with or notification to any governmental or regulatory authority, domestic or foreign, except (a) as described in Section 3.08 of the Disclosure Schedule and (b) to the extent applicable, upon issuance of shares of Common Stock pursuant to Article V of this Agreement and upon a conversion of the Shares as provided for in the Articles, the notification requirements of the HSR Act.

SECTION 3.09. Financial Information. True and complete copies of (i)

the audited balance sheets of the Company for each of the fiscal years ended as of June 30, 1992 and June 30, 1993, and the related audited statements of income and cash flows of the Company, together with all related notes thereto, accompanied by the reports thereon of the Company's Accountants (collectively, the "Financial Statements") and (ii) the unaudited balance sheet of the Company

as of August 31, 1993, and the related unaudited statements of income and cash flow, together with all related notes thereto (collectively referred to herein as the "Interim Financial Statements"), are set forth in Section 3.09 of the

Disclosure Schedule. The Financial Statements and the Interim Financial Statements (i) were prepared in accordance with the books of account and other financial records of the Company, (ii) present fairly the financial condition, results of operations and cash flows of the Company as of the dates thereof or for the periods covered thereby, (iii) have been prepared in accordance with U.S. GAAP applied on a basis consistent with the past practices of the Company and (iv) include all adjustments (consisting only of normal recurring accruals) that are necessary for a fair presentation of the financial condition of the Company, the results of the operations and cash flows of the Company as of the dates thereof or for the periods covered thereby; provided, however, that the

Interim Financial Statements are subject to normal year-end adjustments, none of which are expected to be material in amount, and to the inclusion of footnotes with respect to the matters covered by the footnotes in the Financial Statements.

SECTION 3.10. Absence of Certain Changes, Events and Conditions;

Conduct in the Ordinary Course. (a) Since June 30, 1993, except as disclosed

in Schedule 3.10(a) of the Disclosure Schedule, there has not been any change having a Material Adverse Effect. Except as disclosed in Schedule 3.10(a) of the Disclosure Schedule, there are no conditions known to the Company existing, with respect to the research, markets, proposed development and marketing plans, products, facilities, existing and prospective technologies, capabilities or personnel of the Company that reasonably would be expected to have a Material Adverse Effect.

(b) Since June 30, 1993, the Company has been operated only in the ordinary course. As amplification and not limitation of the foregoing, except as disclosed in Schedule 3.10(b) of the Disclosure Schedule, the Company has not, since June 30, 1993:

(i) permitted or allowed any of the assets or properties (whether tangible or intangible) of the Company to be subjected to any Encumbrance, other than Permitted Encumbrances;

(ii) made any loan to, guaranteed any indebtedness of or otherwise incurred any indebtedness on behalf of any Person;

(iii) failed to pay any creditor any amount owed to such creditor when due;

(iv) redeemed any of the capital stock or declared, made or paid any dividends or distributions (whether in cash, securities or other property) to the holders of capital stock of the Company;

(v) made any material changes in the customary methods of operations of the Company;

(vi) merged with, entered into a consolidation with or acquired an interest in, any Person or acquired a substantial portion of the assets or business of any Person or any division or line of business thereof, or otherwise acquired any material assets other than in the ordinary course of business consistent with past practice;

(vii) made any capital expenditure or commitment for any capital expenditure in excess of \$200,000 individually or \$750,000 in the aggregate;

(viii) issued or sold any capital stock, notes, bonds or other securities, or any option, warrant or other right to acquire the same, of, or any other interest in, the Company;

(ix) entered into any agreement, arrangement or transaction with any of its directors, officers, employees or shareholders (or with any relative, beneficiary, spouse or Affiliate of such Person);

(x) made any change in any method of accounting or accounting practice or policy used by the Company, other than such changes required by U.S. GAAP;

(xi) disclosed any secret or confidential Intellectual Property (except by way of issuance of a patent) or permitted to lapse or go abandoned any Intellectual Property (or any registration or grant thereof or any application relating thereto) to which, or under which, the Company has any right, title, interest or license; or

(xii) agreed, whether in writing or otherwise, to take any of the actions specified in this Section 3.09 or granted any options to purchase, rights of first refusal, rights of first offer or any other similar rights or commitments with respect to any of the actions specified in this Section 3.10, except as expressly contemplated by this Agreement.

SECTION 3.11. Employee Benefit Plans. (a) With respect to each

employee benefit plan, program, arrangement and contract (including, without limitation, any "employee benefit plan", as defined in Section 3(3) of ERISA),

maintained or contributed to by the Company or any of its ERISA Affiliates or with respect to which the Company or any of its ERISA Affiliates could incur liability under Section 4069, 4201 or 4212(c) of ERISA (the "Company Benefit Plans"), the Company has made available to the Purchaser a true and correct copy

of (i) the most recent annual report (Form 5500) filed with the IRS, (ii) such Company Benefit Plan, (iii) each trust agreement relating to such Company Benefit Plan, (iv) the most recent summary plan description for each Company Benefit Plan for which a summary plan description is required and (v) the most recent determination letter issued by the IRS with respect to any Company Benefit Plan

qualified under Section 401(a) of the Code.

(b) Except as set forth in Section 3.11(b) to the Disclosure Schedule, none of the Company Benefit Plans promises or provides retiree medical or life insurance benefits to any person. Each Company Benefit Plan intended to be qualified under Section 401(a) of the Code has received a favorable determination letter from the IRS to the effect that it is so qualified and nothing has occurred since the date of such letter to affect the qualified status of such plan. Except for the Stock Option Plans, none of the Company Benefit Plans in effect on the date hereof would result, separately or in the aggregate, in the payment of any material "excess parachute payment" within the

meaning of Section 280G of the Code. Each Company Benefit Plan has been operated in all material respects in accordance with its terms and the requirements of applicable Law. Except as set forth in Section 3.11(b) to the Disclosure Schedule, none of the Company Benefit Plans is subject to Title IV of ERISA, and neither the Company nor any of its ERISA Affiliates has incurred, or reasonably expects to incur, any direct or indirect liability under or by operation of Title IV or ERISA.

(c) With respect to the Company Benefit Plans, other than claims for benefits, no event has occurred and, to the knowledge of the Company, there exists no condition or set of circumstances, in connection with which the Company or any of its ERISA Affiliates could be subject to any liability under the terms of such Company Benefit Plans, ERISA, the Code or any other applicable Law, which would, individually or in the aggregate, have a Material Adverse Effect.

SECTION 3.12. Leased Real Property. (a) The Company owns no real

property.

(b) Section 3.12(b) of the Disclosure Schedule contains a list of all of the Leased Real Property. Except as described in such Section of the Disclosure Schedule, (i) there is no material violation of any law, rule or regulation by the Company or known to the Company relating to any of the Leased Real Property, (ii) the Company is in peaceful and undisturbed possession of the Leased Real Property, and so long as the lease remains in effect, there are no contractual or legal restrictions that preclude or restrict the ability to use the premises for the purposes for which they are currently being used and (iii) the Company has not leased or subleased any parcel or any portion of any parcel of Leased Real Property to any other Person, nor has the Company assigned its interest under any lease or sublease listed in Section 3.12(b) of the Disclosure Schedule to any third party.

(c) The Company has, or has caused to be, delivered to the Purchaser true and complete copies of all leases and subleases listed in Section 3.12(b) of the Disclosure Schedule. Each of such leases and subleases is in full force and effect and constitutes a legal, valid and binding obligation of the respective parties thereto, and except as set forth on Schedule 3.12(c) of the Disclosure Schedule, the Company is not in default or breach of (with or without the giving of notice or the passage of time) any such leases or subleases. To the knowledge of the Company, no third party is in material breach of any of such leases or subleases.

SECTION 3.13. Intellectual Property. (a) Except as set forth in

Schedule 3.13

of the Disclosure Schedule: (i) all the Owned Intellectual Property is owned by the Company, free and clear of any Encumbrance and (ii) no Actions have been made or asserted or are pending (nor, to the best knowledge of the Company after due inquiry, has any such Action been threatened) against the Company either (A) based upon or challenging or seeking to deny or restrict the use by the Company of any of the Owned Intellectual Property or (B) alleging that any services provided, or products manufactured or sold by the Company are being provided, manufactured or sold in violation of any patents or trademarks, or any other rights of any Person. To the best knowledge of the Company after due inquiry, no Person is using any patents, copyrights, trademarks, service marks, trade names, trade secrets or similar property that are confusingly similar to the Owned Intellectual Property or that infringe upon the Owned Intellectual Property or upon the rights of the Company therein. Except as disclosed in Section 3.12 of the Disclosure Schedule, the Company has not granted any license or other right to any other Person with respect to the Owned Intellectual Property. The consummation of the transactions contemplated by this Agreement will not result in the termination or impairment of any of the Owned Intellectual Property.

(b) Except as set forth on Section 3.13(b) of the Disclosure Schedule, each license and sublicense with respect to the Licensed Intellectual Property:

(i) is valid and binding and in full force and effect and represents the entire agreement between the respective licensor and licensee with respect to the subject matter of such license or sublicense;

(ii) except as otherwise set forth in Section 3.13(b)(ii) of the Disclosure Schedule, will not cease to be valid and binding and in full force and effect on terms identical to those currently in effect as a result of the consummation of any of the transactions contemplated by this Agreement, nor will the consummation of the transactions contemplated by this Agreement constitute a breach or default under such license or sublicense or otherwise give the licensor or sublicensor a right to terminate such license or sublicense;

(iii) no Actions have been made or asserted or are pending (nor, to the best knowledge of the Company after due inquiry, has any such Action been threatened) against the Company either (A) based upon or challenging or seeking to deny or restrict the use by the Company of any of the Licensed Intellectual Property or (B) alleging that any Licensed Intellectual Property is being licensed, sublicensed or used in violation of any patents or trademarks, or any other rights of any Person; and

(iv) to the knowledge of the Company, no Person is using any patents, copyrights, trademarks, service marks, trade names, trade secrets or similar property that are confusingly similar to the Licensed Intellectual Property or that infringe upon the Licensed Intellectual Property or upon the rights of the Company therein.

(c) Except as otherwise disclosed in Section 3.13(c) of the Disclosure Schedule, with respect to each such license or sublicense of Licensed Intellectual Property: (i) the Company has not received any notice of termination or cancellation under such license or

sublicense and no licensor or sublicensor has any right of termination or cancellation under such license or sublicense except in connection with the default of the Company thereunder, (ii) the Company has not received any notice of a breach or default under such license or sublicense, which breach or default has not been cured and (iii) the Company has not granted to any other Person any rights, adverse or otherwise, under such license or sublicense.

(d) Neither the Company nor (to the knowledge of the Company) any other party to such license or sublicense of Licensed Intellectual Property is in breach or default in any material respect, and, to the best knowledge of the Company after due inquiry, no event has occurred that, with notice or lapse of time would constitute such a breach or default or permit termination, modification or acceleration under such license or sublicense.

(e) Except as set forth in Section 3.13(e) of the Disclosure Schedule, the Company is not aware of any reason that would prevent any pending applications to register trademarks, service marks or copyrights or any pending patent applications from being granted.

(f) The Company has taken all reasonable security measures to protect the secrecy, confidentiality and value of all Intellectual Property required to conduct its business. Each founder, officer, director and employee of the Company has executed a Proprietary Information and Inventions Agreement in the Company's standard form, each such agreement is in full force and effect as of the date hereof and to the best of the Company's knowledge, none of the Company's current or former officers, employees or consultants is or will be in violation thereof. The Company does not believe it is or will be necessary to utilize any inventions of any of its employees or consultants (or people it currently intends to hire) made prior to their employment by or consultancy to the Company, other than inventions which have been licensed to the Company.

(g) Section 3.13(g) of the Disclosure Schedule sets forth a complete list of all patent applications in which the Company has an interest. The Company believes that the inventions described in such applications are patentable, that the claims made therein should issue in all material respects and that the patents, if issued, would cover all techniques currently known to the Company to grow human stem cells in culture.

(h) Except as disclosed in Section 3.13(h) of the Disclosure Schedule, no consultant to or employee of the Company has granted any license or other right to any Person other than the Company with respect to the Owned Intellectual Property. The Company is not aware that any of its employees or consultants is obligated under any contract (including licenses, covenants or commitments of any nature) or any order of any court or administrative agency, that would interfere with the use of such employee's or consultant's best efforts to promote the interests of the Company or that would conflict with the Company's business as proposed to be conducted.

SECTION 3.14. Environmental Matters. Except as would not have a

Material Adverse Effect, the Company, to the best of its knowledge, (a) is not violating and has not in the past violated any Environmental Law or Permit, (b) is not exposed to any claims of liability for any off-site disposal or contamination, (c) has not received notice of any claim or threatened

claim relating to any Environmental Permit, Environmental Law or otherwise relating to any Hazardous Substance and (d) is not aware of any circumstance likely to result in claims, liability, investigation, monitoring or remediation costs or restrictions on the ownership, use, or transfer of any Real Property or Environmental Permit pursuant to any Environmental Law. With respect to its period of ownership or use of any property, there has not been any contamination, release or threat of release at any currently or formerly owned, leased or used real property that would have a Material Adverse Effect.

SECTION 3.15. Litigation. There is no pending or, to the knowledge

of the Company, threatened litigation, arbitration or governmental investigation or legal, administrative or regulatory proceeding against the Company or to which any of its properties is or would be subject that (a) if adversely determined, would have a Material Adverse Effect or (b) relates to this Agreement or the Distribution Agreement or the transactions contemplated hereby and thereby. Except as set forth in Schedule 3.15 of the Disclosure Schedule, there are no material citations, fines or penalties heretofore asserted against the Company under any federal, state or local law that remain unpaid or that otherwise bind the assets of the Company.

SECTION 3.16. Agreements. Section 3.16 of the Disclosure Schedule

lists each agreement, contract (other than leases of Leased Real Property), license commitment or instrument (including any and all amendments thereto) to which the Company is a party, involving aggregate annual payments of at least \$200,000 or which is material, individually or in the aggregate, to the business, operations or financial condition of the Company, each of which is in full force and effect and constitutes a legal, valid and binding obligation of the respective parties thereto, and except as set forth on Schedule 3.16 of the Disclosure Schedule, the Company is not in default or breach of (with or without the giving of notice or the passage of time) any such agreement or instrument. To the knowledge of the Company, no third party is in material breach of any such agreements. The Company has caused to be delivered to the Purchaser true and complete copies of all such agreements, including all amendments thereto.

SECTION 3.17. Certain Interests. (a) Except as disclosed in Section

3.17(a) of the Disclosure Schedule, no officer or director of the Company and no relative or spouse (or relative of such spouse) who resides with, or is a dependent of, any such officer or director:

(i) has any direct or indirect financial interest in any competitor, supplier or customer of the Company, provided, however, that the ownership

of securities representing no more than one percent of the outstanding voting power of any competitor, supplier or customer, and which are listed on any national securities exchange or traded actively in the national over-the-counter market, shall not be deemed to be a "financial interest" so long as the Person owning such securities has no other connection or relationship with such competitor, supplier or customer;

(ii) owns, directly or indirectly, in whole or in part, or has any other interest in any tangible or intangible property which the Company uses or has used in the conduct of the Business or otherwise;

(iii) has outstanding any indebtedness to the Company; or

(iv) has any contract or agreement with the Company.

(b) Except as disclosed in Section 3.17(b) of the Disclosure Schedule, the Company has no Liability or any other obligation of any nature whatsoever to any officer, director or shareholder of the Company or to any relative or spouse (or relative of such spouse) who resides with, or is a dependent of, any such officer, director or shareholder.

SECTION 3.18. Licenses and Permits. Except as would not have a

Material Adverse Effect, the Company, to the best of its knowledge, has all governmental licenses, permits and other governmental authorizations and approvals required for the conduct of its businesses as now conducted, and all such licenses, permits, authorizations and approvals will remain in full force and effect immediately following the consummation of the transactions hereunder.

SECTION 3.19. Private Offering. No form of general solicitation or

general advertising (including, without limitation, advertisements, articles, notices or other communications published in any newspaper, magazine or other medium or broadcast over television or radio, or any seminar or meeting whose attendees have been invited by any general solicitation or general advertising) was used by the Company or any other Person acting on behalf of the Company in respect of the Shares or in connection with the offer and sale of the Shares.

SECTION 3.20. Brokers. No broker, finder or investment banker, other

than Hambrecht & Quist (whose fees shall be paid by the Company), is entitled to any brokerage, finder's or other fee or commission in connection with the transactions hereunder based upon arrangements made by or on behalf of the Company. All arrangements between the Company and Hambrecht & Quist with respect to such fees have been disclosed to the Purchaser.

SECTION 3.21. General Solicitation. The Company has not made any

general advertising or general solicitation with respect to the purchase of the Shares, the Option or any shares of Common Stock into which the Shares may be converted or for which the Option may be exercised, or any other securities of the Company that may be purchased pursuant hereto.

ARTICLE IV

REPRESENTATIONS AND WARRANTIES OF THE PURCHASER

The Purchaser represents and warrants to the Company that:

SECTION 4.01. Organization of the Purchaser. The Purchaser is a

corporation duly organized, validly existing and in good standing under the laws of the State of Colorado.

SECTION 4.02. Authority. The Purchaser has all necessary corporate

power and authority to execute and deliver this Agreement and the Distribution Agreement and to perform its obligations and to consummate the transactions contemplated hereunder and thereunder. The execution, delivery and performance of this Agreement and the Distribution Agreement by the Purchaser have been duly and validly authorized by all necessary corporate action of the Purchaser and no other corporate proceedings on the part of the Purchaser are necessary to authorize this Agreement or the Distribution Agreement or to consummate the transactions contemplated by this Agreement or the Distribution Agreement. This Agreement and the Distribution Agreement have been duly and validly executed and delivered by the Purchaser and, assuming the due authorization, execution and delivery hereof by the Company, constitute the legal, valid and binding obligation of the Purchaser enforceable against the Purchaser in accordance with their terms.

SECTION 4.03. No Conflict. The execution and delivery of this

Agreement and the Distribution Agreement by the Purchaser do not, and the performance of this Agreement and the Distribution Agreement by the Purchaser will not, (i) conflict with or violate the articles of incorporation or by-laws of the Purchaser, (ii) conflict with or violate any law, rule, regulation, order, judgment or decree applicable to the Purchaser or by which it or its properties are bound or affected or (iii) result in any breach of or constitute a default (or an event which with notice or lapse of time or both would become a default) under, or give to others any rights of termination, amendment, acceleration or cancellation of, or result in the creation of an Encumbrance on any of the properties or assets of the Purchaser pursuant to, any note, bond, mortgage, indenture, contract, agreement, lease, license, permit, franchise or other instrument or obligation to which the Purchaser is a party or by which the Purchaser or any of its properties is bound or affected.

SECTION 4.04. Securities Act. The Purchaser is an "accredited

investor", as that term is defined in Regulation D promulgated under the Securities Act. The Purchaser received no general advertising or general solicitation with respect to the purchase of the Shares, the Option or any shares of Common Stock into which the Shares may be converted for which the Option may be exercised, or any other securities of the Company that may be purchased pursuant hereto. The Purchaser is acquiring the Shares and the Option, and all shares of Common Stock into which the Shares may be converted, solely for its own account, as principal, for investment purposes only and not with a view to, or for, resale or distribution thereof. The Purchaser has no present intention, agreement or arrangement to resell, assign, transfer or otherwise dispose of all or any part of the Shares, the Option or any shares of Common Stock into which the Shares may be converted. The Purchaser understands that in reliance upon the foregoing representation and warranty, the offer and sale of the Shares and the Option are not registered under the Securities Act or any state securities law. The Purchaser will not sell, assign, transfer or otherwise dispose of the Shares, the Option or the Shares of Common Stock into which the Shares may be converted or for which the Option may be exercised except pursuant to a registration under the Securities Act and applicable state securities laws or an exemption therefrom.

SECTION 4.05. Governmental Consents and Approvals. The execution,

delivery

and performance of this Agreement by the Purchaser do not and will not require any consent, approval, authorization or other order of, action by, filing with or notification to any governmental or regulatory authority, domestic or foreign, except (a) as described in Section 4.05 of the Disclosure Schedule and (b) to the extent applicable, upon issuance of shares of Common Stock pursuant to Article V of this Agreement and upon a conversion of the Shares as provided for in the Articles, the notification requirements of the HSR Act.

SECTION 4.06. Brokers. No broker, finder or investment banker, other

than Lehman Brothers Inc. (whose fees shall be paid by the Purchaser), is entitled to any brokerage, finder's or other fee or commission in connection with the transactions hereunder, based upon arrangements made by or on behalf of the Purchaser.

ARTICLE V

ADDITIONAL AGREEMENTS

SECTION 5.01. Access to Information; Confidentiality. The Company

shall, and shall cause its officers, directors, employees, auditors and other agents to, provide to the Purchaser such financial, operating and other data and information with respect to the business and properties of the Company as the Purchaser shall reasonably request to monitor the investment made pursuant hereto and to exercise its rights hereunder. The Purchaser and the Company agree to keep secret and not to disclose to any third party any Confidential Information of the other that may from time to time be received from the other party; provided, however, that the Purchaser may disclose such information to

its Affiliates which agree to be bound by the provisions of this Section 5.01. The Confidential Information exchanged between the parties pursuant to this Agreement shall not be used by the receiving party for any purpose other than for purposes of carrying out covenants or other obligations contained in this Agreement.

SECTION 5.02. Registration Rights. The Company hereby grants to the

Purchaser the registration rights set forth in Exhibit 5.02.

SECTION 5.03. Purchaser's Option. (a) The Company hereby grants to

the Purchaser an irrevocable option (the "Option") to purchase all, but not less than all, of the Option Shares at the Option Price in accordance with this Section 5.03.

(b) The Purchaser may exercise the Option at any time during the three-year period commencing on the closing date of the Initial Public Offering (the "Option Period"). Upon the expiration of the Option Period, the right to

exercise the Option under this Section 5.03 shall expire and be of no further force and effect. Notwithstanding any such expiration, the Purchaser shall be entitled to acquire the Option Shares with respect to which it has exercised the Option in accordance with the terms hereof during the Option Period.

(c) If the Purchaser wishes to exercise the Option, it shall deliver to the Company a written notice; the date such notice is delivered to the Company by the Purchaser being the "Option Notice Date") specifying (i) the

Purchaser's intention to acquire the Option Shares and

(ii) a place and date not earlier than five business days nor later than fifteen business days (the "Option Closing Date") from the Option Notice Date for the

closing of such acquisition (the "Option Closing"). The Purchaser shall also

deliver to the Company at the Option Closing an opinion of counsel (it being agreed that Shearman & Sterling shall be deemed satisfactory) in form and substance reasonably satisfactory to the Company and its counsel or other evidence reasonably satisfactory to the Company and its counsel that the acquisition of the Option Shares by the Purchaser complies with the Securities Act and with any applicable state securities laws.

(d) On the Option Closing Date, the Purchaser shall pay to the Company, in immediately available funds by wire transfer to a bank account designated in writing by the Company, an amount equal to the Option Price multiplied by the number of Option Shares.

(e) At the Option Closing, simultaneously with the delivery of the consideration specified in paragraph (d) of this Section 5.03, the Company shall deliver to the Purchaser a certificate or certificates representing the Option Shares registered in the name of the Purchaser.

(f) The Option may be transferred to any Affiliate of the Purchaser but is not otherwise transferable without the prior written consent of the Company.

(g) (i) In the event that, at any time following the exercise of the Option, the Company issues (a "Post-Option Issuance") any Out of the Money

Option Stock, it shall deliver written notice of such intention (the "Post-

Option Issuance Notice") to the Purchaser within 30 days after the date of such

Post-Option Issuance. The Post-Option Issuance Notice shall set forth the number of shares of Common Stock issued and the applicable Out of the Money Option Price.

(ii) In connection with each Post-Option Issuance, the Purchaser shall have the right (the "Post-Option Purchase Right") to purchase from the Company

at the Option Price the number of shares of Common Stock equal to 30 percent of the aggregate of the total number of shares of Out of the Money Option Stock issued in such Post-Option Issuance plus the number of shares of Common Stock to be issued to the Purchaser upon exercise of the Post-Option Purchase Right.

(iii) In the event that the Purchaser wishes to exercise its Post-Option Purchase Right, it shall deliver to the Company, within thirty days after the date of the Post-Option Issuance a written notice in which the Purchaser agrees to purchase at the Option Price the number of shares of Common Stock which the Purchaser is entitled to purchase upon exercise of the Post-Option Purchase Right.

SECTION 5.04. Purchaser's Preemptive Rights. (a) In the event that

the Company proposes to issue (a "Post-Determination Issuance") any New Voting

Securities, and such issuance will occur at any time following the date when the conversion price for the Shares has been determined in accordance with the Restated Articles of Incorporation (the "Conversion Determination Date"), it

shall deliver written notice of such intention (the "Post-Determination Issuance

Notice") to the Purchaser not less than 30 days prior to (i) the date of initial

filing of a registration statement, in the case of a Public Offering or (ii) the expected date of issuance,

in the case of any other Post-Determination Issuance. The Post-Determination Issuance Notice shall set forth in reasonable detail the terms of such Post-Determination Issuance, including, without limitation, (A) a description, and the number, of New Voting Securities proposed to be issued, (B) in the case of a Public Offering, the estimated price to the public, underwriting discount and commissions, expenses and underwriters of the Public Offering, (C) in the case of a Private Placement, the sales price, to the extent then known by the Company, and the identity of the proposed purchasers, and (D) in the case of a Non-Cash Transaction, a description of such transaction, including, without limitation, the consideration and the parties thereto. If information concerning the identity of proposed purchasers in a Private Placement becomes known to the Company subsequent to the delivery of the Post-Determination Issuance Notice, the Company shall, promptly after gaining such knowledge, deliver such information to the Purchaser in writing.

(b) In connection with each Post-Determination Issuance, the Purchaser shall have the right (the "Post-Determination Preemptive Right") to

purchase from the Company at the Applicable Preemptive Price simultaneously with, and otherwise upon the terms and subject to the conditions of, the Post-Determination Issuance up to the number of shares of Common Stock or other Voting Securities, as the case may be, necessary to permit the Purchaser to maintain the percentage of the outstanding Common Stock owned by the Purchaser and the percentage of Total Voting Power the Purchaser had, in each case, immediately prior to such Post-Determination Issuance (including, for purposes of calculating such percentage, all shares of Common Stock or other Voting Securities that the Purchaser has the right to acquire upon exercise of options or warrants, conversion or exchange of other securities or otherwise, if the Option has not yet been exercised, excluding the shares of Common Stock subject to the Option).

(c) In the event that the Purchaser wishes to exercise its Post-Determination Preemptive Right, it shall deliver to the Company, not later than ten days prior to the proposed date of the initial filing of the registration statement, in the case of a Public Offering, and the proposed date of issuance, in any other case, a written notice (a "Post-Determination Subscription Notice")

in which the Purchaser specifies the number of New Voting Securities which the Purchaser elects to purchase and in which the Purchaser agrees to purchase such specified number of New Voting Securities at the Applicable Preemptive Price subject to the same conditions as the Post-Determination Issuance.

(d) In the event that the Company issues (such issuance being a "Pre-Determination Issuance") any New Voting Securities during the period beginning

on the date hereof and ending on and including the Conversion Determination Date, then the Purchaser shall have the option (the "Pre-Determination

Preemptive Rights) to purchase from the Company at the Applicable Preemptive

Price for each such Pre-Determination Issuance up to the number of New Voting Securities issued in each such Pre-Determination Issuance equal to the Applicable Percentage. The "Applicable Percentage" means the greater of (i) the

percentage of outstanding Common Stock (including any other securities representing common equity) and (ii) the percentage of Total Voting Power, in either case that would have been held by the Purchaser if the Shares had been converted into shares of Common Stock immediately

prior to such Pre-Determination Issuance at the conversion price of the Shares on the Conversion Determination Date (including, for purposes of calculating such percentage, all shares of Common Stock or other Voting Securities that the Purchaser has the right to acquire upon exercise of options or warrants, conversion or exchange of other securities or otherwise, but if the Option has not yet been exercised, excluding the shares of Common Stock subject to the Option).

(e) In the event that the Purchaser wishes to exercise the Pre-Determination Preemptive Right, it shall deliver to the Company, at any time during the period commencing on the Conversion Determination Date and ending thirty days thereafter, a written notice in which the Purchaser specifies the number of New Voting Securities which the Purchaser elects to purchase and in which the Purchaser agrees to purchase such specified number of New Voting Securities at the Applicable Preemptive Prices. The closing of the purchase of New Voting Securities upon the Purchaser's exercise of the Pre-Determination Preemptive Right shall take place within five days of the receipt of the written notice referred to in the immediately preceding sentence.

SECTION 5.05. Company Put Option. (a) The Company may, at its

option, require the Purchaser to purchase (the "Company Option") in accordance

with the terms of this Section 5.05, Equity Securities in conjunction with either (i) the Initial Public Offering if the aggregate proceeds to the Company therefrom, net of underwriting discounts, commissions and other expenses, are not less than \$17.5 million in cash (including the purchase price payable by the Purchaser pursuant to this Section 5.05) (a "Qualifying IPO") or (ii) any

Private Placement of Equity Securities in which the proceeds to the Company, net of expenses, are not less than \$10 million in cash (including the purchase price payable by the Purchaser pursuant to this Section 5.05) (a "Qualifying Private

Placement").

(b) In the event that the Company wishes to exercise the Company Option, it shall deliver written notice of such exercise (the "Put Notice") to

the Purchaser not less than 30 days prior to (i) the closing date of a Qualifying Private Placement or (ii) the date of the filing with the Securities and Exchange Commission of a registration statement for the Qualifying IPO. Upon delivery of the Put Notice, the Purchaser shall be obligated to purchase from the Company, upon the same terms and subject to the same conditions as the underwriters in the case of a Qualifying IPO, and the other purchasers of Equity Securities in the case of a Qualifying Private Placement, the number of Equity Securities equal to not more than 25 percent of (x) the Equity Securities purchased by the underwriters (excluding Equity Securities purchased by such underwriters pursuant to any over-allotment option) in the case of a Qualifying IPO or (y) the Equity Securities purchased by other purchasers in the case of a Qualifying Private Placement.

(c) Notwithstanding any other provision of this Section 5.05 to the contrary, (i) the Purchaser shall not be required to purchase Equity Securities having an aggregate purchase price of more than \$5 million pursuant to the Company Option; (ii) the Purchaser shall not be required to purchase pursuant to the Company Option any Equity Securities being offered in conjunction with any securities other than Equity Securities; (iii) the Purchaser shall not be required to purchase Equity Securities if such purchase is prohibited by law, if any regulatory

approval required to effect any purchase of Equity Securities upon exercise of the Company Option cannot be obtained or during any waiting period under the HSR Act or during any other period in which regulatory approvals are sought by the parties hereto pursuant to Section 5.10, but such purchase shall take place as promptly as practicable after any requisite waiting period has passed and any required notification period has expired or been terminated, or such approval has been obtained; and (iv) the Purchaser shall not be required to purchase Equity Securities pursuant to the Company Option if the Company (A) becomes insolvent, (B) a bankruptcy petition is filed with respect to the Company or any of its Subsidiaries, (C) is adjudicated as a bankrupt pursuant to an involuntary petition in bankruptcy, (D) suffers appointment of a temporary or permanent receiver, trustee or custodian for its business or for all or part of its assets, where such appointment is not discharged within thirty days, (E) makes an assignment for the benefit of creditors, (F) is admitted to the benefits of any procedure for the settlement or postponement of debts, (G) becomes a party to dissolution proceedings or (H) takes any corporate action with respect to any of the foregoing.

(d) If the Company exercises the Company Option with respect to any Qualifying IPO or Qualifying Private Placement, the Purchaser shall have the right to purchase from the Company in connection with such Qualifying IPO or Qualifying Private Placement, in lieu of any rights granted to the Purchaser pursuant to Section 5.04, up to a number of Equity Securities equal to the greater of (i) forty percent of the Equity Securities sold in such Qualifying IPO or Qualifying Private Placement or (ii) the number of Equity Securities, if any, that the Purchaser would have had a right to acquire in accordance with Section 5.04, notwithstanding the Purchaser's right granted in this Section 5.05(d).

(e) In the event that the Purchaser wishes to exercise the right granted in Section 5.05(d), it shall deliver to the Company, not later than ten days prior to (i) the proposed date of the initial filing of the registration statement, in the case of a Qualifying IPO, or (ii) the closing date, in the case of a Qualifying Private Placement, a written notice in which the Purchaser specifies the number of New Voting Securities which the Purchaser elects to purchase and in which the Purchaser agrees to purchase such specified number of New Voting Securities upon the same terms and subject to the same conditions as the underwriters in the case of a Qualifying IPO, and the other purchasers of Equity Securities in the case of a Qualifying Private Placement. Such right must be exercised by the Purchaser in accordance with the procedures set forth in Section 5.04.

SECTION 5.06. Standstill Agreement. Until the earlier of (a) October __, 1998 or (b) the Purchaser's exercise of the Option in accordance with Section 5.03, the Purchaser shall not, without the prior approval of the Board, acquire, agree to acquire, or make any proposal to acquire, directly or indirectly any securities of the Company, except for the acquisition of shares of Common Stock upon conversion of the Shares and in accordance with Article V of this Agreement.

SECTION 5.07. Purchaser's Right of First Negotiation. If the Company receives any proposal concerning, or otherwise wishes to pursue, a merger, consolidation or other transaction in which all or a majority of the Company's equity securities or Voting Securities,

all or substantially all of the Company's assets, or any material portion of the assets used by the Company in performing its obligations under the Distribution Agreement would be acquired outside of the ordinary course of business of the Company by any Person (a "Business Combination"), the Company shall deliver

written notice (a "Business Combination Notice") of such proposal or intention

to the Purchaser, in the case of a proposal, setting forth the terms of the proposal in reasonable detail. Upon receipt of a Business Combination Notice, the Purchaser shall have the exclusive right to negotiate with the Company concerning a Business Combination, which right shall expire (such period being the "Exclusivity Period") upon the earliest to occur of (a) the thirtieth day

following the commencement of the Exclusivity Period if the Purchaser shall have failed to commence good faith negotiations with the Company with respect to a Business Combination during such thirty day period, (b) either the Purchaser or the Company shall, following such thirty-day period, notify the other that it has reasonably determined that continued negotiations are unlikely to result in a Business Combination and (c) on the 120th day following the date of the Business Combination Notice if the Purchaser and the Company fail to enter into a definitive agreement to effect a Business Combination within such 120 day period. During the Exclusivity Period, the Company shall not engage in any discussions, negotiations, arrangements or understandings with, or provide any non-public or confidential information to, any Person other than the Purchaser with respect to a Business Combination. The Company and the Purchaser agree that all communications between the parties during the Exclusivity Period will be kept strictly confidential and the contents of those communications will not be disclosed to any other person except as, and to the extent, required by applicable law. For one year following the Exclusivity Period, the Company may only enter into a Business Combination with a Person other than the Purchaser if the terms of the Business Combination with such other Person, taken as a whole, are more favorable to the Company and its stockholders than the most favorable terms of a Business Combination proposed to the Company by the Purchaser during the Exclusivity Period.

SECTION 5.08. Legend. The Purchaser agrees that all certificates

representing the Shares and the shares of Common Stock to be issued upon conversion of the Shares or pursuant to this Article V shall bear the following legend:

"THE SHARES REPRESENTED BY THIS CERTIFICATE HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED, OR SECURITIES LAWS OF ANY STATE AND NEITHER THE SECURITIES NOR ANY INTEREST THEREIN MAY BE SOLD OR OTHERWISE TRANSFERRED IN THE ABSENCE OF SUCH REGISTRATION OR AN EXEMPTION THEREUNDER."

The Purchaser agrees to comply with the foregoing transfer restriction legend; and the Purchaser acknowledges that a transfer restriction will be maintained by the Company's stock transfer agent. The legend set forth in this Section 5.08 shall be removed by delivery of substitute certificate(s) without such legend if the Purchaser shall have delivered to the Company an opinion of counsel (it being agreed that Shearman & Sterling shall be deemed satisfactory) in form and substance reasonably satisfactory to the Company and its counsel, to the effect that such legend is not required for purposes of compliance with the Securities Act.

SECTION 5.09. Board Observer; Board Representation. (a) During the

period (such period being the "Observation Period") commencing on the

Purchaser's acquisition of any Equity Securities pursuant to Section 5.05 and ending on the earlier to occur of (i) the Purchaser's exercise of the Option and (ii) the Purchaser's sale of any of such Equity Securities acquired pursuant to Section 5.05, the Purchaser shall be entitled to have present at all meetings of the Board one Person designated by the Purchaser and reasonably acceptable to the Company (the "Purchaser Observer"). During the Observation Period, the

Company (i) shall deliver notice of all meetings of the Board to the Purchaser Observer simultaneously with, and in the same form as, notice to the directors of the Company and (ii) shall deliver to the Purchaser copies of all written materials furnished to the Board simultaneously with the delivery of such written materials to the Board.

(b) From and after the Purchaser's exercise of the Option, (i) the Purchaser shall have the right to designate a percentage of directors of the Company (such persons being the "Purchaser Designees") equal to the percentage

of outstanding shares of Common Stock, on a fully diluted basis, owned by the Purchaser, rounded down to the next whole number, and (ii) at least one Purchaser Designee shall be a member of each Committee of the Board as long as the Purchaser owns at least 25% of the outstanding shares of Common Stock; provided, however, that if at any time following such exercise of the Option,

but only for so long as the Purchaser continues to own a majority of the outstanding shares of Common Stock, the Purchaser owns a majority of the outstanding shares of Common Stock, the Purchaser Designees shall constitute a majority of the directors of the Company and a majority of the members of each Committee of the Board. The Company agrees to take all action permitted by the MBCA necessary to cause the Purchaser Designees to become members of the Board. If the Board is divided into more than one class, the Purchaser Designees shall be distributed as equally as possible among such classes.

(c) The Board shall recommend to the stockholders of the Company for election the Purchaser Designees who are nominated by the Company to serve as members of the Board, and the Company shall use its reasonable best efforts to solicit proxies from stockholders to vote in favor of such Purchaser Designees. In the event that a vacancy is created on the Board at any time by the death, disability, retirement, resignation or removal (with or without cause) of a Purchaser Designee, the Purchaser shall cause such Purchaser Designee to be elected to the Board to fill such vacancy.

SECTION 5.10. Regulatory Approvals. If the Purchaser's acquisition

of any of the shares of Common Stock or Voting Securities subject to issuance pursuant to this Agreement (including, without limitation, the Common Stock or Voting Securities issuable upon conversion of the Preferred Stock or pursuant to Article V of this Agreement), requires approval of, or prior notification to, any regulatory authority pursuant to the HSR Act or otherwise, the Purchaser shall promptly file the required application for approval or notice and shall expeditiously process such notice or application, as the case may be, and the Company shall use all reasonable efforts to cooperate with the Purchaser in the filing of any such notice or application and the obtaining of any such approval. If the closing of the acquisition of shares of Common Stock or Voting Securities pursuant to this Article V cannot be consummated by reason of any applicable judgment, decree, order, law or regulation, such Closing shall take

place as promptly as practicable after the date on which such restriction has expired or been terminated; without limiting the foregoing, if prior approval of, notification to or filing with, any regulatory authority is required pursuant to the HSR Act or otherwise, such closing shall take place as promptly as practicable after any requisite waiting period has passed and any required notification period has expired or been terminated, or such approval has been obtained.

SECTION 5.11. Reservation of Shares. The Company shall at all times

reserve and keep available, free from preemptive rights (other than those of the Purchaser), out of its authorized and unissued Common Stock and Voting Securities the number of shares of Common Stock and Voting Securities subject to issuance upon conversion of the Shares

(the "Reserve Amount"). The Company shall not take any corporate action which

would require an adjustment in the number of shares of Common Stock and Voting Securities, unless either (i) immediately after such corporate action is taken and the transactions contemplated thereby are consummated, the number of authorized and unissued shares of Common Stock would equal or exceed the Reserve Amount, or (ii) concurrently with the taking of such corporate action, the Company shall take such corporate action as may be necessary to increase its authorized and unissued shares of Common Stock to such number as shall equal or exceed the Reserve Amount. The Company shall from time to time as necessary to fulfill the commitments made in this Article V authorize and make available, free from preemptive rights (other than those of the Purchaser), the number of shares of Common Stock and Voting Securities subject to issuance pursuant to this Article V.

SECTION 5.12. Voting Rights; Rights Plan. (a) The Company shall not

take any action to amend the By-Laws or Restated Articles of Incorporation so as to make Chapter 7B of the MBCA, or any successor thereto, applicable to any acquisition of shares of Common Stock or other Voting Securities by the Purchaser. In the event that the Restated Articles are amended so as to make Chapter 7B of the MBCA, or any successor thereto, applicable to any acquisition of shares of Common Stock or other Voting Securities by the Purchaser, the Company shall take such actions as shall be necessary and permitted by the MBCA so that (a) the shares of Common Stock or other Voting Securities that the Purchaser is entitled to acquire upon conversion of the Shares or pursuant to Article V hereof will, upon such issuance, and (b) the Shares will, in accordance with their terms, be duly accorded full voting rights. The Company shall use its best efforts, including the solicitation of votes by proxy, to obtain such votes of shareholders of the Company as shall be necessary to accord the Purchaser with such full voting rights.

(b) The Company shall not adopt a shareholder rights plan, enter into any agreement, arrangement or understanding or grant any warrants, options, rights or any other privileges which, upon acquisition by the Purchaser of shares of Common Stock or other Voting Securities upon conversion of the Shares or pursuant to Article V hereof, would result in the Purchaser, in its capacity as a holder of such securities, being subject to different rights and obligations as all other holders of Common Stock or Voting Securities, as a result of such acquisition.

SECTION 5.13. Survival of Representations and Warranties. The

representations and warranties of the Company in Article III and the Purchaser in Article IV shall survive the

Closing until October , 1996.

SECTION 5.14. Company's Right of First Negotiation. If the Purchaser

elects to pursue a sale of all of the Company's Equity Securities and Voting
Securities acquired pursuant to this Agreement (a "Purchaser's Equity Sale"),

the Purchaser shall deliver written notice (a "Purchaser's Equity Sale Notice")

of such intention to the Company. Upon receipt of a Purchaser's Equity Sale
Notice, the Company shall have the exclusive right to negotiate with the
Purchaser concerning a Purchaser's Equity Sale, which right shall expire upon
the thirtieth day following the receipt of such notice. The Company and the
Purchaser agree that all communications between the parties during such period
will be kept strictly confidential and the contents of those communications will
not be disclosed to any other person except as, and to the extent, required by
applicable law.

ARTICLE VI

TERM, TERMINATION, AMENDMENT AND WAIVER

SECTION 6.01. Term. Unless otherwise terminated by a written

instrument executed by each of the Company and the Purchaser, this Agreement
shall be in full force and effect until the expiration or termination of the
Distribution Agreement in accordance with the terms thereof, whereupon the
rights and obligations of the parties under this Agreement shall terminate.

SECTION 6.02. Amendment. This Agreement may not be amended or

modified except by an instrument in writing signed by each of the parties
hereto.

SECTION 6.03. Waiver. Either party hereto may (a) waive any

inaccuracies in the representations and warranties contained herein or in any
document delivered pursuant hereto and (b) waive compliance with any of the
agreements contained herein. Any such extension or waiver shall be valid if set
forth in an instrument in writing signed by the party to be bound thereby. The
failure of either party to assert any of its rights hereunder shall not
constitute a waiver of any such rights.

ARTICLE VII

GENERAL PROVISIONS

SECTION 7.01. Notices. All notices, requests, claims, demands and

other communications hereunder shall be in writing and shall be given (and shall
be deemed to have been duly given upon receipt) by delivery in person, by cable,
telecopy, telegram or telex or by registered or certified mail (postage prepaid,
return receipt requested) to the respective parties at the following addresses
(or at such other address for a party as shall be specified by like notice):

(a) if to the Purchaser:

Cobe Laboratories, Inc.
1185 Oak Street
Lakewood, Colorado 80215
Attention: Edward Wood
Telecopy: (303) 231-4160

with a copy to:

Shearman & Sterling
599 Lexington Avenue
New York, New York 10022
Attention: Peter D. Lyons, Esq.
Telecopy: (212) 848-7179

(b) if to the Company:

Aastrom Biosciences, Inc.
P.O. Box 376 - (Mail)
Ann Arbor, Michigan 48105
Dominos Farms, Lobby L - (Direct Delivery)
Attention: R. Douglas Armstrong, Ph.D.
President and Chief Executive Officer
Telecopy: (313) 665-0485

with a copy to:

Gray, Cary, Ames & Frye
401 B Street, Suite 1700
San Diego, California 92101
Attention: T. Knox Bell, Esq.
Telecopy: (619) 236-1048

SECTION 7.02. Entire Agreement; Assignment. This Agreement

constitutes the entire agreement between the parties with respect to the subject matter hereof and supersedes all prior agreements and undertakings, both written and oral, between the parties with respect to the subject matter hereof. This Agreement shall not be assigned by operation of law or otherwise, other than by the Purchaser to its Affiliates (in which event the Purchaser shall continue to remain fully liable under this Agreement), without the express written consent of the Purchaser and the Company (which consent may be granted or withheld in the sole discretion of the Company or the Purchaser). Any assignment to an Affiliate of the Purchaser shall not become effective until such Affiliate has agreed to be bound by the terms of this Agreement.

SECTION 7.03. Parties in Interest. This Agreement shall be binding

upon and inure solely to the benefit of each party hereto and in Exhibit 5.02, and nothing in this

Agreement, express or implied, is intended to or shall confer upon any other Person any rights, benefits or remedies of any nature whatsoever under or by reason of this Agreement.

SECTION 7.04. Governing Law. This Agreement shall be governed by,

and construed in accordance with, the laws of the State of New York applicable to contracts executed in and to be performed entirely within that state.

SECTION 7.05. Headings. The descriptive headings contained in this

Agreement are included for convenience of reference only and shall not affect in any way the meaning or interpretation of this Agreement.

SECTION 7.06. Severability. If any term or other provision of this

Agreement is invalid, illegal or incapable of being enforced by any law, rule, regulation or public policy, all other terms and provisions of this Agreement shall nevertheless remain in full force and effect so long as the economic or legal substance of the transactions contemplated hereby is not affected in any manner materially adverse to any party. Upon such determination that any term or other provision is invalid, illegal or incapable of being enforced, the parties hereto shall negotiate in good faith to modify this Agreement so as to effect the original intent of the parties as closely as possible in an acceptable manner in order that the transactions contemplated hereby are consummated as originally contemplated to the greatest extent possible.

SECTION 7.07. Counterparts. This Agreement may be executed in one or

more counterparts, and by the different parties hereto in separate counterparts, each of which when executed shall be deemed to be an original but all of which taken together shall constitute one and the same agreement.

SECTION 7.08. Specific Performance. The parties hereto agree that

irreparable damage would occur in the event any of the provisions of this Agreement were not to be performed in accordance with the terms hereof and that the parties shall be entitled to specific performance of the terms hereof, in addition to any other remedy at law or equity.

SECTION 7.09. WAIVER OF TRIAL BY JURY. THE PURCHASER AND THE COMPANY

HEREBY WAIVE ALL RIGHT TO TRIAL BY JURY IN ANY ACTION, PROCEEDING, OR
COUNTERCLAIM (WHETHER BASED UPON CONTRACT, TORT OR OTHERWISE) RELATED TO THIS
AGREEMENT OR THE TRANSACTIONS CONTEMPLATED HEREBY.

IN WITNESS WHEREOF, the Purchaser and the Company have each caused
this Agreement to be executed by its duly authorized officer as of the date
first written above.

COBE LABORATORIES, INC.

By: /s/ MATS WAHLSTROM

Name: Mats Wahlstrom
Title: President

AASTROM BIOSCIENCES, INC.

By: /s/ R. DOUGLAS ARMSTRONG

Name: R. Douglas Armstrong
Title: President and
Chief Executive Officer

AMENDMENT TO STOCK PURCHASE AGREEMENT

This Amendment is entered into as of October 29, 1996 by and between Cobe Laboratories, Inc., a Colorado corporation (the "Purchaser") and Aastrom Biosciences, Inc., a Michigan corporation (the "Company") with respect to that certain Stock Purchase Agreement between the Purchaser and the Company, dated as of October 22, 1993 (the "Stock Purchase Agreement").

1. Pursuant to Section 5.04 of the Stock Purchase Agreement, the Purchaser has certain preemptive rights to purchase additional capital stock of the Company. Pursuant to Section 5.05 of the Stock Purchase Agreement, the Company has a "put option" to require the Purchaser to purchase certain additional capital stock in the Company.

2. As specified in the definition set forth in the Stock Purchase Agreement, the "Applicable Preemptive Price" for the Purchaser to pay for purchasing the Company's capital stock in a public offering of stock by the Company is the public offering price, less underwriting discounts and commissions (e.g., a 7% underwriter's discount).

3. If the Company exercises its "put option" as specified in Section 5.05 of the Stock Purchase Agreement, the price per share payable by the Purchaser is the public offering price per share, less underwriting discounts and commissions (e.g., a 7% underwriter's discount).

4. The Purchaser and the Company hereby amend the Stock Purchase Agreement, and particularly the sections referenced above, so as to provide for the Purchaser to pay the same purchase price per share as is paid by a public purchaser in the public stock offering, if and when the Purchaser purchases capital stock of the Company pursuant to Section 5.04 and/or 5.05 pursuant to a public stock offering, without the Purchaser being entitled to a price discount for the underwriter's discounts or commissions. This foregoing amendment applies only to capital stock purchased by the Purchaser from the Company at the time of the Company's initial public offering of stock.

5. The Purchaser is agreeing to the foregoing modifications to the stock purchase price in consideration and recognition of the terms in that certain Stock Purchase Agreement (for Series F Preferred stock) between the Purchaser and the Company, and other good and valuable consideration, receipt of which is hereby acknowledged by the Purchaser.

6. Terms defined in the Stock Purchase Agreement shall have the same meaning in this Amendment.

7. Excepting only as otherwise set forth above, all other terms and provisions of the Stock Purchase Agreement shall remain in full force and effect.

IN WITNESS WHEREOF, the Company and the Purchaser each have caused this Amendment to be executed by its duly authorized officer as of date first written above.

COBE LABORATORIES, INC.

By: /s/ Edward C. Wood

AASTROM BIOSCIENCES, INC.

By: /s/ R. Douglas Armstrong

DISTRIBUTION AGREEMENT

Between

COBE BCT, INC.

and

AASTROM BIOSCIENCES, INC.

Dated as of October 22, 1993

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DISTRIBUTION AGREEMENT

DISTRIBUTION AGREEMENT dated as of October 22, 1993 between AASTROM BIOSCIENCES, INC., a Michigan corporation (the "Supplier"), and COBE BCT, INC., a Colorado corporation (the "Distributor").

W I T N E S S E T H:

WHEREAS, the Supplier wishes to create, develop and manufacture and supply Products (as defined below) and to have the Products marketed worldwide;

WHEREAS, the Distributor wishes to sell, market and distribute the Products worldwide; and

WHEREAS, the Supplier wishes that the Distributor distribute the Products worldwide;

NOW, THEREFORE, in consideration of the premises and mutual covenants and agreements hereinafter set forth, the Supplier and the Distributor agree as follows:

ARTICLE I

DEFINITIONS

SECTION 1.01. Definitions. As used in this Agreement, the following terms shall have the following meanings:

"ACL" has the meaning specified in Section 2.04(b).

"Actual International Direct Sales" means for any Direct Sales Country

the unit Sales of any of the Products other than Spare Parts by the Distributor to Stem Cell Therapy Customers in such Direct Sales Country in which the purchase price is due and payable in cash from the purchaser of such Products substantially contemporaneously with (i.e., within 60 days of) such Sales in

such Country expressed in the official currency unit of such Country.

"Actual International Direct Sales Amount" for any Product in any

Direct Sales Country for any calendar month means the Actual International Direct Sales of such Product during such month in such Country multiplied by the greater of (a) the Average International Direct Selling Price for such Product for such Country and (b) the Minimum International Direct Selling Price for such Product for such Country expressed in the official currency unit of such Country.

"Actual Subdistributor Sales" means the unit Sales of the Products

other than Spare Parts by the Distributor to Subdistributors outside the United States (other than Direct Sales Countries) in which the purchase price is due and payable in cash from the purchaser of such Products substantially contemporaneously with (i.e., within 60 days of) such Sales.

"Actual Subdistributor Sales Amount" for any Product for any calendar

month means the Actual Subdistributor Sales of such Product during such month multiplied by the greater of (a) the Average Subdistributor Selling Price for such Product and (b) the Minimum Subdistributor Selling Price for such Product.

"Average Subdistributor Selling Price" means, for any Product for any

calendar month, the aggregate selling price, net of any applicable discounts, less any payments made to Subdistributors, of Actual Subdistributor Sales divided by the quantity of such Product sold during such calendar month.

"Affiliate" means (a) with respect to the Distributor, any Person

other than the Distributor (i) that is controlled, either directly or indirectly, by Investment AB Cardo, (ii) for which a Person controlled, either directly or indirectly, by Investment AB Cardo is the principal manager, or (iii) in which Investment AB Cardo has an equity ownership interest of ten percent or more; and (b) with respect to the Supplier, any Person other than the Supplier (i) that is controlled, either directly or indirectly, by the Supplier, (ii) for which the Supplier is the principal manager or (iii) in which the Supplier has an equity ownership interest of ten percent or more.

"Affiliate Sales" has the meaning specified in Section 2.01(d).

"Agreement" or "this Agreement" means this Distribution Agreement

dated as of October 22, 1993 between the Supplier and the Distributor (including the schedules hereto) and all amendments, modifications and supplements made in accordance with Section 10.01 hereof.

"Average International Direct Selling Price" means, for any Product in

any Direct Sales Country for any calendar month, the aggregate selling price, net of all applicable discounts, less any payments made to Subdistributors (all expressed in the official currency of such Country), of all Actual International Direct Sales of such Product in such Country during such calendar month, divided by the quantity of such Product sold during such calendar month in such Country expressed in the official currency unit of such Country.

"Base Term" has the meaning specified in Section 7.01.

"BIU" has the meaning specified in Section 2.01(a)(i).

"Change of Use" has the meaning specified in Section 2.04(a).

"Co-Marketing Arrangement" has the meaning specified in Section

7.05(b).

"Competitive Product" means any product (other than the Distributor's

Products) that competes with the Products for use by the same Customer such that the Customer might use such product instead of any of the Products.

"Complete System Sale" means the Sale by the Distributor to one or

more Stem Cell Therapy Customers of all of the Products specified in (i), (iii), (vii), (x) and (xi) of Section 2.01(a) at such time as all of the Products specified in (ii), (v), (vi), (viii) and (ix) of Section 2.01(a) are generally available for purchase by Customers and have been delivered to the Distributor or in the Distributor's reasonable judgment, are available for delivery, to the Distributor.

"Confidential Information" means all confidential or secret data,

reports, interpretations, forecasts, records, marketing, sales and other commercial data or reports, trade secret information, know-how methods, procedures, designs, technology, inventions, ideas, specifications, plans, patent applications and related correspondence, or other information that the parties hereto provide to each other in connection with this Agreement, together with analyses, compilations, studies or other documents, whether prepared by their respective agents or attorneys, which contain or otherwise reflect such information; provided, however, that the following shall not constitute

Confidential Information for purposes of this Agreement:

(a) information which was in one of such parties' possession prior to its receipt from the other of such parties;

(b) information which is obtained by one of such parties from a third person who, insofar as is known to such party, is not prohibited from transmitting the information to such party by a contractual, legal or fiduciary obligation to the other of such parties; and

(c) information which is or becomes publicly available through no fault of either of such parties.

"Control" (including the terms "controlled by" and "under common

control with"), with respect to the relationship between or among two or more

Persons, means the possession, directly or indirectly or as trustee or executor, of the power to direct or cause the direction of the affairs or management of a Person, whether through the ownership of voting securities, as trustee or executor, by contract or otherwise, including, without limitation, the ownership, directly or indirectly, of securities having the power to elect a majority of the board of directors or similar body governing the affairs of such Person.

"Customer" means any party to whom Products are sold or reasonably are expected to be sold. Different units within a single Person (e.g., a blood bank, an apheresis center, a transplant center) will be considered separate Customers for purposes of this Agreement if each such unit has the primary decision-making authority for the purchase of the Products, notwithstanding the fact that payment for the Products may be issued by the same Person.

"Customer License" has the meaning specified in Section 2.01(a).

"Customer Service Information" has the meaning specified in Section 2.04(b).

"Deductible" has the meaning specified in Section 3.09(b).

"Deemed International Direct Sales" means, for any Product (other than Spare Parts) in any Direct Sales Country for any calendar month, the aggregate unit sales of such Product by the Distributor to Stem Cell Therapy Customers, other than Actual International Direct Sales.

"Deemed International Direct Sales Amount" for any Direct Sales Country calendar month means the Deemed International Direct Sales of each Product in any Direct Sales Country during such calendar month multiplied by the greater of (a) the Average International Direct Selling Price for such Product in such Direct Sales Country and (b) the Minimum International Direct Selling Price for such Product for any Direct Sales Country expressed in the official currency unit of such Country.

"Deemed Subdistributor Sales" means, for any Product (other than Spare Parts) for any calendar month, the aggregate unit Sales of such Product by the Distributor, other than Actual Subdistributor Sales.

"Deemed Subdistributor Sales Amount" for any calendar month means the Deemed Subdistributor Sales of each Product during such calendar month multiplied by the greater of (a) the Average Subdistributor Selling Price for such Product and (b) the Minimum Subdistributor Selling Price for such Product.

"Direct Sales Countries" has the meaning specified in Section 2.02(c).

"Disposables" has the meaning specified in Section 2.01(a).

"Distributor" has the meaning set forth in the preamble to this Agreement.

"Distributor Customer Service Information" has the meaning specified in Section 2.04(b).

"Distributor Indemnified Person" has the meaning specified in Section

4.12.

"Distributor's Notice of Breach" has the meaning specified in Section

7.02.

"Distributor's Products" means (i) the Spectra Apheresis System, (ii)

the 2991 Blood Cell Processor, (iii) stem cell freezing solutions and protocols,
(iv) immunological tumor purging systems that do not provide for positive
selection of stem cells, (v) all improvements or enhancements to any of the
foregoing and (vi) any

successor product to any of the foregoing that is not a Competitive Product.

"Equipment" has the meaning specified in Section 2.01(a).

"Excess Payments" has the meaning specified in Section 4.09.

"Exchange Rate" means, with respect to any Direct Sales Country for

any calendar month the average monthly market rate at which the official
currency unit of such Country is exchangeable into one U.S. dollar.

"FDA" means the United States Food & Drug Administration.

"Fiscal Year" means any fiscal year ended June 30.

"Growth Medium" has the meaning specified in Section 2.01(a).

"Infringement" has the meaning specified in Section 3.05.

"Intellectual Property Rights" means any rights to any patents, patent

rights, copyrights, trademarks, service
marks, trade names, trademark rights, trade name rights or trade secrets.

"International Direct Monthly Purchase Price" has the meaning

specified in Section 5.02(c).

"International Direct Products" means the Products other than Spare

Parts sold by the Distributor to Stem Cell Therapy Customers in Direct Sales
Countries.

"IP Enforcement Actions" has the meaning specified in Section 3.05.

"IP Enforcement Costs" has the meaning specified in Section 3.05.

"Joint Registration" has the meaning specified in Section 4.07.

"License" has the meaning specified in Section 7.07(a).

"Market Development Program" means the program attached hereto as

Schedule B, to promote and market the Products, as such program may be modified and amended from time to time in accordance with Section 2.04 hereof.

"Milestone Fees" has the meaning specified in Section 5.03(c).

"Minimum Direct International Selling Price" means, for each Product

in each Direct Sales Country, the minimum direct international selling price for such Product in such Country expressed in the official currency unit of such Country.

"Minimum Subdistributor Selling Price" means, for each Product, the

minimum selling price to Subdistributors for such Product.

"Monetary Breach" has the meaning specified in Section 7.03.

"Monthly Parts Purchase Price" has the meaning specified in Section

5.02(e).

"Monthly Purchase Price" means the sum of the U.S. Monthly Purchase

Price, the International Direct Monthly Purchase Price for each Direct Sales Country, the Monthly Parts Purchase Price and the Subdistributor Purchase Price.

"Monthly Report" has the meaning specified in Section 5.03.

"Notice of Breach" has the meaning specified in Section 7.02.

"Objection" has the meaning specified in Section 7.04.

"Party" means a party to this Agreement.

"Permitted Clinical Research Applications" means any clinical or

therapeutic use of the Products for any clinical research or trial that is expected to result in a new application of, or a new FDA-approved indication for, the Products.

"Person" means any individual, partnership, firm, corporation,

association, trust, unincorporated organization or other entity, as well as any syndicate or group that would be deemed to be a person under Section 13(d)(3) of the Securities Exchange Act of 1934, as amended.

"Plan" has the meaning specified in Sections 2.03(e) and (f).

"Policy" has the meaning specified in Section 3.09(a).

"Premiums" has the meaning specified in Section 3.09(a).

"Pricing Information" has the meaning specified in Section 4.11.

"Principal Components of the Market Development Program" has the

meaning specified in Section 2.03(f).

"Principal Components of the Product Development Program" has the

meaning specified in Section 2.03(e).

"Principal Objection" has the meaning specified in Section 2.04(b).

"Product Development Program" means the program attached hereto as

Schedule A, for the design, creation, validation, manufacture and release of the
Products, as such program may be modified and amended from time to time in
accordance with Section 2.04 hereof.

"Products Liability Cap" has the meaning specified in Section 4.09.

"Product Liability Claims" has the meaning specified in Section

3.09(a).

"Products" has the meaning specified in Section 2.01(a).

"Programs" means, collectively, the Market Development Program and the

Product Development Program.

"Purchased Spare Parts" has the meaning specified in Section 5.02(e).

"Retaliatory IP Claims" has the meaning specified in Section 3.05(a).

"Sale" and any grammatical variant thereof means any sale, conditional

sale, installment sale, rental, lease or other arrangement whereby the Products
are placed at the disposal of a Customer in exchange for value received or to be
received.

"Sales Threshold" means (x) \$60 million in any Fiscal Year up to and

including 1998, (y) \$125 million in the Fiscal Year 1999 and (z) \$200 million in
the Fiscal Year 2000 and thereafter.

"SCTIP Rights" has the meaning specified in Section 3.05.

"Sixth Insurance Year" has the meaning specified in Section 4.09.

"Solutions" has the meaning specified in Section 2.01(a).

"Spare Parts" has the meaning specified in Section 2.01(a)(ix).

"Stem Cell Therapy Applications" means applications of the Products

pursuant to which human bone marrow or peripheral blood derived stem and
hematopoietic cells are used primarily for one or more of the following: (a)
restoration of hematopoietic function; (b) augmentation of the recovery of a
previously damaged hematopoietic system; and (c) augmentation of the recovery of

previously damaged bone marrow; provided, however, that such cells have not been

altered through the introduction of a new genetic component. Notwithstanding
anything in this Agreement to the contrary, Stem Cell Therapy Applications shall
not include any of the following applications of the Products: (i) all
diagnostic or other non-therapeutic clinical applications; (ii) all gene therapy
or gene transfer applications; (iii) all non-human applications; (iv) all
Permitted Clinical Research applications; and (v) all applications in which the
Products are labelled not for human use.

"Stem Cell Therapy Customers" means Customers who perform, or are

reasonably expected to perform, Stem Cell Therapy Applications.

"Subdistributor Monthly Purchase Price" has the meaning specified in

Section 5.02(b).

"Subdistributor Products" means Products other than Spare Parts sold

by the Supplier to the Distributor for resale and distribution to
Subdistributors in countries outside of the United States (other than Direct
Sales Countries).

"Subdistributors" has the meaning specified in Section 2.02(a).

"Supplier" has the meaning set forth in the preamble to this

Agreement.

"Supplier Customer Service Information" has the meaning specified in

Section 2.04(b).

"Supplier Deficiency" has the meaning specified in Section 4.09.

"Supplier Indemnified Person" has the meaning specified in Section

3.08.

"Supplier Products Liability Payments" has the meaning specified in

Section 4.09.

"Supplier's New Products" has the meaning specified in Section

2.01(f).

"Supplier's Notice of Breach" has the meaning specified in Section

7.02.

"Supplier's Other Products" means the Supplier's products (other than

the Products) that utilize some or all of the Products as components and that
are not Competitive Products.

"Supplier Products Liability Payments" has the meaning specified in

Section 4.09.

"Supplier's Share" has the meaning specified in Section 4.10.

"Target Prices" has the meaning specified in Section 2.03(f).

"Upcharges" means amounts included in the Distributor's selling price

for Actual U.S. Sales, Actual International Direct Sales, or the Actual Subdistributor Sales of Disposables to a Stem Cell Therapy Customer (in the case of Actual U.S. Sales and Actual International Direct Sales) or to a Subdistributor (in the case of Actual Subdistributor Sales) in any calendar month that reflect the Distributor's depreciation of, and interest on, Equipment or rental, lease or other deferred payments for Equipment, where the value of such Equipment previously has been included in one of the formulae set forth in Section 5.02(a), (b), or (c) in Deemed U.S. Sales, Deemed International Direct Sales or Deemed Subdistributor Sales, respectively.

"Unreimbursed Losses" has the meaning specified in Section 3.09(b).

"U.S. Monthly Purchase Price" has the meaning specified in Section 5.02(a).

"U.S. Products" means the Products other than Spare Parts sold by the Distributor to Stem Cell Therapy Customers in the United States.

"Worldwide Sales" means the sum of the (i) Deemed International Sales Amount, (ii) Deemed U.S. Sales Amount, (iii) Deemed Subdistributor Sales Amount, (iv) Actual International Direct Sales, (v) Actual U.S. Sales and (vi) Actual Subdistributor Sales.

ARTICLE II

APPOINTMENT AS DISTRIBUTOR

SECTION 2.01. Appointment and Acceptance; Products; Exclusivity;

Affiliate Sales. (a) The Supplier hereby appoints the Distributor, and the

Distributor hereby accepts appointment, in each case on the terms and subject to the conditions of this Agreement, as the Supplier's worldwide distributor for Stem Cell Therapy Applications of the following products, or such alterations to, or replacements for, such products as may be developed in accordance with the Product Development Program (collectively, the "Products"):

(i) a biochamber incubation unit (a "BIU") that controls the biological and physical environment during the expansion process;

(ii) a BIU monitor module that provides a central display, an operator input device and a printer;

(iii) an inoculation and harvest unit that facilitates the initial filling and inoculation of cells, as well as the final harvest of cells at the completion of the expansion process;

(iv) a system rack to integrate conveniently the multiple biochamber and incubation units with the companion monitor modules (together with the products described in (i), (ii) and (iii) above and the improvements and enhancements hereto and thereto, the "Equipment");

(v) an incubation and growth medium required by the cell culture, which shall include to the extent required, growth factors, glutamine, antibiotics, serums and other substances ("Growth Medium");

(vi) harvest reagents which facilitate the removal of the expanded cells from the biochamber (together with the Growth Medium and all improvements and enhancements hereto and thereto, the "Solutions");

(vii) a disposable biochamber cartridge where the growth and expansion of cells takes place (together with all improvements and enhancements hereto and the Solutions, the "Disposables");

(viii) all improvements and enhancements to the products described in (i) through (vii) above;

(ix) spare parts for the Equipment ("Spare Parts");

(x) a license for the use of such products solely for Stem Cell Therapy Applications (the "Customer License"); and

(xi) instructions for the use of each of such products, other than the Customer License.

(b) Except as provided in Section 2.01(d), the Distributor and each Subdistributor shall sell the Products only in conjunction with Customer Licenses.

(c) Except as otherwise specifically provided in this Section 2.01 and in Sections 4.01(b) and 7.05(b), the Supplier shall not (i) authorize any Person other than the Distributor to act as a distributor of any of the Products (or any product that includes any Product as a component) to, or for resale to, Customers whose predominant use of the Products is, or reasonably is expected to be, for Stem Cell Therapy Applications or (ii) market, promote, Sell or distribute any of the Products (or any product that includes any Product as a component), directly or indirectly, to, or for resale to, any Stem Cell Therapy Customer.

(d) Notwithstanding any provision of this Agreement to the contrary, the Supplier may Sell the Products to its Affiliates for Stem Cell Therapy Applications by such Affiliates, but not for resale to Persons which are not Affiliates of the Supplier, and may make such Sales with a license for use of the Products for Stem Cell Therapy Applications, and the Distributor may Sell the Products to its Affiliates for applications other than Stem Cell Therapy Applications by such Affiliates, but not for resale to Persons which are not Affiliates of the Distributor, and

may make such Sales with a license for use of the Products for applications other than Stem Cell Therapy Applications (such Sales by either the Distributor or the Supplier being "Affiliate Sales"). If the aggregate purchase price

received by the Supplier for all its Affiliate Sales during any fiscal year exceeds five percent of the Worldwide Sales during such Fiscal Year, the Supplier shall pay to the Distributor, within 90 days after the end of such Fiscal Year, cash in an amount equal to thirty percent of the excess of such aggregate purchase price over the amount equal to five percent of Worldwide Sales during such fiscal year. If the aggregate purchase price received by the Distributor for all its Affiliate Sales during any calendar year exceeds five percent of the aggregate purchase price received by the Supplier for Sales of the Products during such Fiscal Year to Customers that are not Stem Cell Therapy Customers, the Distributor shall pay to the Supplier, within 90 days after the end of such Fiscal Year, cash in an amount equal to ninety percent of the excess of such aggregate purchase price over the amount equal to five percent of such Sales by the Supplier. All calculations pursuant to this Section 2.03(d) of the aggregate purchase price received by the Supplier or the Distributor shall be made in accordance with the calculation of Worldwide Sales. The Supplier and the Distributor shall, promptly following the end of each fiscal year, make available to each other such information as is reasonably necessary to audit the Affiliate Sales of the other party.

(e) The Supplier expressly reserves the right to market, sell and distribute (either directly or through its designees) (i) the Products to its Affiliates for Stem Cell Therapy Applications as provided in Section 2.03(d), (ii) the Products to any Customer for applications other than Stem Cell Therapy Applications, and (iii) the Supplier's Other Products to any Customer for any application. Except as provided in Section 2.03(d), the Supplier shall sell the Products to Customers that are not Stem Cell Therapy Customers only in conjunction with a license to use the Products solely for applications other than Stem Cell Therapy Applications. The Distributor is not authorized by the Supplier to distribute the Products to any Person other than a Stem Cell Therapy Customer.

(f) The Supplier agrees to appoint the Distributor, and the Distributor agrees to accept appointment, as the Supplier's sole worldwide distributor of any of the Supplier's products that are successors to, or replacements of, the Products and are also Competitive Products (the "Supplier's

New Products"). Sales of the Supplier's New Products by the Supplier to the

Distributor pursuant to such distribution arrangement shall be at fixed prices and on other terms to be negotiated by the Supplier and the Distributor in good faith, taking into account the terms of this Agreement, as it is in effect at such time, the respective costs of the Supplier and the Distributor in developing, producing and marketing the Supplier's New Products and market conditions at such time.

SECTION 2.02. Relationship; Subdistributors. (a) The Distributor

shall conduct its business in the purchase and resale of the Products as a principal for its own account. This Agreement does not in any way create the relationship of principal and agent, partners, joint venturers, master and servant, or any similar relationship, between the Supplier and the Distributor.

(b) The Distributor shall have the right to appoint and to use any independent selling representative, agent, associate distributor or subdistributor who agrees to be bound by all applicable terms of this Agreement (collectively, the "Subdistributors") and who is designated in accordance with

Market Development Program. The Distributor shall use all reasonable efforts to cause the Subdistributors to comply with their obligations under this Agreement.

(c) The Distributor shall either Sell the Products directly to Stem Cell Therapy Customers (i.e., through the Distributor's own employed sales force) in each of the countries listed below:

Australia	Holland
Austria	Italy
Belgium	Japan
Canada	Spain
France	Switzerland
Germany	United Kingdom

(collectively, the "Direct Sales Countries"; each being a "Direct Sales

Country"), or make payments to the Supplier in accordance with Section 2.02(e).

(d) The Distributor may Sell the Products to Stem Cell Therapy Customers through Subdistributors, each of whom shall be identified to the Supplier, in countries other than the Direct Sales Countries and the United States.

(e) If the Distributor uses Subdistributors to sell the Products to Stem Cell Therapy Customers in the Direct Sales Countries and the United States, the Distributor shall bear all costs and discounts attributable to the Subdistributor, unless otherwise expressly approved by the Supplier.

SECTION 2.03. Purpose; Development Programs. (a) The Supplier and

the Distributor each acknowledges that it has entered into this Agreement in order to develop a respected image of the Products among Stem Cell Therapy Customers, to develop the Products so that they can be Sold to Stem Cell Therapy Customers as promptly as practicable and to develop a market for the Products among Stem Cell Therapy Customers, in each case in a manner that maximizes the financial returns to both the Supplier and the Distributor.

(b) As the Supplier's worldwide distributor of the Products for Stem Cell Therapy Applications, the Distributor shall use reasonable best efforts to develop and implement a worldwide plan for marketing and Sales of the Products for Stem Cell Therapy Applications so that the Products will be Sold for Stem Cell Therapy Applications worldwide promptly after such Sales become feasible, the market share of the Products for Stem Cell Therapy Applications will be high and the prices of the Products for Stem Cell Therapy Applications, will be commensurate with the market value of the Products, in each case in a

manner that maximizes the financial returns of both the Distributor and the Supplier.

(c) The Supplier shall use reasonable best efforts promptly to develop and produce Products that are high quality, cost competitive, cost effective for Stem Cell Therapy Customers and capable of achieving widespread acceptance among Stem Cell Therapy Customers, in each case in a manner that maximizes the financial returns of both the Supplier and the Distributor.

(d) To achieve the goals set forth in Sections 2.03(a), (b) and (c), the Supplier and the Distributor have developed the Product Development Program and the Market Development Program, each of which will be designed to comply with the applicable standards of the ISO 9000 Series of the International Standards Organization and will be amended from time to time in accordance with the terms of this Agreement.

(e) The Product Development Program will at all times include the following components (the "Principal Components of the Product Development Program"), together with such other components as the Supplier may deem appropriate:

(i) a plan, which shall include, without limitation, a strategy, a rationale, budgets, tactics, contingency plans and staffing and a projected timetable (collectively, a "Plan") to develop the Products for sale to Stem Cell Therapy Customers;

(ii) a Plan for obtaining (A) the approval of (x) the FDA and any other United States governmental authority necessary for the Sale of the Products to Stem Cell Therapy Customers in the United States and (y) the Underwriter's Laboratory and (B) support for the claims set forth in the Market Development Program;

(iii) the specifications of each Product, including, without limitation, specifications for performance and reliability of each Product and each component thereof;

(iv) a Plan for validating the performance and reliability specifications for the Products set forth in the Product Development Program and the Product claims (including, without limitation, cost effectiveness claims) and service goals set forth in the Market Development Program;

(v) a quality assurance Plan;

(vi) a Plan for manufacturing, or causing the Products to be manufactured, so that the Products can be delivered for sale to Stem Cell Therapy Customers in a manner consistent with the Market Development Program, including, without limitation, (A) specifications of, and a timetable

for, the production capacity to be available for the supply of each of the Products; (B) Plans and leadtimes for the production of prototype, pilot and production models; (C) a Plan for identifying, qualifying, contracting with and auditing third parties for the manufacture of the Products; and (D) Plans for addressing situations in which the Distributor's orders for the Products exceeds the Supplier's capacity to deliver the Products; and

(vii) a Plan for developing enhancements to the Products in response to evolving market needs.

(f) The Market Development Program will at all times include the following components (the "Principal Components of the Market Development

Program"), together with such other components as the Distributor may deem

appropriate:

(i) a plan, which shall include, without limitation, a strategy, a rationale, budgets, tactics, contingency plans and staffing and a projected timetable (collectively, a "Plan") to obtain all non-U.S. approvals market,

sell and distribute the Products to Stem Cell Therapy Customers;

(ii) the targets for average prices of the Products for Sales in the United States, in each Direct Sales Country (expressed in the official currency unit of such Country) and elsewhere outside the United States, including targets for prices to Subdistributors, all subject to approval by Supplier ("Target Prices");

(iii) the Minimum U.S. Selling Price and Minimum Subdistributor Selling Price and the Minimum International Direct Selling Price in each of the Direct Sales Countries (expressed in the official currency unit of such Country) of each of the Products, as approved by the Supplier;

(iv) a mechanism for monitoring the development and growth of the market for the Products;

(v) criteria for targeting Customers and targets for sales volume and market share in each of the countries where the Products are to be sold, all as agreed upon by the Supplier and the Distributor;

(vi) criteria for targeting Customers and targets for sales volume and market share in each of the countries where the Products are to be sold, all as agreed upon by the Supplier and the Distributor;

(vii) a warranty program for the Products, as agreed upon by the Supplier and the Distributor, as well as a program for providing customer service and customer support to Stem Cell Therapy Customers beyond the scope of such warranties;

(viii) a Plan for developing customer relations, Customer contacts, Sales lead follow up and monitoring customer satisfaction with, the Products and, the Distributor's and each Subdistributor's performance;

(ix) a program for the Distributor's training of Stem Cell Therapy Customers and for the Supplier's training of the Distributor's personnel who will provide training to the Distributors' and the Subdistributors' personnel who will provide such training to Stem Cell Therapy Customers and to the Distributor's and the Subdistributors' personnel who will provide customer engineering and customer support to Stem Cell Therapy Customers;

(x) guidelines and procedures for coordinating contacts of Stem Cell Therapy Customers by the Supplier with contacts by the Distributor; and

(xi) a Plan for forecasting demand for the Products by Stem Cell Therapy Customers.

SECTION 2.04. Review of Program and ACL. (a) The Supplier and the

Distributor contemplate that the Programs will be amended to address issues that cannot yet be addressed and also will be amended in response to unforeseen events, changes in circumstances and evolving market needs. Accordingly, the Supplier and the Distributor shall meet no more than four times per year to discuss amendments to each of the Programs.

(b) Before the beginning of each Fiscal Year during the term of this Agreement, the Supplier and the Distributor shall mutually establish an annual commitment list (the "ACL"), which shall set forth: (i) the principal

commitments and specific objectives that either the Supplier or the Distributor reasonably believes is important to achieve during the next Fiscal Year to accomplish the objectives set forth in Sections 2.03(a), (b) and (c) of this Agreement and to discharge the obligations of the Supplier and the Distributor under the Programs; (ii) those objectives or commitments of either the Supplier or the Distributor that require mutual agreement or coordination between the Distributor and the Supplier; and (iii) any change from the ACL of the preceding year, the Product Development Program or the Market Development Program, in either case that will materially affect either the timing of, or the mechanism for, the development of the Products for, or the delivery and/or marketing of the Products to, Stem Cell Therapy Customers. No provision of the ACL shall be changed, amended, or modified without the prior approval of the Supplier and the Distributor. Each of the Supplier and the Distributor shall use reasonable best efforts diligently to achieve each of the goals and objectives set forth on the ACL. If the Supplier and the Distributor are unable to reach mutual agreement on the inclusion of any commitment or objective on the ACL, then the Supplier and the Distributor will negotiate in good faith for 30 days in an attempt to resolve such disagreement. If the parties are unable to resolve such disagreement during such 30-day period, then either the Supplier or the Distributor may submit such disagreement to arbitration in accordance with Section 10.03. The Parties shall use their reasonable

best efforts to cause such arbitration to result in a decision within 40 days after submission thereto.

(c) In connection with the preparation of the ACL and as otherwise reasonably required, the Market Development Program and the Product Development Program shall, at all times, include each of the Principal Components thereof set forth in Section 2.03 of this Agreement and such other items as are reasonably required to achieve the goals and objectives set forth in Sections 2.03(a), (b) and (c) of this Agreement. The Supplier and the Distributor shall give each other such information as is reasonably necessary to evaluate, and shall give due consideration to the views and recommendations of the other with respect to, all components of each of the Programs. The Product Development Program and the Market Development Program shall include sufficient details to enable the Distributor and the Supplier, respectively, to have a reasonable basis to assess the probability of achieving the goals and objectives set forth in the ACL and in Sections 2.03(a), (b) and (c) of this Agreement. Subject to the right of objection (and resolution of such objection) set forth below, the Supplier shall be free to amend the Product Development Program without the consent of the Distributor, and the Distributor shall be free to amend the Market Development Program without the consent of the Supplier. The Supplier may object to any amendment of, or failure to amend, any Principal Component of the Market Development Program, and the Distributor may object to any amendment of, or failure to amend, any Principal Component of the Product Development Program on the basis (i) that such amendment, or failure to amend, is not reasonably consistent with the goals and objectives set forth in the ACL or Sections 2.03(a), (b) and (c) of this Agreement, or (ii) that, as a result of such amendment, or failure to amend, the parties are not reasonably likely to achieve the goals and objectives embodied in such Principal Component. If the Supplier and the Distributor are unable to agree on a Principal Component of either Program the Supplier and the Distributor, each shall endeavor to resolve the disagreement within such 30-day period. If the Supplier and the Distributor are unable to resolve such disagreement within such 30-day period, either party shall be free to implement the Principal Component in question until such disagreement is resolved, unless the other party reasonably believes that the failure to resolve such disagreement will have an immediate adverse effect on the ability of the parties to implement the goals and objectives set forth in the ACL. In that case, either Party may cause the disagreement to be submitted immediately to arbitration in accordance with Section 10.03, and the Parties shall use their reasonable best efforts to cause such arbitration to be decided within 40 days after submission. If neither Party believes that there will be any such immediate adverse effect, then the Parties will continue to endeavor to resolve the disagreement for an additional period of six months. If the Parties are unable to resolve such disagreement within such six-month period, then the disagreement may be submitted to arbitration in accordance with Section 10.03. The Parties shall use their reasonable best efforts to cause such arbitration to result in a decision within a 40 day period.

(d) A copy of the ACL for the Fiscal Year ending June 30, 1994 is attached hereto as Schedule C.

SECTION 2.05. Annual Customer Review; Change of Use. (a) The parties

acknowledge that following the sale of any Product to any Customer, such Customer may subsequently (i) use such Product for applications other than those disclosed to the Supplier or the Distributor prior to such sale or (ii) change its use from Stem Cell Therapy Applications to other applications, or vice versa (a "Change of Use"). Notwithstanding anything in this Agreement to the

contrary, the Distributor, or any Subdistributor, shall not be in breach of this Agreement if the Distributor (or such Subdistributor, as the case may be) acts in good faith and uses reasonable best efforts to ensure that it sells Products only to Stem Cell Therapy Customers, even though a Customer's predominant use of a Product may be for applications other than Stem Cell Therapy Applications. Similarly, notwithstanding anything in this Agreement to the contrary, the Supplier or any of its other distributors shall not be in breach of this Agreement if the Supplier (or such other distributor, as the case may be) acts in good faith and uses reasonable best efforts to ensure that it sells Products only to Persons other than Stem Cell Therapy Customers, even though a Person's predominant use of a Product may be for Stem Cell Therapy Applications.

(b) The Supplier and the Distributor shall meet within three months after the end of each Fiscal Year during the term of this Agreement during which sales of the Products are made by either the Distributor, any Subdistributor or the Supplier or any of its other distributors to determine the extent to which the Distributor has sold Products to Customers other than Stem Cell Therapy Customers, the extent to which the Supplier has sold Products to Stem Cell Therapy Customers and the extent to which Customers of the Distributor or the Supplier have effected a Change of Use. At such meeting or meetings, the Distributor shall make available to the Supplier a survey of the Distributor's Customers whose purchases represent at least 80% of the Sales by the Distributor during such Fiscal Year (the "Distributor Customer Service Information"). The

Distributor Customer Service Information shall also provide a reasonable estimate of the expected predominant use of the Products by such Customers in the following Fiscal Year. The Supplier shall furnish the Distributor with comparable information regarding the Supplier's Sales of Products to Customers other than Stem Cell Therapy Customers (the "Supplier Customer Service

Information"; and, together with the Distributor Customer Service Information, the "Customer Service Information").

(c) If it is determined:

(i) that at the time of the Supplier's Sale of any Equipment to a Customer (other than an Affiliate of the Supplier), the Supplier knew or reasonably should have known that such Customer's intended predominant use of such Equipment was for Stem Cell Therapy Applications, the

Supplier shall pay to the Distributor an amount equal to 40% of all amounts received by the Supplier in payment for such Equipment;

(ii) that a Customer of the Supplier (other than an Affiliate of the Supplier) uses any Disposable purchased from the Supplier for Stem Cell Therapy Applications, the Supplier shall pay to the Distributor an amount equal to 30% of all amounts received by the Supplier as payment for such Disposable;

(iii) that at the time of the Distributor's (or any Subdistributor's) Sale of any Equipment to any Customer (other than an Affiliate), the Distributor (or such Subdistributor) knew or reasonably should have known that such Customer's intended predominant use of such Equipment was not for Stem Cell Therapy Applications, the Distributor (or such Subdistributor) shall pay to the Supplier all amounts received by the Distributor (or such Subdistributor) in payment for such Equipment; and

(iv) that a Customer of the Distributor other than an Affiliate of the Distributor (or any subdistributor) has used any Disposable purchased from the Distributor (or such Subdistributor) for any application other than a Stem Cell Therapy Application, the Distributor (or such Subdistributor) shall pay to the Supplier an amount equal to 90% of all amounts received by the Distributor (or such Subdistributor) in payment for such Disposable.

(d) The Supplier and the Distributor shall make available to each other such information as is reasonably necessary to audit the Sales of the other party described in 2.05(c) above.

(e) If it is determined by the Supplier and the Distributor, based on the Customer Service Information or otherwise, (i) that a Customer of the Supplier has effected a Change of Use, such Customer may be redesignated, at the Supplier's option, as being a Stem Cell Therapy Customer and, accordingly, a Customer that the Distributor will have the responsibility to serve, or (ii) that a Customer of the Distributor has effected a Change of Use, such Customer may be redesignated, at the Distributor's option, as not being a Stem Cell Therapy Customer and, accordingly, a Customer that the Supplier will have the responsibility to serve. Upon any such redesignation, the Supplier and the Distributor shall develop a program that is reasonably acceptable to each party and such Customer for the orderly transition of responsibility for such Customer over a reasonable period of time not to exceed one year.

ARTICLE III

SUPPLIER'S UNDERTAKINGS

SECTION 3.01. Product Development Program; Diligence. The Supplier

shall use reasonable best efforts to implement its obligations under the Product Development Program and the Market Development Program diligently.

SECTION 3.02. Product Specifications. The Supplier shall supply the

Products in accordance with the product specifications set forth in, and the other applicable provisions of, the Product Development Program and the Market Development Program.

SECTION 3.03. Training by the Supplier. (a) The Supplier shall, in

accordance with the provisions of Section 6.2 of Market Development Plan (which provisions may not be changed without the Supplier's approval), provide technical and commercial training with respect to the Products to the Distributor's personnel. To facilitate the Distributor's ability to be self-reliant in providing such training, the Supplier shall provide a license to the Distributor to use such technical information and know-how as the Supplier reasonably believes is necessary for such training. The Supplier shall not charge the Distributor for such training, but all costs incurred by personnel of the Distributor in the course of such training shall be the responsibility of the Distributor.

(b) As reasonably requested in writing by the Distributor, at any time and from time to time, the Supplier shall, at reasonable compensation rates chargeable to the Customer, provide training in applications other than Stem Cell Therapy Applications to the Distributor's Customers who wish to use the Products for applications other than Stem Cell Therapy Applications.

SECTION 3.04. Sole Distributor. Unless this Agreement has been

terminated by the Supplier in part in accordance with Section 7.05(b), the Supplier hereby grants (a) the Distributor the right during the term of this Agreement to indicate in appropriate ways (e.g., on its letterhead and billing

forms and through signs) that it is the only authorized distributor for the Products to Stem Cell Therapy Customers and (b) any Subdistributor that has been approved by the Supplier the right during the term of this Agreement to indicate in appropriate ways (e.g., on its letterhead and billing forms and through

signs) that it is an authorized Subdistributor of the Products to Stem Cell Therapy Customers or that it is the only authorized Subdistributor of the Products to Stem Cell Therapy Customers within a geographic segment.

SECTION 3.05. Enforcement of Intellectual Property Rights. Promptly

upon receipt of notice of any infringement or threatened infringement ("Infringement") by third parties of the Supplier's Intellectual Property Rights

relating to the Sale of the Products to Stem Cell Therapy Customers ("SCTIP

Rights"), the Supplier shall, unless such notice was received pursuant to

Section

4.05 hereof, promptly notify the Distributor of any such Infringement, and, as promptly as practicable thereafter, the Supplier and the Distributor shall jointly determine whether to take action to prevent such Infringement and otherwise to enforce the SCTIP Rights (all such actions being "IP Enforcement Actions"). In making such determination, the Supplier and the Distributor shall

consider the impact that such Infringement is expected to have on Sales of the Products to Stem Cell Therapy Customers, the likelihood that such IP Enforcement Action will be successful, the expected cost of such IP Enforcement Action, the likelihood that such IP Enforcement Action will result in intellectual property claims against the Supplier or the Distributor ("Retaliatory IP Claims") and the

potential impact of any Retaliatory IP Claims on the Supplier and the Distributor. No IP Enforcement Action to enforce the SCTIP Rights will be undertaken without the consent of both the Supplier and the Distributor. If any such IP Enforcement Action is undertaken, the Supplier and the Distributor shall jointly retain a single counsel reasonably satisfactory to each of the Supplier and the Distributor, and all decisions relating to such IP Enforcement Action and the defense of any Retaliatory IP Claims shall be reasonably satisfactory to each of the Supplier and the Distributor. Sixty percent of all costs of prosecuting IP Enforcement Actions relating to SCTIP Rights and defending any Retaliatory IP Claims, including, without limitation, reasonable fees and disbursement of counsel, any reasonable out-of-pocket expenses incurred by the Supplier and the Distributor and any damages awarded against (or amount paid in settlement by) either the Supplier or the Distributor in any Retaliatory IP Claim (all such costs being "IP Enforcement Costs") shall be borne by the

Supplier and forty percent of such IP Enforcement Costs shall be borne by the Distributor, unless, and to the extent that, such IP Enforcement Action also benefits the Supplier's Sales of Products to Persons other than Stem Cell Therapy Customers, in which case the Distributor's share of such IP Enforcement Costs shall be reduced proportionally to reflect the benefit derived by each Party. All amounts received by the Supplier and the Distributor, whether as a result of damages awarded, settlement payments or otherwise, as a result of any IP Enforcement Action relating to SCTIP Rights, shall be shared by the Supplier and the Distributor in proportion to their respective share of the IP Enforcement Costs for such IP Enforcement Action.

SECTION 3.06. Manufacturing and Labeling; Product Name; Parts. (a)

The Supplier shall manufacture the Products, or cause the Products to be manufactured, in accordance with the Product Development Program. The Supplier's obligation under this Section 3.06 to manufacture the Products shall include the affixing on the Products of labels agreed upon by the Supplier and the Distributor; provided, however, that any costs associated with the labeling of Products with the Distributor's name that would not be incurred but for such labeling will be at the Distributor's expense. The Products shall be labeled as a Product of both the Supplier and the Distributor, with the Distributor's name at least as prominent as the Supplier's name, unless otherwise required by law, in which case the Distributor's name shall be as prominent relative to the Supplier's name as shall be permitted by law.

(b) The Supplier shall have the right to name the Products and shall, in exercising such right, give due consideration to the views and recommendations of the Distributor.

(c) The Supplier shall maintain a stock of Spare Parts for the Products in accordance with the Market Development Program. Spare Parts shall be priced in accordance with Section 5.02(e) of this Agreement.

SECTION 3.07. Regulatory Approvals. (a) At its own expense, the

Supplier shall, in accordance with the Product Development Program, use reasonable best efforts diligently to obtain, in the name of the Supplier, all authorizations, consents, orders and approvals of all governmental authorities in the United States that may be or become necessary for the Distributor to sell the Products to Stem Cell Therapy Customers in the United States.

(b) The Supplier shall provide to the Distributor such assistance, including, without limitation, providing at no charge all Products necessary for clinical trials and making any modifications to Products, as the Distributor may reasonably request to obtain the regulatory approvals necessary to sell the Products to Stem Cell Therapy Customers in countries other than the United States specified in the Market Development Program.

SECTION 3.08. Intellectual Property Indemnification. The Supplier

agrees to indemnify and hold harmless the Distributor and its Affiliates and all Subdistributors and their affiliates and their respective officers, directors, employees and agents (each such person being a "Supplier Indemnified Person")

from and against any losses, claims, damages or liabilities and to reimburse each Indemnified Person for all expenses (including reasonable fees and expenses of counsel) as they are incurred, related to, arising out of or in connection with defending any action, claim, suit, investigation or proceeding (other than a Retaliatory IP Claim) in which a Person other than the Distributor claims or alleges that the sale of the Products by the Distributor to any Stem Cell Therapy Customer conflicts with or infringes on the Intellectual Property Rights of, or other intellectual property owned or licensed by, such Person.

SECTION 3.09. Insurance; Indemnification for Product Liability. (a)

The Supplier agrees to obtain an insurance policy or policies (the "Policy") on

terms and conditions and in amounts reasonably acceptable to the Distributor covering losses, claims, damages, liabilities or expenses (including reasonable fees and expenses of counsel) incurred by the Supplier related to, or arising out of, any action, claim, suit, investigation or proceeding, in which a Person claims or alleges that any Product distributed by the Distributor pursuant to this Agreement has caused such Person to sustain any personal injury, property damage, wrongful death or any other tortious harm as a result of any manufacturing defect in (including, without limitation, any latent defect in), or any defective design of, or an inadequacy of warnings on, the Products (such

claims or allegations being a "Products Liability Claims"). The Supplier agrees

to use reasonable best efforts to have all Supplier Indemnified Persons named as additional insureds on the Policy, which shall provide that it may not be cancelled without 30 days' notice to the Distributor and that the Distributor shall have the right, but no obligation, to pay any premiums due under the Policy (the "Premiums"). The Policy shall be primary insurance with respect to

Product Liability Claims, and any insurance obtained by the Distributor shall be excess insurance. The Parties recognize that the nature of product liability claims and insurance available to cover product liability claims will change over the coming years and will vary from country to country. It is the agreement and goal of the Parties to obtain from time to time such liability insurance which protects both the Supplier and the Distributor to the maximum extent reasonably feasible, at prices which are commercially reasonable. To the extent reasonably feasible, both Parties shall endeavor to use the same counsel to defend both the Supplier and the Distributor in any Products Liability Claim. Both the Supplier and the Distributor shall, to the extent it does not increase its own risk of liability, cooperate with each other in the defense of any Product Liability Claim so as to minimize the risk of any liability to the other party.

(b) The Supplier shall pay all Premiums and any losses, claims, damages or liabilities for Products Liability Claims to the extent not payable under the Policy (such losses, claims, damages, liabilities being "Unreimbursed Losses"), including, without limitation (including reasonable fees and expenses

of counsel) any portion of any Unreimbursed Loss the Insurance Carrier is not obligated to pay because of any deductible, self-insured retention or similar provision of the Policy (a "Deductible"). The Supplier shall receive a

contribution from the Distributor toward the Premiums and shall share in the satisfaction of any Unreimbursed Losses in accordance with Sections 4.09(b) and (c) hereof.

(c) The Supplier (i) shall not amend, change or cancel the Policy without the consent of the Distributor (which consent shall not unreasonably be withheld) and (ii) shall inform the Distributor in writing in the event that any products other than the Products distributed by the Distributor are covered by the Policy.

(d) The Supplier shall, subject to the limitation set forth in Section 4.09(c), indemnify and hold harmless each Supplier Indemnified Person from and against any Unreimbursed Losses (except Deductibles).

SECTION 3.10. Forecasting Unit Demand. The Supplier and the

Distributor shall agree upon a process of unit demand forecasting that meets the needs of the Supplier, the Distributor, and any sub-Suppliers to be used by the Supplier. A mechanism that the Supplier and the Distributor believe is workable is described in the Market Development Program, but both the Supplier and the Distributor recognize that this mechanism must be modified periodically as product and component lead times and delivery mechanisms are better understood by the Supplier and the Distributor.

ARTICLE IV

DISTRIBUTOR'S UNDERTAKINGS

SECTION 4.01. Market Development Program; Diligence. (a) The

Distributor shall use reasonable best efforts to implement its obligations under the Market Development Program and the Product Development Program diligently. In performing its obligations under the Market Development Program, the Distributor shall provide to Stem Cell Therapy Customers financing options suitable for the market environment.

(b) Notwithstanding anything in this Agreement to the contrary, if the Distributor identifies to the Supplier potential Stem Cell Therapy Customers in the United States to whom the Distributor reasonably believes it cannot effectively sell the Products, the Supplier may sell the Products to such Stem Cell Therapy Customers, directly, or through a distributor or sales agent (identified to the Distributor) who expressly agrees in writing to be bound by all of the restrictions on sales of the Products which are applicable to the Supplier under this Agreement. Upon the identification of such Stem Cell Therapy Customers by the Distributor to the Supplier, the Distributor shall have no further obligation under this Agreement to attempt to sell Products to such Customers.

SECTION 4.02. Training by the Distributor. (a) The Distributor

shall, in accordance with the Market Development Program, provide commercial and technical training with respect to the Products to its, and the Subdistributors' personnel who will provide training, customer service and support to Stem Cell Therapy Customers.

(b) As reasonably requested in writing by the Supplier, at any time and from time to time, the Distributor shall, at reasonable compensation rates chargeable to the customer, provide training in Stem Cell Therapy Applications to the Supplier's Customers who wish to use the Products for such applications.

SECTION 4.03. Advertising. The Distributor and each Subdistributor

shall submit to the Supplier, prior to its use by the Distributor or such Subdistributor, all advertising copy concerning the Products and shall not use such copy without the consent of the Supplier (which shall not be unreasonably withheld); provided, however, that in no event shall the Supplier have any obligation to share in advertising or other promotional costs incurred by the Distributor or Subdistributor.

SECTION 4.04. Warranties; Service. (a) The Distributor and each

Subdistributor shall extend warranties, which in accordance with the Market Development Program, shall be mutually approved by the Supplier and the Distributor, and perform warranty service on the Products sold to Stem Cell

Therapy Customers by the Distributor or any such Subdistributor, as the case may be.

(b) The Monthly Purchase Price shall be reduced in accordance with Section 5.02 by an amount equal to the costs reasonably incurred by the Distributor in providing warranty service to Stem Cell Therapy Customers in accordance with the Market Development Program. Any costs incurred by the Distributor or any Subdistributor in providing extended warranty or maintenance service beyond the standard warranty period provided in the Market Development Program shall be borne solely by the Distributor or such Subdistributor.

(c) The Distributor and each Subdistributor shall, in accordance with the Market Development Program, provide service and customer support for the Products to Stem Cell Therapy Customers which have purchased Products from the Distributor or such Subdistributor, as the case may be. The provision of such service and support shall be priced so as not to be a disincentive to Stem Cell Therapy Customers to purchase the Products.

(d) The Supplier shall assist the Distributor in providing warranty service and other services to Stem Cell Therapy Customers, as reasonably requested by the Distributor, at prices or rates to be negotiated in good faith by the Supplier and the Distributor.

SECTION 4.05. Notice of Infringement. The Distributor and each

Subdistributor shall promptly notify the Supplier in writing if it becomes aware of any infringement or threatened infringement of any SCTIP Rights.

SECTION 4.06. License. The Distributor hereby grants to the Supplier

a license to the Distributor's trademarks and trade names specified in the Market Development Program for the sole purpose of the Supplier's affixing of such trademarks and trade names to the Products sold to the Distributor pursuant to this Distribution Agreement and the packaging for the Products as contemplated in Section 3.06(a) hereof.

SECTION 4.07. Regulatory Approvals. (a) At its own expense, the

Distributor shall use reasonable best efforts diligently to obtain, in the Supplier's name and the Distributor's name (a "Joint Registration"), all

authorizations, consents, orders and approvals of all non-U.S. governmental authorities, and to complete clinical trials, that may be or become necessary to sell the Products to Stem Cell Therapy Customers in the countries other than the United States specified in the Market Development Program; provided, however, that if the law of one of such countries prohibits or otherwise restricts such Joint Registration, the Distributor shall use reasonable best efforts to obtain such Joint Registration to the extent permitted by such law and otherwise shall use reasonable best efforts to obtain such registrations in the Distributor's name. The Distributor shall be responsible for the cost of all clinical trials (other than the cost of the

Products required for such trial, which shall be provided by the Supplier at no charge) necessary to obtain such non-U.S. approvals.

(b) If this Agreement is terminated in its entirety or with respect to any country other than the United States, the Distributor shall use reasonable best efforts to provide information on clinical trials and such other information (other than confidential business information) as is reasonably necessary to enable the Supplier to obtain registration in its name in such country.

SECTION 4.08. Competitive Products. (a) In order to fulfill its

obligations with respect to promoting the Sale of the Products, except as provided in Section 4.10 of this Agreement, the Distributor and its Affiliates shall not, and shall not attempt to, Sell, directly or indirectly, to any Stem Cell Therapy Customer any Competitive Product for Stem Cell Therapy Applications, other than the Distributor's Products and other products that are sold by the Distributor as an adjunct or complement to the Products; provided, however, this prohibition shall not apply to the Sale of Competitive Products in any geographical area with respect to which this Agreement has been terminated or in which a Co-Marketing Arrangement has been established.

(b) Unless otherwise agreed by the Supplier, each Subdistributor shall agree to be bound by this Section 4.08 prior to the Sale of the Products to such Subdistributor.

SECTION 4.09. Insurance. (a) To assist the Supplier in satisfying

its obligation set forth in Section 3.09(a) hereof to obtain the Policy, the Distributor shall recommend the Supplier to the Distributor's insurance carrier, it being understood that such obligations do not depend on the responsiveness of such carrier.

(b) Within 30 days after the Distributor's receipt of reasonably satisfactory evidence of the payment of the Premium, the Distributor shall pay to the Supplier 40% of the Premium, 40% of amounts which the Supplier is obligated to bear as a Deductible, and 40% of the Unreimbursed Losses; provided, however, that the Distributor's obligation to pay the Premium and the Deductible and the Unreimbursed Losses for the fifth Fiscal Year following the first Fiscal Year in which the Supplier first purchases products liability insurance (such year being the "Sixth Insurance Year") and each year thereafter shall not exceed

0.4% of Worldwide Sales during such Fiscal Year (such amount being the "Products Liability Cap"); and, provided further, that if the Policy at any time covers

products other than the Products distributed by the Distributor pursuant to this Agreement, the Premiums, the Deductibles and the Unreimbursed Losses payable to the Supplier by the Distributor shall be reduced to a percentage equal to 40% multiplied by the percentage of the Supplier's total revenues that is represented by revenues received by the Supplier for Sales of the products by the Distributor pursuant to this Agreement.

(c) If the aggregate unreimbursed amounts paid by the Supplier during any Fiscal Year with respect to Product Liability Claims, including amounts of Premiums, Deductibles and Unreimbursed Losses that are not reimbursed by the Distributor under this Section 4.09 (the "Supplier Products Liability Payments")

exceeds 60% (subject to upward adjustment in accordance with the second proviso of Section 4.09(b)) of the aggregate amounts paid with respect to such liabilities, and the Products Liability Cap for such Fiscal Year exceeds the sum of the aggregate amounts paid by the Distributor to the Supplier under Section 4.09(b) for such Fiscal Year that are paid by the Distributor and not reimbursed by the Supplier, then the Distributor shall pay to the Supplier the amount of such excess (the "Excess Payments"). The Distributor shall make Excess Payments

in each Fiscal Year until the sum of the Excess Payments in such Fiscal Year and all preceding Fiscal Years beginning with the Sixth Insurance Year is equal to the Supplier Deficiency in that Fiscal Year and all preceding Fiscal Years beginning with the Sixth Insurance Year. The "Supplier Deficiency" for any

Fiscal Year shall be equal to the excess of the actual amount of the Products Liability Payments for such Fiscal Year over the amount that such Products Liability Payments would have been but for the Products Liability Cap.

SECTION 4.10. Solutions and Growth Medium. Notwithstanding any other

provision in this Agreement to the contrary, if it is in the Customers' best interests or if sale of the Growth Medium or Solutions is prohibited by local law or regulation or otherwise is commercially impracticable, the Distributor may obtain Solutions and Growth Medium from a source other than the Supplier and sell such other Solutions and Growth Medium to any Stem Cell Therapy Customer. If the Distributor makes any such Sales to Stem Cell Therapy Customers, the Distributor shall pay to the Supplier, in those cases in which the use of such other Solutions or Growth Medium is prohibited by law or otherwise is commercially impracticable, an amount equal to the lesser of: (a) a royalty equal to 10% of the Distributor's net selling price of such sales and (b) an amount equal to 60% of the Distributor's gross margin realized on such sales of the Solutions and/or Growth Medium (said 60% amount being defined as the "Supplier's Share"), and, in those cases in which the use of such other

Solutions or Growth Medium is legally or practically required, the Supplier's Share. Such payments shall be made by the Distributor to the Supplier within 30 days following the month in which the sale occurred.

SECTION 4.11. Information Concerning Pricing. (a) The Distributor

shall provide to the Supplier the following information regarding the prices at which Products are Sold by the Distributor to Stem Cell Therapy Customers pursuant to this Agreement (the "Pricing Information"): the average, highest

and lowest selling prices of each of the Products (specified by catalogue number) in each country and to each Subdistributor. The Supplier and the Distributor shall review the Pricing Information at least once a year. In light of such Pricing Information, the Supplier and the Distributor annually shall (i) agree to Target Prices, the Minimum U.S. Selling Price, the Minimum Subdistributor Selling Price and the Minimum Direct International Selling Price in each of the Direct Sales

Countries for each of the Products and (ii) develop goals and objectives to be included in the ACL for such year to maximize the financial returns of both the Supplier and the Distributor.

(b) The Supplier and the Distributor each shall endeavor in good faith to establish, within three years after the payment of the latter of the Milestone Fees, fixed prices (which shall be revised and adjusted annually) at which the Supplier shall Sell Products to the Distributor pursuant to this Agreement, it being recognized, however that neither party shall be obligated to agree to fixed pricing unless the party determines it to be in its own best interests. Once such prices are established, they shall replace the pricing formulae set forth below in Section 5.02 and shall be consistent with the following goals and objectives: (i) to price the Products to maximize their value; (ii) to share mutually in the revenues and benefits from Sales of the Products; and (iii) to exchange openly information regarding Sales prices and production costs.

(c) Notwithstanding anything in this Agreement to the contrary, the Distributor's obligations under Sections 2.03(a) and (b) and Section 4.01 shall not require the Distributor to make any Sales of Products, which, in the judgment of the Distributor, are reasonably likely to cause the Average U.S. Selling Price, the Average International Direct Selling Price in any Direct Sales Country and the Average Subdistributor Selling Price to be less than the Minimum U.S. Selling Price, or the Minimum International Direct Selling Price in such Direct Sales Country and the Minimum Subdistributor Selling Price, respectively, during the month in which such Sales otherwise would be made.

SECTION 4.12. Indemnification for Product Liability. The Distributor

agrees to indemnify and hold harmless the Supplier and its Affiliates and their respective officers, directors, employees and agents (each such person being a "Distributor Indemnified Person") from and against any losses, claims, damages

or liabilities not subject to the Policy and to reimburse each Distributor Indemnified Person for all expenses (including reasonable fees and expenses of counsel) not subject to the Policy as they are incurred, related to, arising out of or in connection with defending any action, claim, suit, investigation or proceeding in which a Person claims or alleges that the claims made beyond those in the Market Development Program, or the training, service or repair undertaken, by the Distributor, or such Subdistributor, with respect to the Products has caused such Person to sustain any personal injury, property damage, wrongful death or any other tortious harm.

ARTICLE V

DISTRIBUTOR PURCHASES OF THE PRODUCTS

SECTION 5.01. Orders. Orders for Products placed by the Distributor shall conform to, and shall be filled in accordance with, the Programs.

SECTION 5.02. Purchase Price; Periodic Adjustments. (a) The aggregate purchase price to be paid to the Supplier by the Distributor for U.S. Products Sold during any calendar month (the "U.S. Monthly Purchase Price") shall be calculated according to the following formula:

*

where "P" is the U.S. Monthly Purchase Price, "SP" is the aggregate of the Actual U.S. Sales Amount for each of the Products during such calendar month, "DS" is the Deemed U.S. Sales Amount during such calendar month, "U" is the aggregate dollar amount of Upcharges included in the selling price of the Actual U.S. Sales Amount during such calendar month, "F" is the applicable aggregate unreimbursed freight and handling charges for the Actual U.S. Sales, the Deemed U.S. Sales and the Purchased Spare Parts used for warranty service provided in accordance with the Programs during such calendar month borne by the Distributor, "R" is the aggregate amount credited by the Distributor during such calendar month for returns of U.S. Products as reflected in the applicable credit invoices, "W" is the Distributor's cost of providing warranty service during such calendar month (i.e., travel and other out-of-pocket expenses and cost of warranty service

at applicable hourly rates, but excluding the cost of Purchased Spare Parts) to Stem Cell Therapy Customers in the United States pursuant to, and in accordance with, Section 4.04(a), all as reflected in the relevant Monthly Report, and "X" is * (or, if 5.02(d) is applicable, *

(b) The aggregate purchase price to be paid to the Supplier by the Distributor for Subdistributor Products Sold during any calendar month (the "Subdistributor Monthly Purchase Price") shall be calculated according to the following formula:

*

where "P" is the Subdistributor Monthly Purchase Price, "SP" is the aggregate of the Actual Subdistributor Sales Amounts for each of the Products during such calendar month, "DS" is the Deemed Subdistributor Sales Amount during such calendar month, "U" is the aggregate dollar amount of Upcharges included in the selling price of the Actual

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Subdistributor Sales Amount during such calendar month, "F" is the applicable aggregate unreimbursed freight and handling charges for the Actual Subdistributor Sales and the Deemed Subdistributor Sales and the Purchased Spare Parts used for warranty service for Subdistributor Products provided in accordance with the Programs during such calendar month borne by the Distributor, "R" is the aggregate amount credited by the Distributor during such calendar month for returns of Subdistributor Products as reflected in the applicable credit invoices, "W" is the Distributor's cost of providing warranty service on Subdistributor Products during such calendar month (i.e., travel and other out-of-pocket expenses and cost of

warranty service at applicable hourly rates, but excluding the cost of Purchased Spare Parts) to Stem Cell Therapy Customers outside of the United States pursuant to, and in accordance with, Section 4.04(a), and "X" is *

(c) The aggregate purchase price to be paid to the Supplier by the Distributor for International Direct Products Sold in each Direct Sales Country during any calendar month (the "International Direct Monthly Purchase Price")

shall be calculated according to the following formula:

*

where "P" is the International Direct Monthly Purchase Price, "SP" is the aggregate of the Actual International Direct Sales Amount for each of the Products in such Country during such calendar month, "DS" is the Deemed International Direct Sales Amount in such Country during such calendar month, "U" is the aggregate dollar amount of Upcharges included in the selling price of the Actual International Direct Sales Amount during such calendar month, "F" is the applicable aggregate unreimbursed freight and handling charges for the Actual International Direct Sales in such Country, the Deemed International Direct Sales and the Purchased Spare Parts used for warranty service provided in such Country in accordance with the Programs during such calendar month borne by the Distributor, "R" is the aggregate amount credited by the Distributor during such calendar month for returns of International Direct Products in such Country as reflected in the applicable credit invoices, "W" is the Distributor's cost of providing warranty service on International Direct Products in such Country during such calendar month (i.e., travel and other out-of-pocket expenses and cost of warranty service

at applicable hourly rates, but excluding the cost of Purchased Spare Parts) to Stem Cell Therapy Customers in such Direct Sales Country pursuant to, and in accordance with, Section 4.04(a), all as reflected in the relevant Monthly Report, and "X" is * The International Direct Monthly Purchase Price for each Direct Sales Country shall be converted

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from the official currency unit of such Country into U.S. dollars at the Exchange Rate for the month in which the Sales represented by such International Direct Monthly Purchase Price were made.

(d) If Worldwide Sales exceed the Sales Threshold in any Fiscal Year, then the U.S. Monthly Purchase Price for all Sales in excess of such threshold shall be calculated based upon the formula in subsection 5.02(a) above, except that "X" shall equal *

(e) The aggregate purchase price (the "Monthly Parts Purchase Price")

to be paid to the Supplier by the Distributor for Spare Parts purchased by the Distributor, whether purchased for a warranty service in accordance with Section 4.04(a) or otherwise (the "Purchased Spare Parts"), in any calendar month, shall

be calculated according to the following formula:

*

where "P" is the Monthly Parts Purchase Price, "C" is the Supplier's cost of producing such Purchased Spare Parts, "R" is the aggregate price paid by the Distributor to the Supplier for the Spare Parts returned by Stem Cell Therapy Customers during such calendar month and the freight paid the Distributor with respect to such returns, "WC" is the purchase price paid to the Supplier by the Distributor for Spare Parts used for warranty service provided in such month by the Distributor to Stem Cell Therapy Customers pursuant to, and in accordance with, Section 4.04(a).

SECTION 5.03. Monthly Report; Monthly Payment; Distributor Fee. (a)

Within thirty days after the end of each calendar month, the Distributor shall prepare and deliver to the Supplier a report (the "Monthly Report") stating,

among other things, the aggregate amount of Worldwide Sales, specifying sales by the Distributor of U.S. Products and International Products during such month. At the time of delivery of the monthly report, the Distributor shall pay the Monthly Purchase Price. The Distributor shall assume responsibility for all amounts that become uncollectible from its Customers and any collection costs incurred in pursuit of such amounts.

(b) Within five business days after the Distributor's first issuance of an invoice (or invoices) evidencing that the Complete System Sale has occurred, the Distributor shall pay to the Supplier a fee of *

(c) Within thirty business days after final written approval by the FDA of the Products for Sales in the United States for any clinical indications for Stem Cell Therapy Applications, the Distributor shall pay to the Supplier a fee of * (together with the fees specified in Section 5.03(b), the "Milestone Fees").
- -----

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SECTION 5.04. Deliveries. The Supplier shall deliver the Products in

accordance with each firm order by the Distributor. Unless otherwise agreed by the Supplier and the Distributor, delivery shall be F.O.B. at the Supplier's place of manufacture ("ex works"). Title to the Products Sold to the Distributor by the Supplier pursuant to this Agreement shall pass from the Supplier to the Distributor upon the Distributor's acceptance of the Products at the Supplier's place of manufacture. All of the costs of transportation (including insurance) shall be borne by the Distributor and included in "F" in the formulae set forth in Section 5.02 above.

ARTICLE VI

TRADEMARKS AND TRADE NAMES

SECTION 6.01. License. To the extent permitted by law, the Supplier

hereby grants to the Distributor and each Subdistributor a license and right to use during the existence of this Agreement any trademark and trade name of the Supplier associated with the Products for the sole purpose of Selling, and promoting the Sale of, the Products in accordance with this Agreement. The Distributor shall take no steps to register the Supplier's trademarks or trade names.

SECTION 6.02. Licenses to Third Parties. The Supplier shall not grant

to any person other than the Distributor a right or license to use during the term of this Agreement any trademark or trade name of the Supplier for the purpose of Selling, or promoting the Sale of, the Products to Stem Cell Therapy Customers unless the Supplier has established a Co-Marketing Arrangement in accordance with Section 7.05(b).

SECTION 6.03. Effect of Use. Any trademarks and trade names licensed

to the Distributor hereunder are, and shall remain the exclusive property of, the Supplier, and nothing contained herein shall grant or be construed as granting to the Distributor any right, title or interest in the Supplier's trademark or trade name not specifically set forth in Section 6.01. Any trade names or trademarks developed for the Products during the term of this Agreement shall be owned solely by the Supplier, but shall be licensed to the Distributor in accordance with Section 6.01.

SECTION 6.04. Cessation of Use. Upon the later of expiration or

termination of this Agreement or the license rights granted to the Distributor pursuant to Section 7.07 hereof, the Distributor shall forthwith cease any and all use of, and shall not use or have any right to use, any trademark or trade name of the Supplier licensed to the Distributor hereunder.

ARTICLE VII

TERM; TERMINATION

SECTION 7.01. Term. Unless earlier terminated pursuant to Section

7.02 hereof, the term of this Agreement shall commence on the date first above written and end on October 22, 2003 (the "Base Term"). At the end of the Base

Term, the Distributor shall have the option to renew this Agreement for one additional ten-year period, which, except as otherwise specifically provided in this Section 7.01, shall be upon the terms and conditions in effect at the expiration of the Base Term. The Distributor may exercise this option by providing written notice to the Supplier not less than 365 days prior to the expiration of the Base Term. At the end of such additional ten-year term, the parties may extend this Agreement for a subsequent ten-year period only by mutual agreement.

SECTION 7.02. Notice of Breach. If the Supplier has materially

breached its obligations under this Agreement, the Distributor shall deliver to the Supplier written notice of such breach (the "Distributor's Notice of

Breach"). If the Distributor has materially breached its obligations under this Agreement, the Supplier shall deliver to the Distributor written notice of such breach (the "Supplier's Notice of Breach"; and, together with the Distributor's

Notice of Breach, a "Notice of Breach"). Any Notice of Breach shall describe

such breach in reasonable detail.

SECTION 7.03. Cure Period. If the alleged breach by the Supplier or

the Distributor can be cured by the payment of money (a "Monetary Breach"), the

breaching Party may cure such Monetary Breach at any time within ten days after the existence of the Monetary Breach and the amount owed has been established. If the breach is not a Monetary Breach and reasonably can be cured within thirty days, then the breaching Party may cure the breach within thirty days after delivery of the Notice of Breach. If the breach is not a Monetary Breach and reasonably cannot be cured within thirty days, then the breaching Party may submit to the nonbreaching Party within thirty days after delivery of the Notice of Breach a written plan to effect a cure as soon as reasonably practicable, but in any event within one year following the receipt of the Notice of Breach from the nonbreaching party, and the breaching Party shall diligently, promptly and continuously pursue such plan until the breach has been cured.

SECTION 7.04. Objection; Negotiation. (a) If either Party disputes

an assertion by the other Party that it has materially breached this Agreement, as specified in any Notice of Breach, then the allegedly breaching Party may, in lieu of proceeding with a remedy of such alleged breach, deliver to the other Party a written objection (the "Objection") within fifteen days after receipt of

the Notice of Breach. Any Objection shall set forth in reasonable detail the basis for the objection to the breach alleged in the Notice of Breach.

(b) For a period of up to thirty days after the delivery of the Objection, the Parties shall pursue good faith negotiations to attempt to resolve mutually the Parties' differences concerning the Notice of Breach and the Objection. If the Parties have not reached a mutually satisfactory resolution within said thirty days, then either Party may submit the matter for resolution by binding arbitration pursuant to Section 10.03.

SECTION 7.05. Remedy; Partial Termination; Termination Upon

Bankruptcy. (a) If the Supplier fails to cure any material breach within the time periods specified in Section 7.03 above, the Distributor may terminate this Agreement.

(b) If the Distributor fails to cure any material breach within the time periods specified in Section 7.03 above, the Supplier may terminate this Agreement, and the Distributor's right to act as the Distributor, on a worldwide basis, or with respect to specific geographic areas, or the Supplier may permit the Distributor to continue to act as a distributor of the Products but may appoint other distributors of the Products or the Supplier may distribute the Products itself, in each case either on a worldwide basis or with respect to one or more geographic areas (such arrangement being a "Co-Marketing Arrangement").

If the Supplier exercises its right under this Section 7.05(b) to establish a Co-Marketing Arrangement, the prices to be paid to the Supplier by the Distributor for the Products distributed by the Distributor in each geographic area in which a Co-Marketing Arrangement is established shall be fair and reasonable fixed prices for each of the Products determined in good faith negotiations by the Supplier and the Distributor, based upon the amounts paid to the Supplier by the Distributor for each of the Products during the period preceding such termination, which prices shall then be renegotiated annually based upon then current market conditions. Effective one year after delivering written notice to the other Party, either Party may terminate the Distributor's right to Sell in countries where a Co-Marketing Arrangement has been established.

(c) This Agreement shall terminate immediately upon written notice by either party to the other (i) in the event that a bankruptcy petition is filed with respect to the party notified pursuant to this subparagraph or (ii) in the event that the party notified pursuant to this subparagraph (A) becomes insolvent; (B) is adjudicated as a bankrupt pursuant to an involuntary petition in bankruptcy; (C) suffers appointment of a temporary or permanent receiver, trustee or custodian for its business or for all or part of its assets, where such appointment is not discharged within thirty days; (D) makes an assignment for the benefit of creditors; (E) is admitted to the benefits of any procedure for the settlement or postponement of debts; (F) becomes a party to dissolution proceedings; or (G) takes any corporate action with respect to any of the foregoing.

(d) The Distributor may terminate this Agreement upon twelve months' advance written notice to the Supplier in the event that any Person other than the Distributor during the term of this Agreement beneficially owns more than 50 percent (measured either by value or voting rights) of the outstanding Common Stock or voting securities of the Supplier.

(e) The Distributor may terminate this Agreement at any time after December 31, 1997 if it reasonably determines that the Supplier is unlikely to be able to produce Products that can be sold to Stem Cell Therapy Customers on a competitive basis on or prior to December 31, 1998. The Supplier may terminate this Agreement at any time after the second anniversary of the payment of the later of the Milestone Fees if the Supplier reasonably determines, taking into account the fact that there is no established market for the Products, that the Distributor is unlikely to be able to develop a market for the Products among, or to market the Products effectively to, Stem Cell Therapy Customers.

SECTION 7.06. Other Remedies. In the event of a breach of this

 Agreement, the nonbreaching Party shall be entitled to pursue, in addition to the remedies specified in this Article VII, any and all equitable or legal remedies available to it as a result of the breach, through the arbitration proceeding or the limited court actions as permitted by Section 10.03. If either Party elects to terminate this Agreement in accordance with this Article VII, such termination shall not preclude the nonbreaching Party from pursuing such additional remedies and collecting any damages to which the nonbreaching Party may be entitled.

SECTION 7.07. Effect of Termination by Distributor. (a) In the event

 that the Distributor terminates this Agreement in accordance with Section 7.05(a) hereof, and the Distributor has paid all of the Milestone Fees, then the Supplier shall (i) grant to the Distributor, effective upon notice by the Distributor to the Supplier following such termination, a non-exclusive perpetual license with no rights to grant a sublicense (other than a sublicense to manufacture) (the "License") of all patents and other intellectual property

 necessary or useful to manufacture, use, market and sell the Products to Stem Cell Therapy Customers solely for the use, manufacture, marketing and sale of the Products for Stem Cell Therapy Applications and (ii) provide to the Distributor all technical or other information relating to the processes covered by the License. In addition, the Distributor shall, if requested by the Supplier, manufacture products for the Supplier's use and sale that are similar to the Products sold in the Stem Cell Therapy Market. The prices to be paid to the Distributor by the Supplier for the Products manufactured by the Distributor shall be fixed prices for each of the Products, based upon the amounts paid to the Supplier by the Distributor for each of the Products during the period preceding such termination, as negotiated in good faith by the Distributor and the Supplier. Such negotiated prices shall be applicable for one year, and shall be renegotiated and redetermined annually based upon the then current market conditions.

(b) Under the License, the Distributor shall pay to the Supplier on a monthly basis a royalty fee equal to 15% of the sales price to Customers (net of freight, delivery and returns) for Products sold during each month using such License, subject to reduction for any amounts payable by the Distributor to any third party pursuant to any agreement between the Supplier and such third party with respect to any Intellectual Property Rights granted to the Distributor under the License.

(c) The License shall not affect any other right or remedy of the Distributor arising from the Supplier's nonperformance of this Agreement.

SECTION 7.08. Attorneys' Fees and Costs. In the event of any

arbitration or court proceedings with respect to a breach, an alleged breach, a dispute as to the interpretation of this Agreement, or any other dispute concerning this Agreement, the Party who most prevails in such proceedings shall be entitled to recover from the other Party the reasonable attorneys' fees and other reasonable costs incurred by the prevailing Party in connection with such proceedings, in such amounts as the arbitrator or the court deems appropriate and fair. The arbitrator in such arbitration proceedings shall determine the prevailing Party, and the amount of attorneys' fees and other costs to be paid by the other Party to the prevailing Party.

SECTION 7.09. Interest. If a Party fails to pay any amount when due,

such amount shall thereafter bear interest until such amount, together with such interest, is paid in full at a rate equal to the rate announced from time to time by Citibank as its base rate of interest plus two percent.

SECTION 7.10. Transition Upon Termination. (a) Upon any termination

of this Agreement, in whole or in part, the Distributor and the Supplier each shall use reasonable and good faith efforts to accomplish an orderly transition of marketing responsibilities, from the Distributor to the Supplier (or the Supplier's designee).

(b) If this Agreement is terminated the Distributor shall make available to the Supplier (i) a list of each Customer and Subdistributor which purchased Equipment from the Distributor, identifying the Equipment purchased by each such Customer and Subdistributor, (ii) a list of each Customer and Subdistributor which purchased Disposables during the 24 calendar months immediately preceding such termination, identifying the types and quantities of Disposables purchased by each such Customer and Subdistributor during the last 24 months, and (iii) a copy of each customer record of service performed within the last 24 calendar months for the Customers listed in subparagraphs (i) and (ii) above. Notwithstanding the foregoing, however, if the Supplier establishes a Co-Marketing Arrangement pursuant to Section 7.05(b) pursuant to which the Distributor is allowed to continue to distribute Products in one or more specific geographical areas, then the Distributor shall not

be required to furnish to the Supplier the foregoing lists and records for such geographical areas.

ARTICLE VIII

CONFIDENTIALITY

SECTION 8.01. Confidentiality. (a) The Distributor and the Supplier

agree to keep secret and not to disclose to any third party any Confidential Information of the other that may from time to time be received from the other party in connection with the transactions contemplated by this Agreement; provided, however, that the Distributor may disclose such information to its Affiliates. The Confidential Information exchanged by the parties in connection with this Agreement shall not be used by the receiving party for any purpose other than for purposes of carrying out this Agreement during its term. The Supplier may disclose the Distributor's Confidential Information to the Supplier's employees and agents to the extent necessary to enable such employees and agents to perform the Supplier's responsibilities under this Agreement, and the Distributor may disclose the Supplier's Confidential Information to the Distributor's employees and agents and the Distributor's Subdistributors and their employees and agents to enable (i) such employees and agents to perform the Supplier's responsibilities under the Agreement and (ii) such Subdistributors to the extent necessary to assist the Distributor in the performance of its obligations under this Agreement.

(b) The foregoing confidentiality obligations are subject to an exception for any disclosure that becomes legally required by subpoena or other legal process; provided, however, that the Party who so becomes legally obligated shall give written notice to the other Party of such required disclosure as promptly as practicable after the Party becomes aware of such disclosure requirements.

SECTION 8.02. Survival of Covenants to Keep Secret. The parties'

obligations under this Article VIII shall survive expiration or termination of this Agreement.

SECTION 8.03. No License. Except as otherwise provided in this

Agreement, nothing in this Agreement shall be construed to constitute a grant of any licensing rights from the Supplier to the Distributor to make the Products or to use the Products (other than a demonstration use for marketing to potential customers).

ARTICLE IX

FORCE MAJEURE

SECTION 9.01. Force Majeure. (a) If either party is rendered unable,

in whole or in part, to carry out its obligations under this Agreement by reason of force majeure, and if such party gives prompt written notice to the other party describing the details giving rise to such party's claim of force majeure, then the party claiming force majeure shall be excused from performing its obligations hereunder, but only for so long as that party remains unable by reason of force majeure so to perform. Such cause of the party's inability to perform shall be remedied to the extent possible with all reasonable speed. As used herein, force majeure means Acts of God, labor disputes, acts of public enemies, wars, blockades, insurrections, riots, epidemics, quarantine restrictions, landslide, lightning, earthquakes, fires, storms, floods, washouts, arrests, restraints of rulers and people, civil disturbances, acts of any governmental or local authority, inability to obtain transport or supplies for any reason, and other acts that are not within the control of the party claiming excuse from performance and that could not have been avoided or overcome by such party using due diligence. The lack of financial resources shall not constitute force majeure.

(b) If any event of force majeure materially impairs the Distributor's ability to sell the Products or the Supplier's ability to manufacture the Product, then during the pendency of that force majeure event, the Supplier may sell the Products or the Distributor may manufacture the Products (as the case may be) that would otherwise have been sold by the Distributor or manufactured by the Supplier, but for the force majeure event.

ARTICLE X

MISCELLANEOUS PROVISIONS

SECTION 10.01. Amendment; Alteration. No amendment, change,

alteration, modification of, or addition to, this Agreement shall be effective unless in writing and properly executed by each of the parties hereto.

SECTION 10.02. Notice. All notices, requests, claims, demands,

waivers and other communications hereunder shall be in writing (including telecopier or facsimile or similar writing) and shall be given or made (and shall be deemed to have been duly given or made upon receipt) if delivered in person,

by courier service, by cable, telegram, telex, telecopier or facsimile or by registered or certified mail (postage prepaid, return receipt requested) as follows:

(a) if to the Distributor:

Cobe BCT, Inc.
1185 Oak Street
Lakewood, CO 80215
Telecopy: 303-231-4160
Attention: Edward Wood

(b) if to the Supplier:

Aastrom Biosciences, Inc.
(Mail: P.O. Box 376)
Ann Arbor, MI 48105
(Direct Delivery:
Dominos Farms, Lobby L)
Telecopy: 313-665-0485
Attention: R. Douglas Armstrong, PhD
President and
Chief Executive Officer

or to such other address as either party may have furnished to the other in writing in accordance herewith. All notices, requests, claims, demands, waivers and other communications hereunder shall be deemed to have been received on the date of personal delivery, cable, telegram, telex, telecopier (with copy by mail) or facsimile transmission (with copy by mail), or on the fifth business day (or, in the case of international post, on the fifteenth business day) after the mailing thereof, except that notices of changes of address shall be effective only upon receipt.

SECTION 10.03. Arbitration. All claims and disputes relating to this

Agreement shall be subject to binding arbitration, at the option of the Supplier or the Distributor, in Chicago, Illinois in accordance with the Arbitration Rules of the American Arbitration Association. Written notice of demand for arbitration shall be filed with the other party to this Agreement and with the American Arbitration Association within a reasonable time after the dispute has arisen. Any award or decision rendered in such arbitration process may be entered as a judgement against a Party in any court of competent jurisdiction over the Party. Nothing in this Section shall limit either the Supplier's or the Distributor's right to obtain a preliminary injunction or temporary restraining order pertaining or relating to an arbitrable dispute or controversy against the other party, pending resolution of said dispute or controversy by the arbitration process. The Distributor and the Supplier hereby irrevocably submit to the jurisdiction of any state or federal court in Michigan or Colorado in any action or proceeding arising out of or relating to this Agreement or any other agreement or transaction

contemplated hereby, or any arbitration award or decision arising from this Agreement. The Distributor and the Supplier hereby irrevocably waive, to the fullest extent they may effectively do so, the defense of an inconvenient forum to the maintenance of such action or proceeding.

SECTION 10.04. Governing Law. This Agreement shall be governed by,

and construed in accordance with, the laws of the State of New York applicable to contracts executed in and to be performed entirely within that state.

SECTION 10.05. Waiver. Either party hereto may waive compliance with

any of, or extend the time for performance of, the agreements contained herein. Any such waiver or extension shall be valid if set forth in an instrument in writing signed by the party to be bound thereby. The failure of either party to assert any of its rights hereunder shall not constitute a waiver of any such rights.

SECTION 10.06. Entire Agreement; Assignment. This Agreement

constitutes the entire agreement between the parties with respect to the subject matter hereof and supersedes all prior agreements and undertakings, both written and oral, between the parties with respect to the subject matter hereof. This Agreement shall not be assigned by operation of law or otherwise, other than by the Distributor to its Affiliates, without the express written consent of the Distributor and the Supplier (which consent may be granted or withheld in the sole discretion of the Supplier or the Distributor); provided that any

assignment by the Distributor to its Affiliates does not relieve the Distributor of its obligations hereunder.

SECTION 10.07. Parties in Interest. This Agreement shall be binding

upon and inure solely to the benefit of each party hereto, and nothing in this Agreement, express or implied, is intended to or shall confer upon any other Person any rights, benefits or remedies of any nature whatsoever under or by reason of this Agreement.

SECTION 10.08. Severability. If any term or other provision of this

Agreement is invalid, illegal or incapable of being enforced by any law, rule, regulation or public policy, all other terms and provisions of this Agreement shall nevertheless remain in full force and effect so long as the economic or legal substance of the transactions contemplated hereby is not affected in any manner materially adverse to any party. Upon such determination that any term or other provision is invalid, illegal or incapable of being enforced, the parties hereto shall negotiate in good faith to modify this Agreement so as to effect the original intent of the parties as closely as possible in an acceptable manner in order that the transactions contemplated hereby are consummated as originally contemplated to the greatest extent possible.

SECTION 10.09. Headings. The descriptive headings contained in this

Agreement are included for convenience of reference only and shall not affect in any way the meaning or interpretation of this Agreement.

SECTION 10.10. Counterparts. This Agreement may be executed in one or

more counterparts, and by the different parties hereto in separate counterparts,
each of which when executed shall be deemed to be an original but all of which
taken together shall constitute one and the same agreement.

SECTION 10.11. Approvals. Whenever a matter is subject to the

approval of the other Party, a Party shall not unreasonably withhold its
approval.

IN WITNESS WHEREOF, the Distributor and the Supplier each have caused
this Agreement to be executed by its duly authorized officer as of the date
first above written.

COBE BCT, INC.

By: /s/ EDWARD WOOD

Edward Wood
President

AASTROM BIOSCIENCES, INC.

By: /s/ R. DOUGLAS ARMSTRONG

R. Douglas Armstrong, Ph.D.
President and Chief
Executive Officer

SCHEDULE A

PRODUCT DEVELOPMENT PROGRAM

*

*CONFIDENTIAL PORTION REDACTED AND FILED
SEPARATELY WITH THE COMMISSION

SCHEDULE B

*

*CONFIDENTIAL PORTION REDACTED AND FILED
SEPARATELY WITH THE COMMISSION

Revision of Schedule C of the 11/1/93 Distribution Agreement
1994-1995 Annual Commitment List

*

*CONFIDENTIAL PORTION REDACTED AND FILED
SEPARATELY WITH THE COMMISSION

SUPPLEMENTAL AGREEMENT

This Agreement is entered into as of March 29, 1995, by and between Aastrom Biosciences, Inc., a Michigan corporation ("Aastrom"), Cobe Laboratories, Inc., a Colorado corporation ("Cobe Lab"), and Cobe BCT, Inc., a Colorado corporation ("Cobe BCT"), with respect to the following facts:

A. Pursuant to Section 5.05 of that certain Stock Purchase Agreement between Aastrom and Cobe Lab, dated October 22, 1993 (the "Stock Purchase Agreement"), Aastrom has a "put option" to require Cobe Lab to purchase stock issued by Aastrom in a "Qualifying Private Placement" (as defined in the Stock Purchase Agreement), under certain circumstances.

B. Pursuant to Section 5.03 of the Distribution Agreement between Aastrom and Cobe BCT, dated as of October 22, 1993 (the "Distribution Agreement"), Cobe BCT is obligated to pay to Aastrom a \$5 million fee upon the occurrence of specified events (the "Milestone Fees").

C. Aastrom is in the process of offering for sale a new series of preferred stock, designated as Series D Preferred Stock.

WHEREFORE, the parties hereto mutually agree as follows:

1. Cobe Lab agrees that if Aastrom sells shares of its Series D Preferred Stock in a private placement on or before April 22, 1995 in which (i) the cash proceeds to Aastrom from such sales to investors other than Cobe Lab equal at least \$5 million, and (ii) persons other than holders of Series A Preferred Stock and Series B Preferred Stock and their affiliates purchase shares of Series D Preferred Stock having an aggregate purchase price of at least \$1 million (the "Private Placement"), then upon request by Aastrom by May 31, 1995, Cobe Lab will purchase shares of Series D Preferred Stock having an aggregate purchase price of \$5 million for the same price per share and on the same terms and conditions as such other investors; provided, that such terms and conditions must be reasonably satisfactory to Cobe Lab (the "Cobe Share Purchase").

2. Aastrom, Cobe Lab and Cobe BCT agree that if the Cobe Share Purchase is consummated:

(i) The Private Placement will not be deemed to be a Qualifying Private Placement for purposes of Section 5.05 of the Stock Purchase Agreement, and Aastrom will retain its "put option" for the next Qualifying Private Placement or a Qualifying IPO;

(ii) Upon the consummation of the Cobe Share Purchase, Section 1.01 of the Distribution Agreement shall be amended by deleting the

definition of "Milestone Fees" and replacing such definition with the following words:

"Milestone Events" means each of (i) the Distributor's first issuance of an invoice (or invoices) evidencing that the Complete System Sale has occurred and (ii) the final written approval by the FDA of the Products for Sales in the United States for any clinical indications for Stem Cell Therapy Applications."

(iii) Upon the consummation of the Cobe Share Purchase, Section 4.11(b) of the Distribution Agreement shall be amended by deleting the words "within three years after the payment of the latter Milestone Fee" and replacing such words with the words "within three years after the later to occur of the Milestone Events");

(iv) Upon the consummation of the Cobe Share Purchase, Section 5.03 of the Distribution Agreement shall be amended by deleting paragraphs 5.03(b) and 5.03(c) in their entirety and by redesignating paragraph 5.03(a) as Section 5.03;

(v) Upon the consummation of the Cobe Share Purchase, Section 7.05(e) of the Distribution Agreement shall be amended by deleting the words "the second anniversary of the payment of the later of the Milestone Fees" and replacing such words with the words "the second anniversary of the later to occur of the Milestone Events"; and

(vi) Upon the consummation of the Cobe Share Purchase, Section 7.07(a) of the Distribution Agreement shall be amended by deleting the words "and the Distributor has paid all of the Milestone Fees," and replacing such words with the words "and both Milestone Events have occurred".

IN WITNESS WHEREOF, the parties have executed and delivered this Agreement as of the date set forth above.

AASTROM BIOSCIENCES, INC.

COBE LABORATORIES, INC.

By:/s/ R. Douglas Armstrong

By:/s/

COBE BCT, INC.

By:/s/ Edward C. Wood, Jr.

AMENDMENT
to
RESTATED DISTRIBUTION AGREEMENT
between
COBE BCT, INC. and
AASTROM BIOSCIENCES, INC.

This Amendment is made as of September 11, 1995, to that certain Restated Distribution Agreement dated as of October 22, 1993, between AASTROM Biosciences, Inc., a Michigan corporation (the "Supplier"), and Cobе BCT, Inc., a Colorado corporation (the "Distributor") (the "Restated Distribution Agreement").

1. The terms which are defined in the Restated Distribution Agreement shall have the same meaning in this Amendment as defined in the Restated Distribution Agreement.

2. The definition of "Stem Cell Therapy Applications" in the Restated Distribution Agreement is hereby amended to add the words "or umbilical cord blood" on the second line, so that the first two and one-half lines read as follows:

"Stem Cell Therapy Applications" means
applications of the Products pursuant to which human
bone marrow or peripheral blood or umbilical cord blood
derived stem and hematopoietic cells are used primarily
for one or more of the following:...

3. There shall be added to Section 1.01 of the Restated Distribution Agreement: new defined terms, as follows:

"Lymphoid Cell" means lymphoid stem cell (e.g.,
any cell capable of generating cells solely of lymphoid
lineage) and any cell derived therefrom, including but not
limited to, the subcortical thymocyte, cortical thymocyte,
medullary thymocyte, lymphocyte, B-cell, plasma cell,
immunoblast, lymphoplasmacytoid cell and the NK-cell.

"Lymphoid Cell Applications" means any
expansion, selection or genetic manipulation,
including genetic transformation, of Lymphoid Cells,
provided that either the starting cell population is a
lymphoid selected cell mixture, or that the mature
lymphoid cell production is not derived ex vivo from a
pre-lymphoid cell-type (e.g., multipotent stem cell).

4. The first sentence in Section 2.01(d) of the Restated Distribution Agreement is hereby amended to add the words "(excluding, however, for Lymphoid Cell Applications)" in two locations, so that the first sentence as amended reads as follows:

(d) Notwithstanding any provision of this Agreement to the contrary, the Supplier may Sell the Products to its Affiliates for Stem Cell Therapy Applications by such Affiliates, but not for resale to Persons which are not Affiliates of the Supplier, and may make such Sales with a license for use of the Products for Stem Cell Therapy Applications, and the Distributor may Sell the Products to its Affiliates for applications other than Stem Cell Therapy Applications (excluding, however, Lymphoid Cell Applications) by such Affiliates, but not for resale to Persons which are not Affiliates of the Distributor, and may make such Sales with a license for use of the Products for applications other than Stem Cell Therapy Applications (excluding, however, for Lymphoid Cell Applications) (such permitted Sales by either the Distributor or the Supplier being "Affiliate Sales").

5. Excepting only as otherwise set forth above, all other terms and provisions of the Restated Distribution Agreement shall remain in full force and effect.

IN WITNESS WHEREOF, the Distributor and the Supplier each have caused this Amendment to be executed by its duly authorized officer as of the date first written above.

COBE BCT, INC.

By: /s/ EDWARD WOOD

Edward Wood, President

AASTROM BIOSCIENCES, INC.

By: /s/ R. DOUGLAS ARMSTRONG

R. Douglas Armstrong, Ph.D.,
President and Chief Executive Officer

AMENDMENT TO
RESTATED DISTRIBUTION AGREEMENT

This Amendment is made as of October 29, 1996 to that certain Restated Distribution Agreement dated as of October 22, 1993, between Aastrom Biosciences, Inc., a Michigan corporation (the "Supplier") and Cobe BCT, a Colorado corporation (the "Distributor") (the "Restated Distribution Agreement").

1. With respect to the Purchase Price payable by the Distributor to the Supplier for the Product as specified in Article V of the Restated Distribution Agreement, the parties hereby agree that the Distributor shall be entitled to a 5% discount on the Purchase Price for all of the Product purchased until the aggregate of said discount equals a total of \$350,000, increased by 25% per annum, compounded annually, from December 15, 1996, until the date the first \$200,000 in aggregate discounts are actually realized and credited. Said aggregate discount, including the compounded increase, shall hereinafter be called the "Aggregate Discount". If the Aggregate Discount has not been realized by the second anniversary of the first commercial sale of the Product by the Distributor, then the discount on subsequent sales of the Product from the Supplier to the Distributor shall be at 10% (rather than 5%), until the Aggregate Discount is realized by the Distributor.

2. An example of the calculations for the Aggregate Discount specified in Section 1 above is as follows:

a. First Product sold to Distributor (12/15/97)	
b. First \$200,000 discount credit at 5% actually realized by Distributor (12/15/98)	
c. Aggregate Discount (\$350,000 x 1.25/2/) as of 12/15/98:	546,875
d. Less \$200,000 discount credit at 5% actually realized as of 12/15/98:	(200,000) -----
e. Net balance of Aggregate Discount as of 12/15/98:	346,875
f. Further \$300,000 discount credit at 5% actually realized from 12/16/98 to 12/15/99:	(300,000) -----
g. Net balance of Aggregate Discount as of 12/15/99:	46,875
h. Further \$46,875 discount credit at 10% actually realized after 12/15/99:	(46,875) -----
i. Aggregate Discount is fully realized.	

3. The Supplier has agreed to the foregoing discount in consideration and recognition of the assistance which the Distributor has given to the Supplier in the development of the Product.

4. Terms defined in the Restated Distribution Agreement shall have the same meaning in this Amendment.

5. Excepting only as otherwise expressly set forth above, all other terms and provisions of the Restated Distribution Agreement shall remain in full force and effect.

IN WITNESS WHEREOF, the Distributor and the Supplier each have caused this Amendment to be executed by its duly authorized officer as of the date first written above.

COBE BCT, INC.

By: /s/ Edward C. Wood

AASTROM BIOSCIENCES, INC.

By: /s/ R. Douglas Armstrong

LICENSE AGREEMENT

by and between

AASTROM BIOSCIENCES, INC.,
a Michigan corporation

and

JOSEPH G. CREMONESE

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LICENSE AGREEMENT

This License Agreement is entered into and made effective as of July 17, 1992, by and between AASTROM BIOSCIENCES, INC., a Michigan corporation ("Licensee") whose address is Post Office Box 376, Ann Arbor, Michigan 48106, and JOSEPH G. CREMONESE, an individual ("Licensor") whose address is 227 Maple Drive, Greensburg, Pennsylvania 15601, with respect to the facts set forth below.

RECITALS

A. Licensee is engaged in development of cell culture technology, including products which are automated culture systems or bioreactors.

B. Licensor has disclosed to Licensee certain technology described in Patent '292 (defined below), a copy of which has been delivered to Licensee.

C. Licensor has the exclusive right to grant a license to the technology described in Patent '292 and the Licensed Patents and Licensed Technology (defined below).

D. Licensor desires to grant to Licensee, and Licensee wishes to acquire, an exclusive worldwide right and license to the technology described in Recital C, subject to the terms and conditions set forth herein.

AGREEMENT

NOW, THEREFORE, in consideration of the mutual covenants and conditions set forth herein, Licensor and Licensee hereby agree as follows:

1. Definitions. Capitalized terms shall have the meaning set forth

below.

Affiliate. The term "Affiliate" shall mean any entity which

directly or indirectly controls, is controlled by or is under common control with Licensee. The term "control" as used herein means the possession of the power to direct or cause the direction of the management and the policies of an entity, whether through the ownership of a majority of the outstanding voting securities or by contract or otherwise.

Combination Product. The term "Combination Product" shall have the

meaning as defined in Section 2.4.1 below.

Component Product. The term "Component Product" shall have the

meaning as defined in Section 2.5.1 below.

Confidential Information. The term "Confidential Information" shall

mean any and all proprietary or confidential information of Licensor or Licensee which may be exchanged between the parties at any time and from time to time during the term of this Agreement. Information shall not be considered confidential to the extent that it:

a. Is publicly disclosed through no fault of any party hereto, either before or after it becomes known to the receiving party; or

b. Was known to the receiving party prior to the date of this Agreement, which knowledge was acquired independently and not from the other party hereto (or such party's employees or agents); or

c. Is subsequently disclosed to the receiving party in good faith by a third party who has a right to make such disclosure; or

d. Has been published by a third party as a matter of right.

Licensed Patents. The term "Licensed Patents" shall mean Patent

'292, plus all patents issued based on divisionals, continuations, continuations-in-part, reissues, re-examinations and extensions of Patent '292, together with all corresponding foreign patents, and together with all related pending patent applications and inventor's certificates, and together with all patents and patent applications covering improvements to the inventions described in the foregoing. Without limiting the generality of the foregoing, Licensed Patents shall include U.S. Patent No. 4,839,292; Canadian Patent Application Serial No. 577,082, filed September 7, 1988; European Patent Application Serial No. 88,201,922.7, filed September 6, 1988, designating the following countries: Austria, Belgium, France, Greece, Italy, Luxembourg, Netherlands, Spain, Sweden, Switzerland, Liechtenstein, United Kingdom, and West Germany; and a new patent application which is being prepared and is entitled "Cell Growth and Perfusion Bag".

Licensed Product. The term "Licensed Product" shall mean any

product or process which cannot be developed, manufactured, used or sold without infringing on the valid claims of the Licensed Patents.

Licensed Technology. The term "Licensed Technology" shall mean the

Licensed Patents, plus all improvements thereto developed by Licensor, and all related data, know-how and technology.

Net Sales. The term "Net Sales" shall mean the gross amount

received by Licensee, or its Affiliates and sublicensees, or any of them, on sales of Licensed Products, net of (i) discounts actually given, (ii) credits for claims, allowances, retroactive price reductions or returned goods, (iii) prepaid freight (iv) sales taxes or other governmental charges paid in connection with sales of Licensed Products (but excluding what is commonly known as income taxes), and (v) the patent protection expenses described in the last sentence of this paragraph. For purposes of determining Net Sales, a sale shall be deemed to have occurred when a Licensed Product is shipped for delivery and paid for. Sales of Licensed Products by Licensee or its Affiliates or a sublicensee thereof to any Affiliate or sublicensee which is a reseller thereof shall be excluded, and only the subsequent sales of such Licensed Products by Affiliates or sublicensees to unrelated parties shall be deemed Net Sales hereunder. In the event that a Licensed Product is a Combination Product, then the Net Sales from said Licensed Product/Combination Product shall be determined in accordance with the formula set forth in Section 2.4 below. In the event that a Licensed Product is a Component Product, then the Net Sales from said Licensed Product/Component Product shall be determined in accordance with the formula set forth in Section 2.5 below. To the extent Licensee incurs any expenses (such as attorneys' fees or settlement payments, as examples) to protect the Licensed Patents against claims of invalidity, or to enforce the Licensed Patents against infringers, or to defend against claims that the Licensed Products infringe the patents of third parties, then said expenses shall be a deduction against the gross amounts for calculating Net Sales.

Patent '292. The term "Patent '292" shall mean U.S. Patent No.

4,839,292 entitled "Cell Culture Flask Utilizing a Membrane Barrier," issued to Licensors on June 13, 1989.

PTO. The term "PTO" shall mean the United States Patent and

Trademark Office.

2. License Terms and Conditions.

2.1 Grant of License. Licensors hereby grants to Licensee an

exclusive, worldwide license to use, make, have made and sell all products and/or processes utilizing the Licensed Technology, with the full right to grant sublicenses, subject to the terms of this Agreement.

2.2 Reimbursement of Patent Costs. As a part of the consideration

for the exclusive license granted pursuant to Section 2.1 hereof, Licensee shall reimburse Licensors for Licensors's out-of-pocket costs incurred for patent attorney fees and patent application filing fees in connection with the Licensed Patents, up to an aggregate maximum of \$25,000. Such reimbursement shall be subject to Licensors's presentation of appropriate documentation of Licensors's payment of such expenses.

No payment shall be payable by Licensee hereunder unless and until the issue of the validity of the claims as now stated in the Licensed Patents as described in Section 3.1 hereof is resolved favorably to Licensor's reasonable satisfaction, or, upon the expiration of one (1) year after the date of this Agreement if no request for re-examination of the Licensed Patents is made within such period. All payments made by Licensee to Licensor pursuant to this Section 2.2 shall be credited against Licensee's obligation to pay royalties as set forth in Section 2.3 hereof.

2.3 Royalties.

2.3.1 Percentage Royalty. As additional consideration for

the exclusive license granted pursuant to Section 2.1 hereof, Licensee shall pay to Licensor a continuing royalty on a country-by-country basis in the amount of (i) three percent (3%) of Net Sales of Licensed Products made, used or sold in any country where the Licensed Technology utilized therein is protected by a valid patent.

2.3.2 Credits Against Royalties. Licensee shall be entitled

to a credit against royalties payable hereunder in an amount equal to the payments made by Licensee under Sections 2.2 and 3.4 hereof.

2.3.3 Minimum Annual Royalty. From and after January 1,

1997, Licensee shall pay to Licensor minimum annual royalties as set forth herein. The minimum annual royalty for the calendar year 1997 shall be \$20,000. For the three years thereafter, the minimum annual royalty for each subsequent calendar year shall increase by \$10,000, such that for all years after and including the calendar year 2000, the minimum annual royalty shall be \$50,000. Any percentage royalties accrued and paid to Licensor (but not taken as a credit pursuant to Section 2.3.2 hereof) for any calendar year shall be credited against the minimum royalty payable for such calendar year. The payment of any shortfall between actual royalties paid and the minimum annual royalty applicable to such calendar year shall be payable to Licensor within sixty (60) days after the last day of such calendar year. Licensor's sole remedy for any failure by Licensee to pay the minimum annual royalty required hereunder shall be to convert the exclusive license granted hereunder to a nonexclusive license upon the expiration of sixty (60) days' written notice of Licensor's intention to so convert the license, without Licensee's payment of any delinquent minimum annual royalty. Such conversion would not relieve Licensee from payment of royalties as described in Section 2.3.1.

2.3.4 Most Favored Licensee. If this license becomes non-

exclusive and if Licensor grants a license to use the Licensed Patents to any third party at a royalty rate lower than three percent (3%), then the royalty rate payable by

Licensee under this Agreement shall be reduced to the same rate payable by the third party.

2.4 Combination Product.

2.4.1 Definition of Combination Product. As used herein, the term "Combination Product" shall mean a Licensed Product which cannot be manufactured, used or sold without (i) infringing the Licensed Patents, and also (ii) infringing one or more patents held by Licensee or a third party (referred to herein as "other patent rights").

2.4.2 Net Sales of Combination Product. The Net Sales

of a Combination Product shall be determined in accordance with the following formula:

$$X = \frac{A}{B} \times C, \text{ where}$$

X = the Net Sales attributable to the portion of the Combination Product which is attributable to the Licensed Patents, on which Net Sales Licensee shall pay the royalty rate set forth in Section 2.3.1; and

A = the value of the contribution of the Licensed Patents (as compared to the value of the contributions of the rights) used in the Combination Product; and

B = The aggregate value of all patent rights used for the Combination Product, consisting of both the Licensed Patents and all other patent rights used in the Combination Product; and

C = the Net Sales for the Combination Product.

The values described above shall be determined by the parties hereto in good faith. In the absence of agreement as to said values, the values shall be determined by arbitration in accordance with the provisions of Section 10.2 hereof.

2.5 Component Product.

2.5.1 Definition of Component Product. As used herein,

the term "Component Product" shall mean a Licensed Product which is a distinct component of a product which contains multiple components (including, as an example of additional components, proprietary methods sold or licensed with the Component Product).

2.5.2 Net Sales of Component Product. The Net Sales of a

Component Product shall be determined in accordance with the following formula:

$$X = \frac{A}{B} \times C, \text{ where}$$

X = the Net Sales attributable to the Component Product, on which Licensee is obligated to pay the royalty rate set forth in Section 2.3.1; and

A = the value of the Component Product, based upon costs to manufacture the Component Product, or the sales price of the Component Product if it is sold separately; and

B = The value of the aggregate product, with all components (including methods sold or licensed with the Component Product), including the Component Product, based upon the same criteria as used for A above; and

C = the Net Sales for the aggregate product.

The values described above shall be determined by the parties in good faith. In the absence of agreement as to said values, the values shall be determined by arbitration in accordance with the provisions of Section 10.2 hereof.

2.6 Quarterly Payments.

2.6.1 Sales by Licensee. With regard to Net Sales made

by Licensee or its Affiliates, royalties shall be payable by Licensee quarterly, within ninety (90) days after the end of each calendar quarter, based upon Net Sales of Licensed Products during such preceding calendar quarter, commencing with the calendar quarter in which the first commercial sale of any Licensed Product is made.

2.6.2 Sales by Sublicensees. With regard to Net Sales

made by sublicensees of Licensee or its Affiliates, royalties shall be payable by Licensee quarterly, within one hundred twenty (120) days after the end of each calendar quarter, based upon the Net Sales of Licensed Products by such sublicensee during such preceding calendar quarter, commencing with the calendar quarter in which the first commercial sale of any Licensed Product is made by such sublicensee.

2.7 Term. The term of this Agreement and the license granted

hereunder shall commence on the date set forth in the preamble paragraph of this Agreement, and unless sooner

terminated by Licensee upon delivery of thirty (30) days' written notice or in accordance with the provisions of Section 8.1 hereof, the term of this Agreement and the license granted hereunder shall expire when the last patent licensed hereunder has expired.

2.8 Sublicense Rights. Licensee shall have the sole and

exclusive right to grant sublicenses to any party with respect to the rights conferred upon Licensee under this Agreement, provided, however, that any such sublicense shall be subject in all respects to all of the provisions contained in this Agreement (but not including the payment of patent costs pursuant to Sections 2.2 and 3.4 hereof and the obligation to pay minimum annual royalties pursuant to Section 2.3.3 hereof). Licensee shall pay Licensor, or cause its Affiliates or sublicensees to pay Licensor, the same royalties on all Net Sales of such Affiliate or sublicensee the same as if such Net Sales had been made by Licensee. Each Affiliate and sublicensee shall report its Net Sales to Licensor through Licensee, which Net Sales shall be aggregated with any Net Sales of Licensee for purposes of determining the Net Sales upon which royalties are to be paid to Licensor. Any royalties paid to Licensor with respect to Net Sales of any Affiliate or any sublicensee of Licensee or any Affiliate shall be credited against Licensee's minimum annual royalty obligations hereunder.

2.9 Duration of Royalty Obligations. The royalty obligations

of Licensee as to each Licensed Product shall terminate on a country-by-country basis concurrently with the expiration of the last to expire of the patents licensed hereunder utilized by or in such Licensed Product in each such country. Notwithstanding any other provision of this Agreement, in the event that, based upon a challenge by a party other than Licensee, its Affiliates or sublicensees, the existing favorable claims of the Licensed Patents are held to be invalid by the PTO or any competent court of law, Licensee may terminate this Agreement and Licensee thereafter shall have no further obligation to pay any royalties hereunder.

2.10 Reports. Licensee shall furnish to Licensor at the same

time as each royalty payment is made by Licensee, a written report of Net Sales of Licensed Products and the royalty due and payable thereon, including a description of any offsets or credits deducted therefrom, on a product-by-product and country-by-country basis, for the calendar quarter upon which such royalty payment is based.

2.11 Records. Licensee shall keep, and cause its Affiliates

and sublicensees to keep, complete records and accounts of all sales of Licensed Products in sufficient detail to enable the royalties payable on Net Sales of each Licensed Product to be determined. Licensor shall have the right to appoint an independent certified public accounting firm approved by Licensee, which approval shall not be unreasonably withheld,

to audit, upon delivery of advance written notice and during normal business hours without interruption of normal business operations, the records of Licensee, its Affiliates and sublicensees as necessary to verify the royalties payable pursuant to this Agreement. Licensee, its Affiliates and sublicensees shall pay to Licensor an amount equal to any additional royalties to which Licensor is entitled as disclosed by the audit. Such audit shall be at Licensor's expense. Licensor may exercise its right of audit hereunder no more frequently than once in any calendar year. The accounting firm shall disclose to Licensor only such information as is necessary to verify the accuracy of the royalty payments required hereunder, and all such information shall be treated as Confidential Information by Licensor. Licensee, its Affiliates and sublicensees shall preserve and maintain all records required for audit for a period of three (3) years after the calendar quarter to which the record applies.

2.12 Foreign Taxes. Any tax required to be withheld by

Licensee under the laws of any foreign country for the account of Licensor shall be paid by Licensee for and on behalf of Licensor to the appropriate governmental authority and deducted from any royalties payable by Licensee hereunder.

3. Patent Matters.

3.1 Validity of Licensed Patents. The parties hereto

acknowledge that there may be an issue concerning the validity of some of the claims of the existing Licensed Patents. In order to resolve such issue, Licensee may, in the exercise of its sole discretion and at its sole expense, request a re-examination of the existing Licensed Patents by the PTO and the applicable foreign agencies. Each of the parties hereto shall exercise good faith and due diligence in their efforts to establish the validity of the existing Licensed Patents.

3.2 Patent Prosecution and Maintenance. From and after the

date of this Agreement, the provisions of this Section 3.2 shall control the prosecution and maintenance of the Licensed Patents. Licensee shall direct and control (i) the maintenance of Patent '292 and the re-examination of Patent '292 described in Section 3.1 hereof; (ii) the preparation, filing and prosecution of all other domestic and foreign patent applications relating to Licensed Technology (including any interferences and foreign oppositions); and (iii) the maintenance of any patents issuing therefrom. Licensee shall select the patent attorney, and the fees and expenses incurred by Licensee with respect to services performed by such patent counsel and any filing or other fees shall be paid as set forth below in Section 3.4. Licensor shall assist Licensee and patent counsel retained by Licensee as necessary to accomplish the patent processes described hereunder. Licensor shall sign all documents which are reasonably necessary to enable Licensee to prosecute and maintain all patent matters. Licensee shall use good faith and due diligence in determining

which foreign countries, in addition to the U.S.A., in which to file for and maintain patent rights, depending on the commercial benefits Licensee can reasonably anticipate in each country. In as much as Licensee is paying the patent costs, the ultimate decision as to all of these patent prosecution and maintenance matters shall be made by Licensee.

3.3 Information to Licensor. Licensee shall keep Licensor

informed with regard to the patent application, re-examination and maintenance processes. Licensee shall deliver to Licensor copies of all patent applications, amendments, related correspondence, and other related matters.

3.4 Patent Costs. The parties hereto agree that the exclusive

license granted hereunder is in part in consideration for Licensee's assumption of patent costs and expenses as described herein. Licensee shall pay for all expenses incurred by Licensee pursuant to Sections 3.1 and 3.2 hereof, in addition to patent costs paid by Licensee as set forth in Section 2.2 hereof.

3.5 Ownership. Patent '292 and the patent applications filed

and the patents obtained by Licensee pursuant to Section 3.2 hereof shall be owned solely by Licensor, and included in the exclusive license granted hereunder.

3.6 Infringement Actions.

3.6.1 Prosecution and Defense of Infringements. Licensee

shall have the right but not the obligation to prosecute any and all infringements of any patent licensed hereunder and to defend all charges of infringement arising as a result of the exercise by Licensee, its Affiliates or sublicensees of the rights granted hereunder. Licensee may enter into settlements, stipulated judgments or other arrangements respecting such infringement, at its own expense. Licensor shall permit any action to be brought in his name if required by law, and Licensee shall hold Licensor harmless from any costs, expenses of liability respecting all such infringements or charges of infringement, except such infringements as shall result from any breach of warranty made by Licensor herein. Licensor agrees to provide all necessary assistance of a technical nature which Licensee may require in any litigation arising with respect to the Licensed Technology. In the event Licensee elects not to prosecute any infringement, Licensee shall notify Licensor in writing promptly and Licensor shall have the right to prosecute such infringement on his own behalf. If Licensee elects to prosecute an infringement, then Licensor shall not be entitled to do so.

3.6.2 Allocation of Recovery. Any damages or other

recovery from an infringement action undertaken by Licensee pursuant to Section 3.6.1 shall be retained by Licensee as its exclusive property; but any such recovery, net of

Licensee's costs of litigation, shall be treated as "Net Sales" and Licensee shall pay a royalty thereon pursuant to Section 2.3.1 above. If Licensee elects to not prosecute an infringement, and Licensor does prosecute said infringement, then Licensee shall retain any recovery received from said prosecution.

4. Obligations Related to Commercialization.

4.1 Commercial Development Obligation. In order to

maintain Licensee's exclusive license rights granted hereunder in force, Licensee shall use reasonable efforts and due diligence to develop the Licensed Technology into commercially viable Licensed Products, as promptly as is reasonably and commercially feasible, and thereafter to produce and sell reasonable quantities of Licensed Products. Licensee shall keep Licensor generally informed as to Licensee's progress in such development, production and sale, including its efforts, if any, to sublicense Licensed Technology.

4.2 Milestone. If Licensee has not, by July 1, 1998,

pursued reasonable efforts and due diligence to develop the Licensed Technology into commercially viable Licensed Products, such that there is a reasonable probability of Net Sales forthcoming, then Licensor may require Licensee to pay to Licensor a one-time payment of Fifty Thousand Dollars (\$50,000) as a condition to retaining the exclusivity of the license granted hereunder in force. If said payment is so required and not paid, then Licensee's rights under this Agreement shall become non-exclusive and no minimum royalties shall thereafter be payable. If Licensor concludes that Licensee has failed to pursue said reasonable efforts and due diligence, then Licensor shall give written notice of said conclusion to Licensee, and Licensee shall have three months after receipt of said notice to cure the failure. If there is a dispute as to whether there is a failure or a cure, the dispute shall be resolved by arbitration pursuant to Section 10.2 below.

4.3 Governmental Approvals and Marketing of Licensed

Products. Licensee shall be responsible for obtaining all necessary governmental approvals for the development, production, distribution, sale and use of any Licensed Product, at Licensee's expense. Licensee shall have sole responsibility for any warning labels, packaging and instructions as to the use of Licensed Products and for the quality control for any Licensed Product.

4.4 Product Liability Indemnity. Licensee hereby agrees

to indemnify, defend and hold harmless Licensor from and against any liability or expense arising from any product liability claim asserted by any party as to any Licensed Product made or sold by Licensee or its Affiliates and sublicensees, other than any claim which arises due to a breach by Licensor of any warranty made herein.

5. Representations and Warranties. Licensor hereby represents and

warrants that (i) he is the rightful owner of the Licensed Technology, (ii) the Licensed Technology is not subject to any lien, license, assignment, security interest or other encumbrances, (iii) he has made full disclosure to Licensee of all communications with respect to the Licensed Technology with the PTO and any foreign patent agencies, (iv) he has the power and authority to enter into this Agreement and grant the license provided for hereunder, and (v) except as disclosed to Licensee, Licensor has no knowledge that the Licensed Technology infringes any patents or other intellectual property rights of third parties, or that any third party is in any way infringing the Licensed Technology covered by this Agreement.

6. Interests in Intellectual Property Rights.

6.1 Preservation of Title. Licensor shall retain full

ownership and title to Licensed Technology, Patent '292 and any other patents licensed hereunder and shall use his reasonable best efforts to preserve and maintain such full ownership and title.

6.2 Ownership of Improvements.

6.2.1 Developed by Licensee. Any improvements to

Licensed Technology conceived, developed or reduced to practice by Licensee, its Affiliates or sublicensees or their employees shall remain the sole and exclusive property of such party, and shall not be included in Licensed Technology hereunder.

6.2.2 Developed by Licensor. Any improvements to

Licensed Technology conceived, developed or reduced to practice by Licensor during the term of this Agreement shall be included in Licensed Technology and subject to the exclusive license granted hereunder.

7. Confidentiality and Publication.

7.1 Treatment of Confidential Information. The parties agree

that during the term of this Agreement, and for a period of three (3) years after this Agreement terminates, a party receiving Confidential Information of the other party will (i) maintain in confidence such Confidential Information to the same extent such party maintains its own proprietary industrial information, (ii) not disclose such Confidential Information to any third party without prior written consent of the other party and (iii) not use such Confidential Information for any purpose except those permitted by this Agreement.

7.2 Publications. In order to protect the rights granted to

Licensee hereunder, Licensor shall submit to Licensee copies of proposed publications of Licensor which contain subject matter relating to intellectual property licensed hereunder and

afford Licensee sixty (60) days to review such proposed publications. Upon timely written request by Licensee, Licensors shall delay any such publication to facilitate the preparation and filing of a patent application, which delay shall not exceed ninety (90) days from the date Licensee requests such delay.

8. Termination.

8.1 Termination Upon Default. Upon the failure of a party to

perform any obligation required of it or him to be performed hereunder, and the failure to cure within thirty (30) days after receipt of written notice from the other party specifying in reasonable detail the nature of such default, the non-defaulting party may deliver to the defaulting party written notice of intent to terminate, such termination to be effective upon the date set forth in such notice.

Such termination rights shall be in addition to and not in substitution for any other remedies that may be available to the non-defaulting party. Termination pursuant to this Section 8.1 shall not relieve the defaulting party from liability and damages to the other party for breach of this Agreement. Waiver by either party of a single default or a succession of defaults shall not deprive such party of any right to terminate this Agreement arising by reason of any subsequent default.

8.2 Transfer Upon Bankruptcy or Insolvency. In the event of

the bankruptcy or insolvency of Licensee, this Agreement and the rights granted to Licensee hereunder may be transferred by Licensee or any trustee appointed for the estate of Licensee, provided such transferee shall agree in writing to comply with all of the terms and conditions set forth herein and to cure any financial defaults by Licensee.

8.3 Rights Upon Expiration. Neither party shall have any

further rights or obligations upon the expiration of this Agreement other than the obligation of Licensee to make any and all reports and payments for the final quarter period. Provided, however, that upon such expiration, each party shall be required to continue to abide by its non-disclosure obligations as described in Section 7.1, and Licensee shall continue to abide by its obligation to indemnify Licensors as described in Section 4.4 for products sold prior to the termination.

8.4 Rights Upon Termination. Notwithstanding any other

provision of this Agreement, upon any termination of this Agreement prior to the regularly scheduled expiration date of this Agreement, the license granted hereunder shall terminate. Except as otherwise provided in Section 8.5 of this Agreement with respect to work-in-progress, upon such termination, Licensee shall have no further right to develop, manufacture or sell any Licensed Products, or to otherwise use any Licensed Technology. Any such termination shall not relieve either party from any obligations accrued to the date of such termination. Upon such

termination, each party shall be required to abide by its nondisclosure obligations as described in Section 7.1, and, provided termination was not initiated by Licensee due to Licensor's breach hereunder, Licensee shall continue to abide by its obligations to indemnify Licensor as described in Section 4.4 for products sold prior to the termination.

8.5 Work-in-Progress. Upon any early termination of this

Agreement and the license granted hereunder, Licensee shall be entitled to finish any work-in-progress and to sell any completed inventory of Licensed Products which remain on hand as of the date of termination, so long as Licensee pays to Licensor the royalties applicable to such sales in accordance with the terms and conditions as set forth in this Agreement .

9. Binding Upon Successors and Assigns. This Agreement shall be

binding upon and inure to the benefit of any successors in interest and assigns of Licensor and Licensee. Any such successor or assignee shall expressly assume in writing the performance of all the terms and conditions of this Agreement to be performed by the assigning party.

10. General Provisions.

10.1 Independent Contractors. The relationship between

Licensor and Licensee is that of independent contractors. Licensor and Licensee are not joint venturers, partners, principal and agent, master and servant, employer or employee, and have no other relationship other than independent contracting parties. Licensor and Licensee shall have no power to bind or obligate each other in any manner, other than as is expressly set forth in this Agreement.

10.2 Arbitration. Any matter or disagreement arising under

this Agreement shall be submitted for decision to a panel of three neutral arbitrators with expertise in the subject matter to be arbitrated. One arbitrator shall be selected by each party and the two arbitrators so selected shall select the third arbitrator. The arbitration shall be conducted in accordance with the Rules of the American Arbitration Association. The decision and award rendered by the arbitrators shall be final and binding. Judgment upon the award may be entered in any court having jurisdiction thereof. Any arbitration shall be held in Ann Arbor, Michigan, or such other place as may be mutually agreed upon in writing by the parties.

10.3 Entire Agreement; Modification. This Agreement sets

forth the entire agreement and understanding between the parties as to the subject matter hereof. There shall be no amendments or modifications to this Agreement, except by a written document which is signed by both parties.

10.4 Governing Law. This Agreement shall be construed and

enforced in accordance with the laws of the State of Michigan.

10.5 Severability. If any one or more of the provisions of

this Agreement is held to be invalid or unenforceable by a court of competent jurisdiction, it shall be considered severed from this Agreement and shall not serve to invalidate the remaining provisions thereof. The parties shall make a good faith effort to replace any invalid or unenforceable provision with a valid and enforceable provision such that the objectives contemplated by them when entering this Agreement may be realized.

10.6 No Waiver. Any delay in enforcing a party's rights under

this Agreement or any waiver as to a particular default or other matter shall not constitute a waiver of such party's rights to the future enforcement of its rights under this Agreement, excepting only as to an express written and signed waiver as to a particular matter for a particular period of time.

10.7 Attorneys' Fees. In the event of a dispute between the

parties hereto or in the event of any default hereunder, the party prevailing in the resolution of any such dispute or default shall be entitled to recover its reasonable attorneys' fees and other costs incurred in connection with resolving such dispute or default.

10.8 Notices. Any notices required by this Agreement shall be

in writing, shall refer to this Agreement and shall be sent by registered or certified mail, postage prepaid, or by telefax, telex or cable, charges prepaid, or by overnight courier, charges prepaid to the addresses set forth below unless subsequently changed by written notice to the other party:

For Licensee: Aastrom Biosciences, Inc.
 Post Office Box 376
 Ann Arbor, Michigan 48106
 Attention: R. Douglas Armstrong, Ph.D.
 President/CEO
 Fax No.: (313) 665-0485

For Licensor: Joseph G. Cremonese
 227 Maple Drive
 Greensburg, Pennsylvania 15601
 Fax No.: (412) 838-7780

Notice shall be deemed delivered upon the earlier of (i) when received, (ii) three (3) days after deposit into the mail, or (iii) the date notice is sent via telefax, telex or cable,

(iv) the day immediately following delivery to overnight courier (except Sunday and holidays).

IN WITNESS WHEREOF, the parties have executed this Agreement by their duly authorized representatives as of the date set forth above.

LICENSOR:

LICENSEE:

AASTROM BIOSCIENCES, INC.

/s/ Joseph G. Cremonese

By: /s/ R. Douglas Armstrong

Joseph G. Cremonese
7-17-92

R. Douglas Armstrong, Ph.D.
President/CEO
8/5/92

July 7, 1993

Mr. Joseph G. Cremonese
227 Maple Drive
Greensburg, PA 15601

Dear Joe,

In follow-up to our discussion, this letter is to formalize our understanding for extension of our license agreement. More specifically, we mutually agree to allow AASTROM a 1-month extension to initiate a re-examination request for Patent #4,839,292, as per sections 2.2 and 3.1 of our July 17, 1992, License Agreement. All other provisions of the License Agreement are unmodified.

To represent your agreement with this, please sign as indicated below.

Thank you.

Sincerely,

/s/ R. DOUGLAS ARMSTRONG

R. Douglas Armstrong, Ph.D.
President and CEO

RDA:pp

I agree to the terms as indicated above.

/s/ JOSEPH G. CREMONESE 7/8/93

Joseph G. Cremonese

COLLABORATIVE PRODUCT DEVELOPMENT AGREEMENT
(Instrument)

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EXHIBITS

A	General Description of the System and the Instrument
B	Specifications and Functional Requirements for the Instrument
C	Time and Quantity Schedule - Preproduction Units
C1	Pricing for Precommercial Units
D	Manufacturing Drawings for the Instrument
E	Compensation Schedule for Design Work and Manufacturing Preproduction Units
F	Summary of Manufacturing Agreement for Phase II

COLLABORATIVE PRODUCT DEVELOPMENT AGREEMENT

(Instrument)

This Collaborative Product Development Agreement (the "Agreement") is entered into as of May 10, 1994, by and between Aastrom Biosciences, Inc., a

Michigan corporation ("Aastrom"), and SeaMED Corporation, a Delaware corporation ("SeaMED").

A. Aastrom is in the final stages of research and development for a proprietary Cell Expansion System which is used for stem cell growth (the "System"). The System includes an instrument or instruments (the "Instrument") and a disposable biochamber cartridge. Aastrom has completed a working prototype model of the System; and Aastrom now needs to complete the design of the Instrument and to obtain (i) pre-production models defined as pre-revision Rev. A specification units (hereinafter called "preproduction units") of the Instrument for laboratory and clinical evaluation, and (ii) pre-commercial models, defined as units made once the release occurs for Rev. A specification units (hereinafter called "precommercial units") of the Instrument for laboratory and clinical evaluation. Attached hereto as Exhibit A is a general description of the System, including the Instrument.

B. SeaMED has expertise and experience in the development and manufacture of medical instruments which are somewhat similar to the Instrument, and SeaMED is prepared to collaborate with Aastrom for completing the necessary design work on the Instrument to enable SeaMED to produce preproduction units and precommercial units of the Instrument for laboratory and clinical evaluation as outlined in the SeaMED Project Plan, Drawing Number 908180, draft dated 2-2-94.

C. As further described in this Agreement, (i) the design and manufacture of preproduction units and precommercial units of the Instrument shall be referred to as Phase I, and (ii) the subsequent manufacture of commercial units (defined as any unit that is sold) of the Instrument shall be referred to as Phase II.

D. Pursuant to the terms of this Agreement, during Phase I SeaMED shall (i) collaborate with and assist Aastrom to design the preproduction units and precommercial units of the Instrument, and (ii) manufacture the preproduction units and precommercial units of the Instrument. At least six months prior to the expected commencement of Phase II, Aastrom and SeaMED shall pursue good faith negotiations for entering into a Manufacturing Agreement for SeaMED to manufacture the commercial units of the Instrument, as further described in

Section 6 of this Agreement. Because of foreign governmental approval requirements, it is possible that there still will be some preproduction units and precommercial units being made during Phase I, while at the same time there will be some commercial units being made during Phase II.

E. Aastrom has contracted with Roecker Design Group, and Aastrom may also contract with other design specialists for assistance with specified aspects of the System and/or Instrument (collectively called the "Other Design Contractors").

AGREEMENT

NOW, THEREFORE, the parties hereby agree as follows:

1. Responsibilities of Aastrom.

1.1 Project Management. Aastrom shall be responsible for overall

project management relating to the development of the Instrument.

1.2 Specifications. Aastrom shall collaborate with SeaMED and the

Other Design Contractors on completing the design work for the Instrument. With assistance from SeaMED as more fully described in Section 2 below, Aastrom shall develop the final specifications and functional requirements for the preproduction units and precommercial units (including applicable test criteria) (the "Specifications"). Upon completion of the Specifications, Aastrom shall promptly provide SeaMED with a copy of the Specifications, and the Specifications shall be incorporated herein as Exhibit B hereto.

2. Responsibilities of SeaMED.

2.1 Design Collaboration. SeaMED shall collaborate with Aastrom

and the Other Design Contractors on completing the design work for the Instrument. The time schedule for completing such design work shall be as set forth in Exhibit C. Without limiting the foregoing, SeaMED shall:

(a) Assist Aastrom with respect to planning for all manufacturing issues that are likely to arise in connection with the design work and development of the Instrument, including issues relating to the Phase I and Phase II manufacturing process development and validation, component sourcing, and the creation of Device Master record documentation requirements;

(b) Review the Instrument software design and documentation, and provide third party quality assurance, including specification review, code audits, verification and validation testing, to ensure to the best of

SeaMED's ability that they are in compliance with all applicable guidelines of the U.S. Food and Drug Administration;

(c) Assist Aastrom to establish a reliability goal for the Instrument, calculate the reliability of the preproduction units and precommercial units at certain established review points during the design and development of the Instrument, and perform demonstration tests on pilot production units produced by SeaMED; and

(d) Determine all necessary requirements for certification of the Instrument by UL, CSA, IEC, TUV and EC, and to review the design of the Instrument at various key points during the product development stage to determine compliance with such requirements, and coordinate the testing of the Instrument for compliance with such requirements and the submission of the Instrument for certification by each of such entities.

(e) Prepare working drawings for manufacturing and testing the preproduction units and the precommercial units of the Instrument, including without limitation, (i) specifications for component parts to be acquired from specified vendors, (ii) drawings and specifications for component parts, (iii) test and acceptance procedures and criteria, (iv) subassembly specifications, drawings and requirements, (v) costed bill of materials, and (vi) product specific manufacturing procedures, device master record, routing and processes (collectively called the "Manufacturing Drawings"), which Manufacturing Drawings shall be subject to the prior written approval of Aastrom, shall be owned by Aastrom, and shall ultimately be incorporated herein as Exhibit D. If said manufacturing drawings reference general policies and procedures of SeaMED, such as SeaMED's Quality System, then such general policies and procedures shall remain the property of SeaMED, but Aastrom shall be given a copy of the same. As modifications are made from time to time to the Manufacturing Drawings by mutual agreement, SeaMED shall furnish to Aastrom an updated copy thereof.

(f) To the extent required for submittal to the U.S. Food and Drug Administration ("FDA") (or comparable foreign agencies) for Aastrom's IDE and/or PMA (or comparable foreign approvals), prepare a detailed description of SeaMED's manufacturing methods, processes, procedures and facility applicable to Aastrom's Instrument.

2.2 Delivery of Preproduction Units. Following Aastrom's approval of the

Manufacturing Drawings prepared by SeaMED, in accordance with the time and quantity schedule specified in Exhibit C attached hereto, and the pricing specified in Exhibit E, SeaMED shall manufacture and deliver to Aastrom at its Ann Arbor, Michigan facility, a number of the preproduction units of the Instrument, in compliance with the Specifications and the Manufacturing Drawings,

for use in clinical tests of the System. The exact number of said preproduction units, and any variations thereof, shall be as specified by Aastrom in a purchase order, subject to SeaMED's reasonable approval, which approval will not be withheld unreasonably. As Aastrom's clinical tests of the System proceed, and depending on the outcome of those tests, Aastrom may place purchase orders for additional units of the preproduction unit; and SeaMED shall manufacture and sell said additional preproduction units on the same terms and conditions as set forth herein. Provided, however, the maximum number of preproduction units shall be as specified in Exhibit C.

2.2.1 Delivery of Precommercial Units. Once Aastrom has released

for manufacture the Rev. A specifications for the precommercial units, SeaMED shall manufacture and deliver to Aastrom at its Ann Arbor, Michigan facility, a number of the precommercial units of the Instrument, in compliance with the Rev. A Specifications and the related manufacturing Drawings, for use in clinical tests of the System. The exact number of said precommercial units shall be specified by Aastrom in a purchase order, subject to SeaMED's reasonable approval, which approval will not be withheld unreasonably. The purchase and sale of the precommercial units shall be in accordance with the terms specified on Exhibit C-1 attached hereto. Delivery of precommercial units will be within twenty (20) weeks after SeaMED receives a firm purchase order for the specified number of units. A specific schedule will be determined at the time of the purchase order placement.

2.3 Maintenance of Adequate Facilities and Manufacturing

Practices. SeaMED shall maintain adequate personnel and facilities to perform

its obligations under this Agreement. SeaMED shall assemble all of the preproduction units and precommercial units in an environment where good manufacturing practices are followed. Inasmuch as SeaMED's FDA facility registration and inspection record are extremely important to Aastrom's ability to obtain prompt FDA approval for Aastrom's System, SeaMED hereby agrees to use its best efforts to maintain in good standing all appropriate FDA facility registrations and inspection records. SeaMED shall immediately report to Aastrom in writing any adverse events, circumstances, or potential problems relating to SeaMED's FDA registrations and inspections that could adversely effect Aastrom's product or the System approval. SeaMed shall furnish to Aastrom a copy of the FDA facility registrations and inspection reports applicable as of the date of this Agreement, plus each subsequent FDA registration or inspection report during the term of this Agreement. SeaMED shall allow Aastrom and its agent to review and inspect SeaMED's facilities, and FDA compliance files, and correspondence to and from the FDA regarding inspections, registrations, and audits that pertain directly to Aastrom's product or the System's regulatory submission. SeaMED will inform Aastrom of any negative findings regarding other products (although the product and company will remain confidential) or processes that may have an impact on

Aastrom's product or regulatory submission. To the extent that European Economic Community standards apply to SeaMED's facility and manufacturing practices for units to be used in Europe, SeaMED will also comply with said standards.

2.4 No Subcontracting. No part of SeaMED's obligations under

this Agreement shall be subcontracted by SeaMED that would impact Aastrom's PMA approval, without the prior written approval of Aastrom.

2.5 Inventory and Insurance. All inventory of components and

materials purchased by SeaMED to make the Instrument shall be owned by SeaMED and shall be insured against risk of loss by SeaMED. Any components and materials purchased by Aastrom and delivered to SeaMED for SeaMED to use to make the Products shall be covered by SeaMED's insurance policy for risk of loss while said items remain in SeaMED's facility, with Aastrom being the loss payee therefor.

2.6 Transit. SeaMED shall arrange for shipment of the Instrument by

a common carrier approved by Aastrom, to a destination specified by Aastrom. Title and risk of loss to the Instrument shall pass from SeaMED to Aastrom when the Instruments are delivered to a common carrier for shipment to Aastrom's designation.

2.7 Financial Condition. Each party shall furnish to the other

party a copy of the party's quarterly financial statements and a copy of the party's annual financial statements, within forty-five (45) days after each quarter-end and ninety (90) days after the party's fiscal year-end. Each party shall give written notification to the other party of any material adverse financial condition affecting the party, including without limitation: (i) the filing of a significant lawsuit against the party, (ii) the lack of cash funds available to pay all obligations of the party as they become due, (iii) the lack of resources available to enable the party to fully and promptly perform its obligations under this Agreement on schedule, or (iv) any other condition which may jeopardize or impair the full and prompt performance by the party of its obligations under this Agreement. Said notification shall be given within five (5) days after the occurrence or realization of said adverse condition.

3. Acceptance Procedures. Delivery of each of the preproduction units

and precommercial units shall be deemed accepted by Aastrom unless SeaMED is notified in writing of Aastrom's rejection of such delivery within thirty (30) days after the delivery date due to a failure thereof to comply with the Specifications and/or the Manufacturing Drawings, including the test criteria. In the event SeaMED receives such notice, SeaMED shall diligently attempt to promptly resolve any such failure, and to deliver a unit which conforms to the

Specifications and the Manufacturing Drawings. In the event SeaMED cannot resolve any such failure and deliver a unit that conforms to the Specifications and the Manufacturing Drawings within thirty (30) days of receipt of such notice, Aastrom may terminate this Agreement pursuant to Section 12 below.

4. Compensation. Aastrom shall compensate SeaMED for SeaMED's

design work and preproduction unit manufacture on a "time and materials" basis, as further described on Exhibit E. Aastrom shall compensate SeaMED for the precommercial units manufactured pursuant to the maximum pricing formula as specified in Exhibit C-1 attached hereto, subject to the definitions and pricing schedule considerations in Section 4.1 of Exhibit F attached hereto. SeaMED shall submit to Aastrom a monthly invoice for said design work, and SeaMED shall invoice for units manufactured upon shipment of the units, and each invoice shall be accompanied by such supporting details as Aastrom may reasonably request. Aastrom shall pay said invoice within thirty (30) days after the invoice and supporting details are received by Aastrom.

5. Warranties.

5.1 SeaMED's Warranty. SeaMED warrants that each of the units

(i) shall be manufactured in full compliance with the Specifications and the Manufacturing Drawings, (ii) shall be free from defects in material and workmanship, and (iii) shall be free from defects in design as to those specific elements for which SeaMED was primarily responsible for the design. As to elements of the unit for which SeaMED was not primarily responsible for the

design, SeaMED is not making any warranty as to design. SeaMED further warrants that the manufacture, assembly and delivery of the units hereunder shall be (i) in compliance with all applicable federal, state and local laws, rules, regulations and executive orders, including without limitation, all of the employee compensation, health and safety and environmental laws applicable to SeaMED's facility, and all U.S. customs laws and regulations, and U.S. Food and Drug Administration ("FDA") regulations, and applicable foreign regulations, and (ii) performed in a professional, workmanlike manner in accordance with prevailing industry standards. SeaMED understands that Aastrom may sell the units to hospital customers or other users. SeaMED agrees that the foregoing warranties are for the benefit of Aastrom and any ultimate end-user of the units.

5.2 Limitation on Liability. SeaMED shall either repair or

replace or provide to Aastrom full credit for the purchase price of any unit which is defective due to SeaMED's failure to comply with the foregoing warranty. Any such warranty repairs or replacements shall be completed within thirty (30) days after the date on which any defective unit is delivered to SeaMED. All shipping and other costs incurred in connection with the repair or replacement of any

defective unit shall be borne by and for the account of SeaMED. Except as specified in Section 8, SeaMED shall have no liability to Aastrom for any consequential damages or loss, including but not limited to loss of profits or goodwill, additional expenses incurred, or other damages.

5.3 Disclaimer of Warranties.

EXCEPT FOR THE WARRANTIES SET FORTH IN THIS SECTION, SEAMED DISCLAIMS ANY AND ALL WARRANTIES, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR ANY IMPLIED WARRANTY OF FITNESS FOR A PARTICULAR PURPOSE.

5.4 Aastrom's Warranty. Aastrom warrants that all elements of

the Instrument units for which SeaMED was not primarily responsible for the design shall be free from defects in design.

6. Phase II Manufacture.

6.1 Manufacturing Agreement. Subject to satisfying the

prerequisites listed below, Aastrom and SeaMED will enter into a Manufacturing Agreement for Phase II manufacture of commercial units of the Instrument in accordance with the terms set forth in Exhibit F attached hereto. At the option and discretion of Aastrom, Aastrom may waive any one or more of said prerequisites. Said prerequisites are:

(a) SeaMED has performed its obligations during Phase I in a diligent, prompt and effective manner, to the reasonable satisfaction of Aastrom, without any defaults by SeaMED.

(b) SeaMED has manufactured the preproduction units and precommercial units of the Instrument during Phase I in full compliance with the Manufacturing Drawings and the Specifications, and SeaMED has delivered the quantities of same on a timely schedule as ordered, and SeaMED has complied fully with its obligations under this Agreement.

(c) SeaMED has successfully controlled the costs to manufacture the preproduction units and precommercial units, on a reasonable and cost effective basis.

(d) SeaMED has adequate facilities, equipment, personnel, governmental approvals, and manufacturing capacity to manufacture the quantities

of the commercial units of the Instruments needed by Aastrom during Phase II; and SeaMED shall furnish to Aastrom reasonable evidence to verify the same.

(e) SeaMED's facility has received all necessary approvals from the FDA and from the European Community (or other necessary foreign agencies) to manufacture the commercial units of the Instrument.

(f) SeaMED's financial condition is sound and stable, such that there are no reasonable doubts as to SeaMED's financial ability to remain in business and perform its obligations contemplated under the Manufacturing Agreement, and SeaMED shall furnish to Aastrom reasonable evidence to verify the same.

(g) SeaMED is able and willing to manufacture the commercial units of the Instrument on a cost effective and efficient basis, on a timely production schedule, and on a high quality basis, pursuant to mutually approved pricing and delivery schedules, all in accordance with the Manufacturing Agreement, and SeaMED shall furnish to Aastrom reasonable evidence to verify the same.

(h) SeaMED maintains the insurance coverage as specified in the Manufacturing Agreement and SeaMED shall furnish to Aastrom reasonable evidence to verify the same.

(i) Aastrom is satisfied with the results of its clinical trials and the market potential for the Instrument, such that Aastrom is prepared to proceed with Phase II and the manufacture and sale of commercial units.

(j) SeaMED approves any modifications to the Phase II Manufacturing Drawings for the Instrument which Aastrom determines to be needed.

(k) SeaMED approves the quantities and delivery schedule determined by Aastrom to be needed to meet the market needs for the commercial units of the Instrument.

If Aastrom concludes that the foregoing prerequisites are satisfied, then Aastrom and SeaMED will enter into a Manufacturing Agreement in accordance with the terms set forth in Exhibit F. Provided however, SeaMED may decline to enter into such a Manufacturing Agreement only if one or more of the following circumstances occurs:

(l) Aastrom has defaulted on its obligations under this Agreement.

6.2 Phase II Manufacturing Drawings and Process. At least six (6)

months prior to the expected commencement of Phase II, (i) SeaMED shall prepare and deliver to Aastrom any recommended revisions to the Manufacturing Drawings for the Instrument that may be needed for efficient and cost-effective manufacturing and testing of the commercial units of the Instrument, and (ii) SeaMED shall prepare and deliver to Aastrom a complete and detailed written package of documents which fully describes the manufacturing process for the manufacturing and testing of the commercial units of the Instrument, including without limitation, all items referenced in Sections 2.1(e) as the Manufacturing Drawings and 2.1(f). The foregoing shall hereinafter collectively be referred to as the "Phase II Manufacturing Drawings and Process." As modifications are made from time to time to said Phase II Manufacturing Drawings and Process by mutual agreement, SeaMED shall furnish to Aastrom an updated copy thereof.

6.3 Transition Cooperation. If this Agreement is terminated,

SeaMED shall provide to Aastrom, or its designee, all necessary Instrument information, documentation, equipment lists, material lists, traceable recordings, tooling, suppliers, Phase II Manufacturing Drawings and Process, and description of manufacturing methods and processes (including device master list) required by governmental agencies, to enable the continued manufacture of the Instrument.

6.4 Compensation. If this Agreement is terminated by SeaMED,

then the transition services specified in Sections 6.2 and 6.3 shall be provided by SeaMED, without charge to Aastrom. If Aastrom terminates this Agreement, then Aastrom shall compensate SeaMED for SeaMED's transition services specified in Section 6.2 and 6.3 above in accordance with the Compensation Schedule attached hereto as Exhibit E.

7. Records; Inspection. SeaMED shall keep accurate and complete

records with respect to its design work and manufacture of the Instrument preproduction units and precommercial units, including all records of time worked and other costs. At Aastrom's request, SeaMED shall allow Aastrom or its designee to inspect and audit such records to verify actual costs and reasonableness of allocation methodologies. Additionally, at Aastrom's request, SeaMED shall allow Aastrom to inspect the facility where the Instrument units are manufactured.

8. Indemnification.

8.1 By SeaMED. SeaMED shall indemnify, defend and hold harmless

Aastrom and its officers, directors, employees and agents for any loss, claim, cost or damage arising out of any claim or action for bodily injury based on the use of any Instrument preproduction units and precommercial units to the extent such loss, claim, cost or damage results, directly or indirectly, (i) from a

breach by SeaMED of its warranties as set forth in this Agreement, or (ii) from any negligent, willful or intentional acts by SeaMED.

8.2 By Aastrom. Aastrom shall indemnify, defend and hold harmless

SeaMED and its officers, directors, employees and agents for any loss, claim, cost or damage arising out of any claim or action for bodily injury based on the use of any Instrument preproduction units and precommercial units to the extent such loss, claim, cost or damage does not result from SeaMED's acts described in Section 8.1 above, but rather results, directly or indirectly, (i) from the negligent, willful or intentional acts of Aastrom or its agents (other than SeaMED), (ii) from a breach by Aastrom of its warranties with respect to the Instrument preproduction unit, or (iii) from any product liability claim related to or arising out of the Instrument preproduction units and precommercial units, other than those claims described in Section 8.1 above.

8.3 Patent Infringement. Aastrom shall indemnify and hold SeaMED

harmless from any loss, damage, or cost (including reasonable attorneys' fees and expenses) arising from any claim that the Instrument or its operation infringes a United States patent, trademark, copyright, or other proprietary right, including trade secrets. SeaMED shall indemnify and hold Aastrom harmless from any loss, damage, or cost (including reasonable attorneys' fees and expenses) arising from any claim that SeaMED's manufacturing processes or methods infringes a United States patent or other proprietary right, including trade secrets.

8.4 Control of Action. In the event any lawsuit for which indemnity

is applicable, Aastrom will control the defense and selection of defense counsel, and SeaMED will be entitled to participate therein by selecting co-counsel reasonably satisfactory to Aastrom. Aastrom shall have the right to direct and control such defense, to settle any dispute, and SeaMED shall be responsible for payment of any settlement to which SeaMED has consented, such consent not to be unreasonably withheld. In conducting the defense and negotiating any settlement, Aastrom's counsel shall give due consideration to suggestions of SeaMED's co-counsel.

8.5 Insurance. SeaMED agrees to provide and maintain at its sole

expense comprehensive general liability insurance, including product liability insurance, covering worldwide sales, covering bodily injury and property damage to third parties for accidents or injuries arising out of the use of the Instrument preproduction units and precommercial units manufactured by SeaMED. Said insurance shall have a combined single limit of \$2 million per occurrence, as a total limit of liability for any one occurrence with respect to bodily injury and property damage, with a deductible of no higher than \$25,000, and with no aggregate annual limit. SeaMED will furnish to Aastrom certificates of insurance evidencing that such insurance is in effect, and that Aastrom is named as an additional insured

party thereunder. Such certificates shall provide that in the event such insurance should be materially adversely changed or terminated for any reason, the insurance company will give Aastrom thirty (30) days' prior written notice of such change or termination.

9. Exclusivity.

9.1 Continuing Prohibition. At all times both during and after

the term of this Agreement, SeaMED shall not make or sell, or enable others to make or sell, the Instrument, excepting only for making and selling the Instrument for Aastrom. Similarly, at all times SeaMED shall not use, or enable others to use, any of Aastrom's proprietary information as further described in Section 10 below.

9.2 No Similar Product. (a) During the term of this Agreement,

and during the term of any similar manufacturing agreement between SeaMED and Aastrom, and for a period of three (3) years thereafter, SeaMED shall not participate in the design or development by any party other than Aastrom of any cell expansion system which uses any technologies which are similar to one or more of the significant proprietary technologies utilized by the Instrument; provided, however, SeaMED may continue to perform its existing customer agreements which are in place as of the date hereof, and SeaMED may manufacture products that have cell culture applications so long as said products are not competitive with Aastrom's Instrument and so long as said products do not use substantially identical subassemblies; (b) During the term of this Agreement, and during the term of any manufacturing agreement between SeaMED and Aastrom, SeaMED shall not manufacture, assemble, produce, ship or in any other way make available for use or distribution, by any party other than Aastrom, any cell expansion system which uses any technologies which are similar to one or more of the significant proprietary technologies utilized by the Instrument.

9.3 No Use of Aastrom's Proprietary Information. Even after the

three (3) years specified in Section 9.2(a) above, SeaMED shall not thereafter render any services or make or sell any product for any other party which services or products use or arise out of technology developed or owned by Aastrom or developed by SeaMED on behalf of Aastrom. Such methods or systems shall include, without limitation, those presently in the course of development by Aastrom and those which shall be developed by SeaMED and/or Aastrom and/or the Other Design Contractors in furtherance of this Agreement. SeaMED acknowledges and agrees that Aastrom has a legitimate business purpose in precluding SeaMED from divulging or otherwise using any and all information derived by SeaMED in the course of performing this Agreement, and that Aastrom intends to use the Instrument and related methods and systems for its own business purpose and competitive advantage in the marketplace.

10. Proprietary Information.

10.1 Aastrom's Property; Use of Property by SeaMED. SeaMED

recognizes the proprietary interest of Aastrom in the techniques, designs, specifications, drawings and other technical data now existing or developed during the term of this Agreement relating to the System. SeaMED acknowledges and agrees that such techniques, designs, specifications, drawings and technical data relating to the System, whether developed by SeaMED alone, in conjunction with others, or otherwise, shall be and is the property of Aastrom. SeaMED shall cooperate fully in communicating to Aastrom or its agents the property described above. SeaMED hereby waives any and all right, title and interest in and to such proprietary information. SeaMED shall have the right to use any technology, information, samples, documents and other proprietary information of Aastrom provided in connection with the collaboration described herein solely and exclusively for the purpose of conducting such development and design efforts related to the Instrument and manufacturing the System for Aastrom and for no other purpose.

10.2 Inventions. As to any improvement to the Instrument, any

component thereof or any disposable used in connection therewith, which is made by SeaMED's employees or agents in the course of SeaMED's work for Aastrom, or as a result thereof, which improvement constitutes a patentable invention, SeaMED hereby agrees to promptly disclose the same to Aastrom, and SeaMED hereby agrees to assign to Aastrom, and SeaMED hereby agrees to cause the inventor/employee to assign to Aastrom, all ownership rights in the invention; and SeaMED shall cause said inventor/employee to sign appropriate patent applications prepared at the expense of Aastrom.

10.3 Nondisclosure. SeaMED acknowledges and agrees that Aastrom

is entitled to prevent Aastrom's competitors from obtaining and utilizing Aastrom's trade secrets. SeaMED agrees during the term hereof and thereafter to hold Aastrom's trade secrets and other confidential or proprietary information in strictest confidence and not to use them for purposes other than performance hereunder, and not to disclose them or allow them to be disclosed, directly or indirectly, to any other person or entity, other than to persons engaged by SeaMED for the purpose of performance hereunder, without Aastrom's prior written consent. SeaMED acknowledges the confidential nature of its relationship with Aastrom and of any information relating to the Instrument, Aastrom, or its distributors, agents, clients or customers which SeaMED may obtain during the term hereof. SeaMED also agrees to place any persons to whom said information is disclosed for purposes of performance hereunder under a legal obligation to treat such information as strictly confidential.

10.4 Confidentiality. The provisions and arrangements made

under this Agreement are confidential between parties. Each party shall protect

confidential information in the same manner it protects its own confidential materials. Neither party shall make any reference to this Agreement or any provision hereof in any publicly disseminated literature, printed matter, or other publicity issued by or for it, except (i) as required by law, (ii) in connection with a public or private offer or sale of securities, a business collaboration or transaction, or a governmental or industry regulatory communication, or (iii) in a fashion and at a time mutually agreed upon by both parties after the execution of this Agreement. After Aastrom has sold an Instrument in the ordinary course of business, SeaMED may add Aastrom to SeaMED's list of customers and may show external product photographs for marketing purposes.

11. Term. The term of this Agreement shall commence on the date

first written above and shall continue in full force and effect until terminated as set forth herein. Either party may terminate this Agreement without cause upon at least six (6) months' prior written notice. Upon any termination of this Agreement, (i) both parties shall fully perform all of their obligations accruing up through the date of termination and (ii) SeaMED will immediately return to Aastrom all tools and tooling, components, work-in-process, preproduction units, and any other items which have been or will be paid for by Aastrom, plus any information, Manufacturing Drawings, description of manufacturing methods and processes required by governmental agencies, and all other items related to the Instrument. Additionally, to the extent applicable, the obligations under Sections 5, 7, 8, 9, 10 and 13 shall survive any termination of this Agreement for a period of ten (10) years after the termination of this Agreement.

12. Default and Termination.

12.1 Breach. The occurrence of any one or more of the

following events shall constitute an event of default hereunder, and upon the expiration of any applicable time period for a cure, shall constitute a breach of this Agreement, giving rise to the rights identified in Section 12.2 hereof:

(a) If Aastrom shall default hereunder in the payment of funds when due and such default continues for a period of thirty (30) days after written notice thereof;

(b) Subject to subsections (d) and (e) below, if either party fails to faithfully perform or observe any agreement or condition to be performed by such party (including without limitation, the delivery obligations set forth on Exhibit C), and if such default continues for a period of thirty (30) days after written notice thereof, specifying the nature of such default;

(c) If any proceeding is commenced by or for either party under any of the bankruptcy laws, or if either party is adjudged insolvent by any court,

makes an assignment for the benefit of creditors, or enters into a general extension agreement with creditors;

(d) If SeaMED shall breach its obligation to timely repair any defective Instrument preproduction unit pursuant to Section 3; or

(e) If SeaMED shall breach its obligations of exclusivity or confidentiality set forth in Sections 9 or 10 hereof.

12.2 Remedy. In addition to all rights and remedies provided

under law, the nondefaulting party shall have the right, in the event of default, to terminate this Agreement and any obligations imposed on such nondefaulting party hereunder, provided, however, that, to the extent applicable, the obligations under Sections 5, 7, 8, 9, 10 and 13 shall survive any termination of this Agreement.

13. Miscellaneous.

13.1 Independent Contractors. The relationship between Aastrom

and SeaMED hereunder shall be that of independent contractors, and nothing in this Agreement shall be deemed to constitute a joint venture, partnership, agency or employer/employee arrangement between the parties. Neither party shall have any authority or power to bind the other party or to contract in the name of, or make any representations or warranties, express or implied, on behalf of the other party, or otherwise create any liability against the other party in any way for any purpose.

13.2 Causes Beyond Control. The parties hereto shall not be

responsible for any loss or breach due to delay in delivery or performance hereunder caused by governmental regulations, controls or directions, outbreak of a state of emergency, hostilities, civil commotion, riots, epidemics, acts of God, other natural casualties, fires, strikes, walkouts or other similar cause or causes beyond the control of the parties. In the event that any party shall be delayed in, or prevented from, performing its obligations under this Agreement as a result of any of the foregoing, such party shall promptly notify the other party of such delay or cessation in performance. In the event that such party is unable to resume performance hereunder within sixty (60) days of the date on which its performance was suspended, the other party shall have the right to terminate this Agreement upon ten (10) days prior written notice.

13.3 Successors and Assigns. The rights and remedies of Aastrom

under this Agreement shall inure to the benefit of the successors, assigns and transferees of Aastrom. SeaMED shall have no right to assign, transfer or otherwise dispose of its rights under this Agreement or to assign the burdens hereof, without the prior written consent of Aastrom.

13.4 Applicable Law. The construction of this Agreement, and the

rights and liabilities of the parties hereto, shall be governed by the laws of
the State of Michigan.

13.5 Severability. Each term, condition or provision of this

Agreement shall be viewed as separate and distinct, and in the event that any
such term, condition or provision shall be held by a court of competent
jurisdiction to be invalid, the remaining provisions shall continue in full
force and effect.

13.6 Entire Agreement; Modification and Waiver. This Agreement

contains the entire agreement and understanding between the parties and
supersedes all prior agreements and understandings between them relating to the
subject matter hereof. This Agreement may not be amended or modified except by
an instrument in writing, signed by duly authorized representatives of both
parties. The waiver, express or implied, by any party of any right hereunder or
of any failure to perform or breach hereof by any other party shall not be
deemed to constitute a waiver of any other right hereunder or of any claim in
respect of any other failure to perform or breach.

13.7 Counterparts. This Agreement may be executed in

counterparts all of which together shall constitute one and the same instrument.

13.8 Dispute Resolution. Any controversy or claim arising out of

or relating to this Agreement, or the breach or interpretation hereof, shall be
resolved through good faith negotiation between the principals of the parties
hereto. Any controversy or claim not resolved by mutual agreement shall be
submitted to binding arbitration in Ann Arbor, Michigan, in accordance with the
rules of the American Arbitration Association ("AAA") as then in effect; and
judgment upon the award rendered in such arbitration shall be final and may be
entered in any court having jurisdiction thereof. Notice of the demand for
arbitration shall be filed in writing with the other party to this Agreement and
with the AAA. In no event shall the demand for arbitration be made after the
date when institution of legal or equitable proceedings based on such claim,
dispute or other matter in question would be barred by the applicable statute of
limitations. This agreement to arbitrate shall be specifically enforceable
under the prevailing arbitration law. The party most prevailing in said
arbitration, as determined by the arbitrator based upon the parties' respective
claims and positions, shall be entitled to recover from the non-prevailing party
all attorneys' fees and other costs incurred in connection with the arbitration
proceeding.

13.9 Notices. All notices and other communications permitted or

required under this Agreement shall be in writing and shall be deemed to have
been given when received at the addresses set forth on the signature page
hereof, or at such other address as may be specified by one party in writing to
the other.

Said written notice may be given by mail, telecopy, rush delivery service, personal delivery or any other means.

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first above written.

AASTROM:

AASTROM BIOSCIENCES, INC.
a Michigan corporation

By: /s/ R. DOUGLAS ARMSTRONG

Name: R. Douglas Armstrong, Ph.D.

Title: President and CEO

P. O. Box 376
Ann Arbor, MI 48106
Attn: R. Douglas Armstrong, Ph.D.
Fax: (313) 665-0485

SEAMED:

SEAMED CORPORATION,
a Delaware corporation

By: /s/ W. ROBERT BERG

Name: W. Robert Berg

Title: President/CEO

11810 North Creek Parkway North
Bothell, WA 98011
Attn: W. Robert Berg
Fax: (206) 487-1736

EXHIBITS

- A General Description of the System and the Instrument
- B Specifications and Functional Requirements for the Instrument
- C Time and Quantity Schedule - Preproduction Units
- C-1 Pricing for Precommercial Units
- D Manufacturing Drawings for the Instrument
- E Compensation Schedule for Design Work and Manufacturing Preproduction Units
- F Summary of Manufacturing Agreement for Phase II

General Description of the System and the Instrument

1.1 The Aastrom Cell Expansion System represents technology for the ex vivo growth and expansion of human stem and hematopoietic progenitor cells. The system is intended to provide cells in sufficient volume and with the necessary characteristics to complete a bone marrow transplantation or a nadir prevention/rescue resulting from therapies such as high dose chemotherapy or radiation. These cells are grown from a small starting population of cells normally obtained from the bone marrow or peripheral blood. The use of Cell Expansion System provides for production of cells that can be infused to augment recovery of a compromised hematopoietic system.

1.2 The Cell Expansion System consists of (1) a disposable biochamber cartridge where the growth and expansion of cells takes place, (2) a biochamber incubation unit and companion monitor module that controls the biological and physical environment during the expansion process, (3) an inoculation/harvest unit that facilitates the initial filling and inoculation of cells as well as the final harvest of cells at the completion of the expansion process, (4) growth medium as required by the cell culture (to which specified growth factors and glutamine are added), (5) harvest reagents which facilitate the removal of the expanded cells from the biochamber, (6) a system rack will be available to conveniently integrate multiple biochamber incubation units with the monitor module.

1.2.1. The disposal biochamber cartridge (DBC) contains the medium contact components for the incubation period and provides a functionally closed environment in which the cell expansion can occur. The cartridge is provided fully assembled in a sterile package.

In addition to a cell growth chamber, the medium contact components include a reservoir for medium supply, a pump mechanism for delivery of the medium to the growth chamber, valves to facilitate filling and harvesting, a reservoir for the collection of waste medium exiting the growth chamber, and a reservoir for the collection of harvested cells.

The cartridge also includes a gas chamber which is supplied with a controlled mixture of gases for pH stability and oxygenation of the growth chamber through a gas permeable, hydrophobic membrane that separates the two chambers.

The cartridge also includes a provision for heat transfer to the growth chamber and away from the medium supply reservoir to facilitate temperature control.

A biochamber key containing a non-volatile memory device is attached to the DBC at the beginning of use and accessed by the system electronics during the cell expansion process to record pertinent data. The key is detached after cell harvest, and archived as part of the patient specific cell expansion record.

- 1.2.2. The biochamber incubation unit (BIU) provides the biological and physical environment to support the cell growth process. The biochamber cartridge is inserted into the BIU after inoculation is complete. The BIU controls: the flow of medium to the growth chamber; the temperature of the growth medium supply compartment; the temperature of the growth chamber compartment; and the concentration and flow rate of gases delivered to the gas chamber. The BIU also monitors the density of cells in the growth chamber and various safety/alarm parameters to assure that the cell expansion process is proceeding as expected.

The unit receives commands from keys on its front panel and communicates with the operator through a central BIU monitor module (BIUMM). An integral BIU display also provides information to the operator. Up to twelve biochamber incubation units can be connected to the monitor module. Each BIU has its own micro processor based control system and operates independently of the monitor module. As such, it will continue to function in the event of failure of the monitor module.

- 1.2.3. The inoculation/harvest unit (IHU) performs the initial filling of the biochamber cartridge with growth medium (supplemented with growth factors) and the inoculation of cells. The same unit also performs the removal of the cells from the growth chamber at the completion of the cell expansion process. The system design provides for the appropriate level of sterility assurance during the inoculation and harvest procedures.

- 1.2.3.1 During initial set up and fill, the operator loads the biochamber cartridge into the IHU, connects the medium supply (supplemented with growth factors) to the cartridge and transfer the medium to the internal reservoir. The operator is prompted to

manually inject the cells into the cartridge at the appropriate time. The process then continues under software control until the cartridge is ready to be placed in the biochamber incubation unit for cell expansion.

1.2.3.2. At the completion of the expansion process, the operator loads the biochamber back into the IHU, attaches the harvest reagents, and harvesting of the expanded cells proceeds under software control. At the completion of the harvest process, the expanded cell product is contained in a single bag to facilitate washing and preparation for direct infusion or cryopreservation.

1.2.4. The standard growth medium for the expansion of hematopoietic cells will be distributed as a separate item in packaging that will facilitate the addition of growth factors and glutamine followed by sterile connection to the biochamber cartridge just prior to use.

1.2.5. The harvest reagents needed for the process will be distributed as separate items in packaging that will facilitate an aseptic connection to the biochamber cartridge for cell harvest.

1.2.6. The system rack conveniently integrates several BIUs and a monitor module. The rack organizes connections to the facility and the inter connections between the various modules.

The Instrument consists of the components described in paragraphs 1.2.2 (BIU), 1.2.3 (IHU), and 1.2.6 (Rack).

EXHIBIT B

Functional Requirements and Specifications for the Instrument

(to be added per Section 1.2)

See generally Exhibit A. See also the SeaMED Project Plan, Drawing Number 908180, draft dated 2-2-94, which is incorporated herein. Additional functional requirements and specifications for the Instrument will be added by Aastrom during the course of the work.

EXHIBIT C

Time and Quantity Schedule --
Preproduction Units

*

*CONFIDENTIAL PORTION REDACTED AND FILED
SEPARATELY WITH THE COMMISSION

*

*CONFIDENTIAL PORTION REDACTED AND FILED
SEPARATELY WITH THE COMMISSION

EXHIBIT D

Manufacturing Drawings for the Instrument

(to be added per Section 2.1(e))

EXHIBIT E

Compensation Schedule for Design Work
and Manufacturing Preproduction Units

*

*CONFIDENTIAL PORTION REDACTED AND FILED
SEPARATELY WITH THE COMMISSION

EXHIBIT F

Summary of Manufacturing Agreement for Phase II

*

*CONFIDENTIAL PORTION REDACTED AND FILED
SEPARATELY WITH THE COMMISSION

COLLABORATIVE PRODUCT DEVELOPMENT AGREEMENT

Bioreactor Assembly
and
Tubing Kit

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Exhibits:

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- A Description of Product
- B Company's Project Plan
- C Specifications for the Product
- D Manufacturing Drawings

COLLABORATIVE PRODUCT DEVELOPMENT AGREEMENT

Bioreactor Assembly

and

Tubing Kit

This Agreement (the "Agreement") is entered into as of 11/8, 1994, by and

between Aastrom Biosciences, Inc., a Michigan corporation ("Aastrom"),
and Ethox Corp., a New York corporation ("Company").

RECITALS

A. Aastrom is in the final stages of research and development for a proprietary, manually operated, bioreactor assembly and custom tubing kit (collectively hereinafter referred to as the "Product" and individually referred to as the "Bioreactor" or the "Tubing Kit"). The Product is more fully described on Exhibit A attached hereto.

B. Aastrom has completed working prototype models of the Product; and Aastrom now needs to obtain pre-production units of the Product for laboratory and clinical evaluation.

C. Company has expertise and experience in the development and manufacture of medical products which are somewhat similar to the Product. Company is prepared to collaborate with Aastrom for completing the necessary design work on the Product to enable Company to manufacture the Product.

D. Company has prepared a Project Plan, attached hereto as Exhibit B, which specifies the Company's resources and activities to be applied and used for performing this Agreement. Said Project Plan includes Company's pricing and an estimate of the time, materials and costs for Company to perform under this Agreement as the design stood at the time on April 10, 1994. With changes in the design and specifications it is contemplated that Company pricing and estimates will be subject to change.

E. Aastrom has contracted with Roecker Design Group, and Aastrom may also contract with other design specialists for assistance with specified aspects of the Product (collectively called the "Other Design Contractors"), subject to the provisions hereof.

AGREEMENT

NOW, THEREFORE, the parties hereby agree as follows:

1. Responsibilities of Aastrom.

1.1 Project Management. Aastrom shall be responsible for

overall project management relating to the development of the Product.

1.2 Specifications. Aastrom shall collaborate with Company and

the Other Design Contractors on completing the design work for the Product. With assistance from Company as more fully described in Section 2 below, Aastrom shall develop the final specifications and functional requirements for the Product, including applicable test criteria (the "Specifications"). It shall be solely Aastrom's responsibility to assure that the Specifications are safe and effective and to make the decision that the Specifications are complete. Upon completion of the Specifications, Aastrom shall promptly provide Company with a copy of the Specifications, and if the parties mutually agree, the Specifications shall be attached as Exhibit C hereto. Prior to completion of the Specifications, the parties shall use the preliminary design specifications referenced on Exhibit C.

2. Responsibilities of Company.

2.1 Design Collaboration. Company shall collaborate with

Aastrom and the Other Design Contractors to assist Aastrom in completing the design work for the Product. Company shall perform its responsibilities under this Agreement in accordance with the Project Plan attached hereto as Exhibit B; provided, however, it is understood that with changes in the design and specifications, it is contemplated that Company's pricing and estimates of time, materials and costs will be subject to change. Without limiting the foregoing, Company shall:

(a) Assist Aastrom with respect to planning for all manufacturing issues that are likely to arise in connection with the design work and development of the Product, including issues relating to the manufacturing process development and validation, component sourcing, and the creation of Device Master record documentation requirements.

(b) Prepare working drawings in accordance with the Specifications for manufacturing and testing the Product (the "Manufacturing Drawings"), which Manufacturing Drawings shall be owned by Aastrom and shall, subject to the prior written approval of Aastrom and Company, ultimately be attached hereto as Exhibit D. Said Manufacturing Drawings shall include the Device Master Record and (i) specifications for component parts to be acquired from specified vendors, (ii) drawings and specifications for component parts, (iii) test and acceptance procedures and criteria, (iv) subassembly specifications,

drawings and requirements, and (v) product specific manufacturing procedures, routing and processes. Said Manufacturing Drawings may reference general policies and procedures of Company, such as Company's quality system; and Company's general policies and procedures shall remain the property of Company. As modifications are made from time to time to the Manufacturing Drawings by mutual agreement, Company shall furnish to Aastrom an updated copy thereof.

(c) Prepare a gamma sterilization validation plan and conduct the required laboratory tests to achieve a 10⁻⁶/ sterility assurance level for the Product.

(d) To the extent required for submittal to the U.S. Food and Drug Administration ("FDA") for Aastrom's IDE and/or PMA, prepare a detailed description of Company's manufacturing methods, processes, procedures and facility applicable to Aastrom's Product.

2.2 Delivery of Products. Following Aastrom's determination that

the Manufacturing Drawings prepared by Company are in accordance with the Specifications, Company shall manufacture and deliver to Aastrom at its Ann Arbor, Michigan facility a number of the prototypes of the Products, in compliance with the Specifications and the Manufacturing Drawings, for use in clinical tests of the Product. The exact number of the Product to be manufactured, and the delivery schedule thereof, shall be as specified by Aastrom in separate purchase orders, subject to Company's approval, which approval will not be withheld unreasonably. Said purchase orders normally will be for 15 units of the Bioreactor at a time, with delivery to be within three weeks, and for 150 units of the Tubing Kit at a time, with delivery to be within eight weeks. The pricing on said purchase orders shall be in accordance with the pricing set forth in Exhibit B; provided, however, it is understood that with changes in the design and specifications, it is contemplated that Company's pricing and estimates of time, materials and costs will be subject to change. As Aastrom's tests of the Product proceed, and depending on the outcome of those tests, Aastrom may place additional purchase orders for the same or larger lot sizes of the Product; and Company shall manufacture and sell said additional units of the Product on the same terms and conditions as set forth above.

2.3 Maintenance of Adequate Facilities and Manufacturing

Practices. Company shall maintain adequate personnel and facilities to perform

its obligations under this Agreement. Company shall manufacture and assemble all of the Product in an environment where good manufacturing practices ("GMP") are followed. Inasmuch as Company's FDA facility registration and inspection record are extremely important to Aastrom's ability to obtain prompt FDA approval for the Product, Company hereby agrees to use its best efforts to maintain in good standing all appropriate FDA facility registrations and inspection records. Company shall immediately report to Aastrom in writing any adverse events, circumstances, or potential problems relating to Company's FDA registrations and inspections that

could adversely affect availability or approval of the Product. Company shall allow Aastrom and its agents (such agent to be acceptable to Ethox, with approval not to be unreasonably withheld) to review and inspect Company's facilities, FDA compliance files, and correspondence to and from the FDA regarding inspections, registrations, and audits that pertain to the Product or the Aastrom's regulatory submission. To the extent Aastrom shall determine that European Economic Community standards apply to Company's facility and manufacturing practices for units of the Product to be used in Europe, Aastrom will provide details of said standards to Company, and Company shall make every reasonable effort to comply with said standards.

2.4 No Subcontracting. No part of Company's obligations under this

Agreement which are being subcontracted by Company will be changed without Aastrom's approval if such change would impact Aastrom's FDA approval, without the prior written approval of Aastrom.

2.5 Inventory Insurance. All inventory of components and materials

purchased by Company to make the Products shall be owned by Company and shall be insured against risk of loss by Company. Any components and materials purchased by Aastrom and delivered to Company for Company to use to make the Products shall be covered by Company's insurance policy for risk of loss while said items remain in Company's facility.

2.6 Transit. Company shall arrange for shipment of the Products by a

common carrier approved by Aastrom, to a destination specified by Aastrom. The costs of shipment and insurance during transit shall be borne by Aastrom. Title and risk of loss to the Products shall pass from Company to Aastrom when the Products are delivered to a common carrier for shipment to Aastrom's designation.

2.7 Financial Condition. Company and Aastrom shall each give written

notification to the other of any material adverse financial condition affecting either, including without limitation the lack of resources available to enable either to fully and promptly perform its obligations under this Agreement on schedule, and any other conditions which may jeopardize or impair the full and prompt performance by either of its obligations under this Agreement. Said notification shall be given within five (5) days after the occurrence or realization of said adverse condition.

3. Acceptance Procedures. Delivery of each unit of the Product

shall be deemed accepted by Aastrom unless Company is notified in writing of Aastrom's rejection of such delivery within thirty (30) days after the delivery date due to a non-conformance with the Specifications and/or the Manufacturing Drawings (which shall include acceptance criteria). In such case, Aastrom shall advise Company of Aastrom's acceptance criteria and the details of how Aastrom believes that there has been a non-conformance. In the event Company receives

such notice and advise, Company shall diligently attempt to promptly resolve any such non-conformance. In the event Company cannot resolve any such non-conformance and deliver a Product that conforms to the Specifications and the Manufacturing Drawings within a time period not to exceed six (6) weeks of receipt of such notice, Aastrom may pursue remedies pursuant to Section 12 below.

4. Compensation. Aastrom shall compensate Company for Company's

assistance, manufacture and assembly of the Products on a "time and materials" basis, as further described on Exhibit B. Company shall submit to Aastrom a monthly invoice for said work, together with such supporting details as Aastrom may reasonably request. Aastrom shall pay said invoice within thirty (30) days after the invoice and supporting details are received by Aastrom.

5. Company's Warranty. Company warrants that each unit of the

Product shall comply in all respects with the Specifications and the Manufacturing Drawings and shall be free from defects in material and workmanship. Company shall either repair or replace or provide to Aastrom full credit for the purchase price of any Product which Aastrom finds to be defective due to Company's failure to comply with said warranty. If credit is not given by Company, then any such warranty repairs or replacements shall be completed within a time period not to exceed six (6) weeks of the date on which Company receives notice of any such non-compliance. All shipping and other costs incurred in connection with the repair or replacement of any such non-complying Product shall be for the account of Company. Company further warrants that the manufacture, assembly and delivery of the Products hereunder shall be (i) in compliance with all applicable federal, state and local laws, rules, regulations and executive orders known or reasonably expected to be known by Company, and (ii) performed in a professional, workmanlike manner in accordance with prevailing industry standards.

THE WARRANTIES SET FORTH IN THIS SECTION 5 ARE EXCLUSIVE AND IN LIEU OF ANY AND ALL OTHER WARRANTIES, EXPRESS OR IMPLIED.

6. Records; Inspection. Company shall keep accurate and complete

records with respect to its work and manufacture of the Product to the extent necessary to attempt to satisfy any FDA requirements and to verify the time worked and material costs invoiced by Company to Aastrom. At Aastrom's request, Company shall allow Aastrom or its accountant to inspect and audit such records. Additionally, at Aastrom's request, Company shall allow Aastrom and/or Aastrom's consultant (such consultant to be subject to Ethox's approval, and such approval will not be unreasonably withheld) to inspect the facility where the Products are manufactured. All inspections shall be upon reasonable notice and during regular business hours and shall require execution of confidentiality agreements satisfactory to Company.

7. Patent Infringement; Insurance.

7.1 Patent Infringement. Aastrom shall indemnify and hold Company

harmless from any loss, damage, or cost (including reasonable attorneys' fees and expenses) arising from any claim that the Product or its operation infringes a United States patent, trademark, copyright, or other proprietary right, including trade secrets. In the event any lawsuit for which indemnity is applicable, Aastrom will control the defense and selection of defense counsel, and Company will be entitled to participate therein (at Company's expense) by selecting co-counsel reasonably satisfactory to Aastrom. Aastrom shall have the right to direct and control such defense, to settle any dispute. Company shall be responsible for payment of any settlement to which Company has consented, and such consent shall not be unreasonably withheld. In conducting the defense and negotiating any settlement, Aastrom's counsel shall give due consideration to suggestions of Company's co-counsel.

7.2 Insurance. Company and Aastrom shall each provide and maintain

\$1 million comprehensive general liability insurance and product liability insurance. Company will furnish to Aastrom, and Aastrom will furnish to Company, certificates of insurance evidencing that such insurance is in effect. Aastrom's requirement hereunder is contingent upon its successful obtaining of such coverage.

8. Exclusivity.

8.1 Continuing Prohibition. At all times both during and after the

term of this Agreement, Company shall not make or sell, or enable others to make or sell, the Product which is the subject of this Agreement, excepting only for making and selling the Product for Aastrom.

8.2 No Similar Product. During the term of this Agreement, (i)

Company shall not manufacture, assemble, produce, ship or in any other way make available for use or distribution, by any party other than Aastrom, any product or system which is functionally similar to the Product, and (ii) Company shall not in any way accept engagement with, or render service to, any other individual, firm or corporation, as a consultant, instructor, expert, designer, manufacturer or producer, or act in any other capacity, which engagement or rendition of services involves the development or production of any product or system which is functionally similar to the Product. As used in this section, a hematopoietic stem cell expansion product or system is not "functionally

similar" if it utilizes distinctly different methods or distinctly different disposable components than are utilized for Aastrom's Product.

8.3 Disclosure. Company advises Aastrom that Company is currently

manufacturing a line of products referred to as the Stericell product line which are used for cell culture, and a product named Stempak which is utilized for

stem cell processing. In addition, Company has contract relationships, and is working with other companies to develop relationships, for cell processing devices which, to the best of Company's belief, function in a significantly different manner than Aastrom's Product.

9. Ownership of Technology; Confidentiality.

9.1 Ownership of Technology.

(a) Except as set forth in Section 9.1(c) below, Aastrom shall retain and own all right, title, and interest in any invention, technology or development, whether or not patentable, which it now has or which arises in connection with the Product during the course of the Company's performance of this Agreement. Any invention made by Company in connection with Company's work with the Product, which invention is an improvement or variation to the Product, shall be owned by Aastrom and assigned to Aastrom by Company. Company shall cooperate with Aastrom and take all steps reasonably required, including executing assignments, to aid Aastrom in securing any patent or other protection which may be appropriate, and Aastrom shall bear the expense in connection therewith.

(b) All tools and tooling which were paid for by Aastrom (either separately or as part of the price for the Product sold by Company to Aastrom) shall be owned by Aastrom. The Manufacturing Drawings (including the device master records) shall be owned by Aastrom.

(c) Company shall retain all of its right, title, and interest in and to its proprietary knowledge in fabrication methods which it currently has, and in and to such additional knowledge in fabrication methods Company may develop at its sole expense (and for which Aastrom is not invoiced) as a part of the Company's performance of this Agreement. As to any fabrication methods developed by Company from efforts for which Aastrom is invoiced, said fabrication methods shall be deemed developed for Aastrom as a "work for hire," and Aastrom shall have sole ownership thereof. Company shall retain a royalty free license to make, use, sell or otherwise promote any such fabrication methods which are developed by Company but owned by Aastrom, so long as such undertaking does not directly or indirectly cause competition to Aastrom products or business activities.

9.2 Confidential Information. The parties recognize that during the

course of Company's performance of this Agreement, it may be necessary that either or both parties be given access to certain Confidential Information of the other. The following subparagraphs shall be applicable to such Confidential Information and the words "Recipient" and "Disclosing Party" shall be

interchangeable as between Aastrom and Company as appropriate under the circumstances.

(a) Title to Confidential Information and Related Documents.

Recipient hereby acknowledges that the Confidential Information and all related documents, drawings, sketches, designs, products, or samples disclosed or furnished hereunder are the sole and exclusive property of Disclosing Party. Recipient hereby agrees to return all such documents, drawings, sketches, designs, products, or samples furnished to it hereunder, together with all copies thereof except for one archive copy, promptly upon the request of Disclosing Party.

(b) Nondisclosure or Use of Confidential Information. Recipient

hereby agrees that it shall hold all Confidential Information disclosed to it in strict confidence, that it will use the same only for the purpose of performing this Agreement and for no other purpose whatsoever, and that it will not disclose the same to any third parties (except to its employees to the extent such disclosure is necessary for purposes of performing this Agreement) except to the extent Disclosing Party agrees to in writing.

(c) Protection of Confidential Information. Recipient agrees that

it will observe reasonable precautions and procedures to protect and preserve all Confidential Information and related documents, drawings, sketches, designs, products, or samples disclosed or furnished to it hereunder, using such precautions which shall be no less rigorous than those used by Recipient to protect its own trade secrets and confidential data. In addition, Recipient warrants that it has or will obtain written agreements of confidentiality with its employees for the protection of information of the subject nature both during and after employment.

(d) Confidential Information. "Confidential Information" as used

herein shall mean all information, discoveries, inventions, improvements or innovations which are maintained as confidential by the party having the same. Provided, however, Confidential Information shall not include information, discoveries, inventions, improvements, or innovations (a) which at the time of disclosure is a part of the public domain; (b) which subsequently becomes a part of the public domain by publication or otherwise through no fault of Recipient; (c) which Recipient can show was contained in its possession at the time of disclosure; (d) which is subsequently disclosed to Recipient by a third party not in violation of any rights of, or obligations to, Disclosing Party; or (e) which is disclosed in a patent or publication anywhere.

9.3 Other Design Contractors. To the extent any Confidential

Information of Company is to be furnished to the Roecker Design Group or any Other Design Contractors, it shall be the obligation of Aastrom to provide Company with confidentiality agreements executed by such design contractors, and said confidentiality agreements shall be in a form reasonably acceptable to Company.

9.4 Privacy of Agreement. Neither party shall make any reference to

this Agreement or any provision hereof in any publicly disseminated literature, printed matter, or other publicity issued by or for it, except (i) as required by law, (ii) in connection with a public or private offer or sale of securities, a business collaboration or transaction, or a governmental or industry regulatory communication, or (iii) in a fashion and at a time mutually agreed upon by both parties after the execution of this Agreement. After release of the product for commercial sale, Company may add Aastrom to Company's list of customers and may show external product photographs for marketing purposes, and Aastrom may add Company to Aastrom's list of vendors and subcontractors.

10. Term. The term of this Agreement shall commence on the date first

written above and shall continue in full force and effect until completion of Aastrom's need for the Products, or until terminated as set forth herein. Either party may terminate this Agreement without cause upon at least six (6) months' prior written notice. Upon any termination of this Agreement, (i) both parties shall fully perform all of their obligations accruing up through the date of termination and (ii) Company will immediately deliver to Aastrom the Manufacturing Drawings, all tools and tooling owned by Aastrom, and any prototypes, components, information, and work-in-process related to the Product. Additionally, to the extent applicable, the obligations under Sections 5, 6, 7, 8, 9 and 12 shall survive any termination of this Agreement.

11. Default and Termination.

11.1 Breach. The occurrence of any one or more of the following

events shall constitute an event of default hereunder, and upon the expiration of any applicable time period for a cure, shall constitute a breach of this Agreement, giving rise to the rights identified in Section 11.2 hereof:

(a) If Aastrom shall default hereunder in the payment of funds when due and such default continues for a period of thirty (30) days after written notice thereof;

(b) If either party fails to faithfully perform or observe any agreement or condition to be performed by such party, and if such default continues for a period of thirty (30) days after written notice thereof, specifying the nature of such default;

(c) If any proceeding is commenced by or for either party under any of the bankruptcy laws, or if either party is adjudged insolvent by any court, makes an assignment for the benefit of creditors, or enters into a general extension agreement with creditors;

(d) If Company shall breach its obligation to timely give credit for or to repair any non-conforming Product prototype pursuant to Section 3; or

(e) If either party shall breach its obligations set forth in Sections 8 or 9 hereof.

11.2 Remedy. In addition to all rights and remedies provided under

law, the nondefaulting party shall have the right, in the event of default, to terminate this Agreement and any obligations imposed on such nondefaulting party hereunder, provided, however, that, to the extent applicable, the obligations under Sections 5, 6, 7, 8, 9, and 13 shall survive any termination of this Agreement.

12. Miscellaneous.

12.1 Independent Contractors. The relationship between Aastrom and

Company hereunder shall be that of independent contractors, and nothing in this Agreement shall be deemed to constitute a joint venture, partnership, agency or employer/employee arrangement between the parties. Neither party shall have any authority or power to bind the other party or to contract in the name of, or make any representations or warranties, express or implied, on behalf of the other party, or otherwise create any liability against the other party in any way for any purpose.

12.2 Causes Beyond Control. The parties hereto shall not be

responsible for any loss or breach due to delay in delivery or performance hereunder caused by governmental regulations, controls or directions, outbreak of a state of emergency, hostilities, civil commotion, riots, epidemics, acts of God, other natural casualties, fires, strikes, walkouts or other similar cause or causes beyond the control of the parties. In the event that any party shall be delayed in, or prevented from, performing its obligations under this Agreement as a result of any of the foregoing, such party shall promptly notify the other party of such delay or cessation in performance. In the event that such party is unable to resume performance hereunder within sixty (60) days of the date on which its performance was suspended, the other party shall have the right to terminate this Agreement upon ten (10) days prior written notice.

12.3 Successors and Assigns. Neither party shall have a right to

assign, transfer or otherwise dispose of its rights under this Agreement or to assign the burdens hereof, without the prior written consent of the other party. Notwithstanding the foregoing, the rights and obligations of a party shall automatically transfer to a successor entity, without the need for any consent, in the event of a merger between the party and the successor, or in the event of a sale of substantially all of the assets of that party to the successors.

12.4 Applicable Law. The construction of this Agreement, and the

rights and liabilities of the parties hereto, shall be governed by the laws of
the State of Michigan.

12.5 Severability. Each term, condition or provision of this

Agreement shall be viewed as separate and distinct, and in the event that any
such term, condition or provision shall be held by a court of competent
jurisdiction to be invalid, the remaining provisions shall continue in full
force and effect.

12.6 Entire Agreement; Modification and Waiver. This Agreement

contains the entire agreement and understanding between the parties and
supersedes all prior agreements and understandings between them relating to the
subject matter hereof. This Agreement may not be amended or modified except by
an instrument in writing, signed by duly authorized representatives of both
parties. The waiver, express or implied, by any party of any right hereunder or
of any failure to perform or breach hereof by any other party shall not be
deemed to constitute a waiver of any other right hereunder or of any claim in
respect of any other failure to perform or breach.

12.7 Counterparts. This Agreement may be executed in counterparts

all of which together shall constitute one and the same instrument.

12.8 Dispute Resolution. Any controversy or claim arising out of or

relating to this Agreement, or the breach or interpretation hereof, shall be
resolved through good faith negotiation between the principals of the parties
hereto. Any controversy or claim not resolved by mutual agreement shall be
submitted to binding arbitration in Cleveland, Ohio, or in such other city as
the parties may mutually agree, in accordance with the rules of the American
Arbitration Association ("AAA") as then in effect; and judgment upon the award
rendered in such arbitration shall be final and may be entered in any court
having jurisdiction thereof. Notice of the demand for arbitration shall be
filed in writing with the other party to this Agreement and with the AAA. In no
event shall the demand for arbitration be made after the date when institution
of legal or equitable proceedings based on such claim, dispute or other matter
in question would be barred by the applicable statute of limitations. This
agreement to arbitrate shall be specifically enforceable under the prevailing
arbitration law. The party most prevailing in said arbitration, as determined
by the arbitrator based upon the parties' respective claims and positions, shall
be entitled to recover from the non-prevailing party all attorneys' fees and
other costs incurred in connection with the arbitration proceeding.

12.9 Notices. All notices and other communications permitted or

required under this Agreement shall be in writing and shall be deemed to have
been given when received at the addresses set forth on the signature page
hereof, or at such other address as may be specified by one party in writing to
the other.

Said written notice may be given by mail, telecopy, rush delivery service, personal delivery or any other means.

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first above written.

AASTROM:

AASTROM BIOSCIENCES, INC.
a Michigan corporation

By:

Name: /s/ R. DOUGLAS ARMSTRONG

Title: President/CEO

Address: P. O. Box 376
Ann Arbor, MI 48106
Attn: James Maluta
Fax: (313) 665-0485

COMPANY:

ETHOX CORP.
a New York corporation

By: /s/ FRANK P. WILTON

Name: Frank P. Wilton

Title: President

Address: 251 Seneca Street
Buffalo, NY
Attn: Frank P. Wilton
Fax: (716) 842-4040

EXHIBITS

- A Description of Product (Bioreactor Assembly and Custom Tubing Kit)
- B Company's Project Plan
- C Specifications for the Product
- D Manufacturing Drawings for the Product

EXHIBIT A

Description of Product

*

*CONFIDENTIAL PORTION REDACTED AND FILED
SEPARATELY WITH THE COMMISSION

EXHIBIT B

Company's Project Plan

*

*CONFIDENTIAL PORTION REDACTED AND FILED
SEPARATELY WITH THE COMMISSION

EXHIBIT C

Time and Quantity Schedule --
Preproduction Units

*

*CONFIDENTIAL PORTION REDACTED AND FILED
SEPARATELY WITH THE COMMISSION

EXHIBIT C-1

Pricing for Precommercial Units/1/

*

*CONFIDENTIAL PORTION REDACTED AND FILED
SEPARATELY WITH THE COMMISSION

EXHIBIT D

Manufacturing Drawings (Device Master Record)
for the Product

(to be added per Section 2.1(b))

*

*CONFIDENTIAL PORTION REDACTED AND FILED
SEPARATELY WITH THE COMMISSION

LICENSE AND SUPPLY AGREEMENT

This License and Supply Agreement, effective as of April 1, 1996,

(the "Effective Date") is made by and between Aastrom Biosciences, Inc., a Michigan corporation having its principal place of business at Lobby L, Domino's Farms, Ann Arbor, Michigan 48106 ("AASTROM") and Immunex Corporation, a Washington corporation having its principal place of business at 51 University Street, Seattle, Washington 98101 ("IMMUNEX").

AGREEMENT

In consideration of the mutual covenants and undertakings set forth herein, IMMUNEX and AASTROM hereby agree as follows:

1. BACKGROUND

1.1 Development and Supply of Products and Technology.

IMMUNEX has discovered and developed Cytokines (Pixykin(R) PIXY321, Flt3 ligand and Leukine(R) GM-CSF) and enzyme-linked immunoassay ("ELISA") reagents for the Cytokines ("Ancillary Materials"), that are collectively referred to herein as "Supplied Products," and certain cell culture technology, that together with Supplied Products are "Licensed Technology," and is the owner of certain patent rights relating to the Licensed Technology ("Licensed Patent Rights") that may be useful in or relate to the field of extracorporeal cell culture and transplantation ("ECCAT"). IMMUNEX intends to supply AASTROM with Supplied Product and to provide a nonexclusive license to AASTROM to the Licensed Technology and Licensed Patent Rights for Supplied Product purchased by AASTROM, subject to the terms of this Agreement.

1.2 Purchase and Use of Supplied Product and Licensed Technology.

AASTROM is a developer of certain ECCAT systems (instrumentation and single-use plastic disposables operated by the instrumentation, referred to herein as the "Systems") and desires to purchase Supplied Products from IMMUNEX for distribution, sale and use with the Systems. AASTROM also desires access to the Licensed Technology and Licensed Patent Rights to make, use and sell the Systems and services incorporating the Licensed Technology or otherwise covered by the Licensed Patent Rights.

2. DEFINITIONS

2.1 All initially capitalized terms shall have the meanings specified below:

"Affiliate" shall mean any entity that directly or indirectly

controls, is controlled by or is under common control with a party to this Agreement. The term "control" as used herein shall mean the possession of the power to direct or cause the direction of the management and the policies of an entity, whether through the ownership of a majority of the outstanding voting securities or by contract or otherwise.

"Ancillary Materials" shall mean ELISA reagents that are useful in

assay or quantification of Cytokines, and other materials made available by IMMUNEX to AASTROM to facilitate use of Licensed Technology.

"Calendar Quarter" shall mean each three-month period commencing

January 1, April 1, July 1 and October 1 of each year during the Term.

"Calendar Year" shall mean each twelve-month period commencing the

first Calendar Quarter following the Effective Date of each year during the
Term.

"Confidential Information" shall mean any and all proprietary or

confidential information owned by AASTROM or IMMUNEX that is provided to the
other party. Confidential Information shall not be deemed to include
information that:

(a) is or becomes known publicly through no fault of the recipient;
(b) is learned by the recipient from a Third Party entitled to
disclose it;

(c) is developed by the recipient independently of information
obtained from the disclosing party;

(d) is already known to the recipient before receipt from the
disclosing party, as shown by prior written records; or

(e) is released with the prior written consent of the disclosing
party.

"Cytokine" shall mean an IMMUNEX cytokine product identified

in Exhibit B.

"Effective Date" shall mean the date set forth in the first

paragraph of this Agreement.

"FDA" shall mean the United States Food and Drug Administration or any

successor agency vested with administrative and regulatory authority to approve
testing and marketing of human pharmaceutical or biological therapeutic products
in the United States.

"Field" shall mean development, manufacture, testing, use and sale of

systems, techniques, equipment, devices and associated technologies for
explanation, separation, culture, testing and transplantation of cells, referred
to collectively as "extracorporeal cell culture and transplantation" ("ECCAT").
The Field excludes all parenteral or in-vivo uses of Cytokines or Supplied
Products, which are expressly reserved to IMMUNEX.

"Force Majeure" shall mean any act of God or the public enemy, any

accident, explosion, fire, storm, earthquake, flood, drought, peril of the sea,
riot, embargo, war or foreign, federal, state or municipal order issued by a
court or other authorized official, seizure, requisition or allocation, any
failure or delay of transportation, shortage of or inability to obtain supplies,
equipment, fuel or labor or any other circumstance or event beyond the
reasonable control of the party relying upon such circumstance or event;
provided, however, that no such Force Majeure circumstance or event shall excuse
any failure or delay beyond a period exceeding one hundred eighty (180) days
from the date such performance would have been due but for such circumstance or
event.

"GMP" shall mean the regulatory requirements for good manufacturing

practices promulgated by the FDA under the Federal Food, Drug and Cosmetic Act,
as amended, 21 C.F.R. et seq.

"Improvement" shall mean any invention or improvement involving a

Cytokine or Licensed Technology that is made by employees of AASTROM, whether
solely or jointly with employees of IMMUNEX.

"Licensed Patent Rights" shall mean the patents and patent

applications identified in Exhibit A; any divisional, continuation or
continuation-in-part applications that

claim priority based upon such applications; any patents that issue in respect of the foregoing applications; and any reissues or extensions of such patents, and any other patents or patent applications owned or controlled by IMMUNEX that are necessary and useful to permit AASTROM to use and sell Licensed Technology in the Field.

"Licensed Technology" shall mean the Cytokines, Ancillary Reagents,

and any related technology, know-how, data, information and results that IMMUNEX has a right to disclose or transfer to AASTROM, and that is necessary or useful to permit AASTROM to use the Cytokines or Ancillary Materials and is transferred to AASTROM.

"Licensed Trademarks" shall mean Cell Software(TM), Leukine(R) and

Pixykin(R).

"Manufacturing Regulatory Documentation" shall mean a Drug Master File

or other Regulatory Filing owned by IMMUNEX and filed with the FDA that contains definitive technical information concerning a Supplied Product.

"Order" shall mean each quantity of a Supplied Product sold to AASTROM

under a separate invoice.

"Person" shall mean any individual, partnership, corporation, firm,

association, unincorporated organization, joint venture, trust or other entity.

"Purchase Order" shall have the meaning specified in Section 3.9

hereof.

"Regulatory Filing" shall mean a filing with a regulatory agency, for

example, the FDA, that concerns a Cytokine or use of a Cytokine in the Field.

"Supplied Product(s)" shall mean Cytokines and Ancillary Materials

produced by IMMUNEX for AASTROM; or, as permitted under this Agreement, produced by AASTROM or a Third Party.

"Supply Price" shall mean the price paid by AASTROM to IMMUNEX to

obtain Supplied Product for sale or distribution to end users of Licensed Technology.

"Systems" shall mean AASTROM's ECCAT systems, consisting of certain

instrumentation and single-use plastic disposables for use with the instrumentation, as well as any related documentation.

"Territory" shall mean North America, consisting of the United States

of America and Canada, and their respective territories and possessions.

"Third Party" shall mean any Person other than a party to this

Agreement or an Affiliate.

3. SUPPLY AND USE OF MATERIALS -----

3.1 Supply of Supplied Products. Subject to the terms of this Agreement, -----

IMMUNEX shall manufacture and sell to AASTROM, and AASTROM shall purchase exclusively from IMMUNEX, AASTROM's requirements of the Supplied Products for sale or use by AASTROM in conjunction with the Systems. AASTROM shall not be obligated to purchase its requirements of GM-CSF from IMMUNEX in countries other than the United States. All Supplied Products shall be sold and delivered to AASTROM in the Territory, and all sales shall be deemed to have been made in the United States.

3.2 Supply Price. The Supply Price applicable to the Supplied Products to

be sold by IMMUNEX to AASTROM pursuant to Section 3.1 hereof shall be that set forth in Exhibit B, which is attached hereto and made a part of this Agreement.

3.3 Supply of Research Quantities of Cytokines for Preclinical Research.

IMMUNEX shall provide reasonable research quantities of Cytokines and Ancillary Materials to AASTROM solely for AASTROM's own use in preclinical research, and not for resale or distribution to any other Person, at no charge to AASTROM.

3.4 Technical Assistance. Upon request and at no charge, IMMUNEX shall make

its employees available (at their normal places of employment or by telephone) to provide reasonable levels of technical assistance to AASTROM concerning AASTROM's use of the Supplied Products or AASTROM's preparation of Regulatory Filings.

3.5 Regulatory Filings. AASTROM shall file and be the owner of record for

all Regulatory Filings developed by AASTROM applicable to use of Supplied Products with the Systems. IMMUNEX shall permit AASTROM to cross-reference its Drug Master Files and Regulatory Filings to enable AASTROM to complete Regulatory Filings applicable to the Systems. IMMUNEX owns, and shall retain all right, title and interest in and to the Manufacturing Regulatory Documentation, and any other Regulatory Filing prepared and submitted by IMMUNEX to obtain or maintain regulatory approval of a Supplied Product. Each party shall, upon request and at no charge to the other, reasonably cooperate with and assist the other in preparing Regulatory Filings. Such cooperation shall extend to reasonable consultation by telephone or at the cooperating party's normal business location, but shall not include preparation of Regulatory Filings for the other party. All nonpublic information provided by one party to the other in preparing Regulatory Filings shall be deemed to be Confidential Information of the disclosing party. AASTROM's or IMMUNEX's right to cross-reference any Regulatory Filings owned by the other shall not extend to any Confidential Information of any Third Party that may be incorporated into a Regulatory Filing.

3.6 Clinical Studies. AASTROM shall be independently and solely responsible

for the design, implementation and evaluation of any human clinical studies used to obtain clinical data for use in preparing Regulatory Filings. AASTROM shall provide IMMUNEX with a complete copy of any clinical study protocol in which Supplied Products are used, as well as copies of any final abstracts or publications concerning the results of such study. AASTROM shall report any serious and unexpected adverse event that occurs in a clinical study involving Supplied Products. This report shall be provided by telephone or fax to the Professional Services Department at IMMUNEX (fax: 800-221-6820) as soon as possible and shall be confirmed and updated in writing within 24 hours after occurrence.

3.7 Manufacture of Product for Clinical Studies and Commercial Sale.

During the term of this Agreement, and for an additional one year period if IMMUNEX notifies AASTROM that it will not renew the Agreement under Section 8.7, and for two additional years should IMMUNEX cease supply per the terms of this Agreement under Section 3.19, IMMUNEX shall use reasonable commercial efforts to manufacture all of the requirements of AASTROM for each Supplied Product and release all quantities ordered by AASTROM in the Calendar Quarter specified in each accepted Purchase Order. IMMUNEX's supply obligations shall be limited in any year, at its option, to the projected number of vials of each Supplied Product specified by AASTROM in the Annual Requirements Forecast. In the event of any supply constraint, IMMUNEX shall allocate the available quantities of Supplied Products among itself and its licensees in a fair and equitable manner. Each Supplied Product released to AASTROM for clinical studies or commercial sale shall be

manufactured in material compliance with current GMP and according to manufacturing information in the Manufacturing Regulatory Documentation. IMMUNEX shall perform sufficient quality control testing of all Supplied Products released to AASTROM to establish compliance with any release specifications required by the Manufacturing Regulatory Documentation.

3.8 Annual Requirements Forecast. AASTROM shall inform IMMUNEX of its

forecasted requirements for each Supplied Product to be released to AASTROM during each Calendar Year ("Annual Requirements Forecast"). Within 30 days following the Effective Date, AASTROM shall provide IMMUNEX with a forecast of its Supplied Product requirements by Calendar Quarter for the remainder of 1996. On or before July 31 of each Calendar Year during the Term, AASTROM shall provide IMMUNEX with a forecast of its Supplied Product requirements for each Calendar Quarter of the following Calendar Year. Each such Annual Requirements Forecast shall not constitute a Purchase Order but rather a non-binding estimate to assist IMMUNEX in scheduling its facilities to manufacture Supplied Products. In the event that AASTROM shall, during the first three Calendar Quarters of any Calendar Year, fail to provide IMMUNEX with Purchase Orders for at least 25% of the quantity of each Supplied Product specified in the Annual Requirements Forecast applicable to such Calendar Year, IMMUNEX shall have the right to cease supply of such Supplied Product pursuant to Section 3.19 hereof following notice to AASTROM. Following the effective date of such notice, IMMUNEX shall provide AASTROM with thirty (30) days in which to submit a Purchase Order that will increase the quantity of Supplied Product subject to AASTROM's Purchase Orders in such Calendar Year to at least 25% of the Annual Requirements Forecast applicable to such Calendar Year.

3.9 Purchase Orders. On or before the first day of each Calendar Quarter

during the Term, AASTROM shall provide IMMUNEX with a Purchase Order specifying the quantity of each Supplied Product to be released to AASTROM in the following Calendar Quarter and a schedule specifying the dates upon which such quantity, or any fraction thereof, is to be released to AASTROM. Following acceptance by IMMUNEX, a Purchase Order shall not be cancelable by AASTROM without the consent of IMMUNEX. AASTROM may submit additional Purchase Orders during each Calendar Quarter which IMMUNEX shall accept, provided that adequate quantities of Supplied Products are available for supply to AASTROM and that such Purchase Orders otherwise comply with all other terms of this Agreement. IMMUNEX shall have no obligation to undertake additional production or vialing campaigns to produce any Supplied Products for AASTROM that have not been specified in an Annual Requirements Forecast or a Purchase Order provided in accordance with this Section 3.9.

3.10 Supplied Product Specifications; Development of New Formulations.

Immediately following the Effective Date, IMMUNEX shall provide Supplied Products to AASTROM in the available vialled formulations and vial sizes specified in the current Drug Master Files applicable to such Supplied Products. As new vialled formulations or vial sizes become available, IMMUNEX shall provide such new formulations or vial sizes to AASTROM and cause the Manufacturing Regulatory Documentation to be amended or supplemented to reflect all specifications applicable to such new formulations or vial sizes. IMMUNEX shall use reasonable commercial efforts to develop a 250 ug vialled formulation of each of PIXY321 and Flt3L. IMMUNEX shall have no obligation under this Agreement to develop any other vial sizes or formulations for AASTROM.

3.11 Specification Changes. Unless otherwise agreed by the parties,

IMMUNEX shall have no obligation to manufacture any Cytokine for AASTROM according to processes or specifications that vary from those set forth in the applicable Manufacturing

Regulatory Documentation. Following the establishment of a standard formulation for each Cytokine, IMMUNEX shall use reasonable commercial efforts to maintain the integrity and consistency of all specifications applicable to Cytokines. In the event that IMMUNEX deems it necessary to revise any specifications, procedures or Manufacturing Regulatory Documentation applicable to a Cytokine, IMMUNEX shall provide reasonable advance notice of any such revision to AASTROM. All specification changes that result in procedures or limits that exceed or differ from those set forth in the Manufacturing Regulatory Documentation shall be submitted to the FDA before being implemented. IMMUNEX shall take reasonable actions in consultation with AASTROM to ensure that any such changes do not compromise any clinical study or Regulatory Filing of AASTROM.

3.12 Quality Control Testing and Release of Products. Following manufacture

of each lot from which any Order is to be provided to AASTROM hereunder, IMMUNEX shall perform all quality control testing required to establish compliance of the lot with applicable specifications. A certificate of analysis shall be issued upon satisfactory completion of quality control testing of such lot. If quality control testing is successfully completed and a Purchase Order has been received, an Order shall be released to AASTROM on the date specified in the Purchase Order (the "Release Date"). Upon the Release Date, (a) IMMUNEX shall ship the Order to a location in the Territory as instructed by AASTROM, (b) upon receipt, title to such Order shall transfer to AASTROM, and (c) AASTROM shall be invoiced for the Order at the Supply Price at that time in effect.

3.13 Documentation. Not later than the time of delivery of each Order,

IMMUNEX shall provide AASTROM with a certificate of analysis applicable to each lot of Supplied Products included in each Order released to AASTROM. IMMUNEX shall document each step of the manufacturing and processing procedure and shall maintain retention samples of each lot in accordance with applicable FDA requirements. Complete batch records for all Supplied Products manufactured for AASTROM shall be maintained at IMMUNEX for inspection at any time by AASTROM at IMMUNEX's place of business upon reasonable notice to IMMUNEX. Any proprietary information of IMMUNEX contained in such batch records shall be deemed to be Confidential Information of IMMUNEX.

3.14 Storage and Shipping. Following release, each Order shall be held for

AASTROM by IMMUNEX in secure storage for use by or shipment to AASTROM or to such other recipient as instructed by AASTROM. All Orders shall be shipped FOB IMMUNEX's United States facility to a location in the Territory as designated by AASTROM with the insurance paid by IMMUNEX. AASTROM shall be responsible for all shipping charges, which shall be itemized on each invoice by IMMUNEX. Title to and risk of loss for each Order shall transfer to AASTROM upon delivery to AASTROM's designated delivery location. AASTROM shall provide IMMUNEX with a specific list of approved carriers that meet AASTROM's specifications for handling during shipment. AASTROM shall be solely responsible for any reshipments of Supplied Products or any shipments of Supplied Products outside the Territory.

3.15 Minimum Order Quantity. IMMUNEX will not act in the capacity of a

distributor of Supplied Products to AASTROM's customers. At any time during the Term of this Agreement, IMMUNEX may establish reasonable minimum Order quantities (which will not exceed, absent AASTROM's consent, one Calendar Quarter's projected purchases as set forth in the applicable Annual Requirements Forecast) if AASTROM does not provide Purchase Orders specifying economically efficient Order quantities, or otherwise increase the prices charged to AASTROM for Supplied Products to include any additional costs incurred in filling Purchase Orders that do not meet reasonable minimum quantities.

3.16 Acceptance; Payment Terms. Payment for each Order released to AASTROM

shall be due forty-five (45) days following delivery and invoice, during which period AASTROM shall perform its acceptance testing. IMMUNEX shall provide AASTROM with descriptions of its release testing procedures and specifications to permit AASTROM to conform its acceptance testing to the methods used by IMMUNEX. If AASTROM provides evidence that such Order fails to meet the release specifications set forth in the Manufacturing Regulatory Documentation that are at that time in effect, payment shall not be due until the failure is corrected. If the results of quality control testing by AASTROM do not agree with those obtained by IMMUNEX, AASTROM shall promptly so notify IMMUNEX and the acceptance period shall be extended forty-five (45) days to enable the parties to retest the Order or otherwise attempt to reconcile their differences. In the event that such differences cannot be resolved by the parties, the parties shall designate an independent testing laboratory to test the Order. The findings of such independent testing laboratory shall be binding on the parties, absent manifest error. The expenses shall be borne by the party adversely affected by such findings. IMMUNEX shall have no obligation to supply additional Orders of Supplied Products to AASTROM if AASTROM declines to accept any Order due to the application of any specifications or acceptance testing procedures that are different from the release testing procedures and specifications employed by IMMUNEX, if such Order otherwise complies with the procedures and specifications employed by IMMUNEX. A late payment charge of 1% of the outstanding unpaid balance per month shall be payable if invoiced charges are not paid when due.

3.17 Facility Visits. Upon reasonable prior notice to IMMUNEX, AASTROM or

its designee may (but shall not be required to) have its representatives audit IMMUNEX's production of Supplied Products for material compliance with current GMP, including observing at any time the manufacture of any Supplied Product, or any quality control or other services provided by IMMUNEX. These representatives shall comply with all applicable safety and security rules while present at facilities owned or operated by IMMUNEX.

3.18 Scheduling of Campaigns; Delays. IMMUNEX shall employ reasonable

commercial efforts to maintain inventories of all Supplied Products sufficient to meet AASTROM's commercial requirements as specified in each Annual Requirements Forecast. IMMUNEX shall promptly advise AASTROM of significant unanticipated delays in the release of any Order. IMMUNEX shall not be liable to AASTROM for any delay in providing any Order, or the documentation relating to any Order, if such delay is caused by Force Majeure.

3.19 Alternate Source of Supply. In the event that IMMUNEX elects to

discontinue supplying AASTROM with any Supplied Product as provided in Section 3.8 above, or is prevented by Force Majeure from supplying AASTROM with any Supplied Product for a period of at least one hundred eighty (180) days, IMMUNEX shall use reasonable commercial efforts to grant AASTROM a nonexclusive license to make or have made the Cytokine corresponding to such Supplied Product for use or sale in the Field and Territory, transfer to AASTROM or its designee (which could include, for example, a mutually acceptable contract manufacturer) all Licensed Technology and any available license rights (apart from facilities, commercially available raw materials or equipment) that are necessary or useful in manufacturing such Cytokine in an alternative facility, and shall use reasonable commercial efforts to cooperate with AASTROM to continue to supply Supplied Product from its inventories to meet AASTROM's requirements for Supplied Product until an alternate source of supply is established. IMMUNEX shall not be obligated to grant such licenses or transfer any technologies in the event that a dispute over acceptance procedures or specifications cannot be resolved as provided in Section 3.16 hereof, or IMMUNEX and AASTROM are unable to resolve any dispute over pricing. In such event, AASTROM

shall be entitled to terminate this Agreement, subject to the liquidated damages provisions of Section 8.4 hereof.

3.20 Place of Payment. Payments by AASTROM to IMMUNEX will be made in

United States Dollars by wire transfer to an account designated by IMMUNEX located in the United States.

4. GRANT OF LICENSE

4.1 License. IMMUNEX hereby grants AASTROM a nonexclusive license under

the Licensed Patents and Licensed Technology, to use and sell the Supplied Products in the Field and Territory. The license granted hereunder includes the right to grant sublicenses to purchasers or distributors of the Systems, to preclinical or clinical investigators, or Affiliates of AASTROM, to use or sell the Supplied Products in the Field and Territory, but excludes the right to sell or to use the Supplied Products outside the Field and Territory. The scope of the Territory to which this license applies may be amended during the Term.

4.2 Expanded Territorial Rights. IMMUNEX and AASTROM each desire to extend

the Territory to which the license granted pursuant to Section 4.1 hereof applies to include all countries in the world ("Expanded Territorial Rights"). IMMUNEX has commenced negotiations with American Cyanamid Company and American Home Products Corporation ("AHP") to obtain rights under prior agreements with such companies enabling IMMUNEX to grant the Expanded Territorial Rights to AASTROM. IMMUNEX shall continue such negotiations, and any other negotiations that it deems reasonably necessary to secure appropriate licenses and rights necessary to extend and protect such Expanded Territorial Rights. Pending resolution of such negotiations, IMMUNEX will not object to the commencement of any clinical trials by AASTROM outside of the Territory using Supplied Products sold to AASTROM in the Territory. If such negotiations are successful, IMMUNEX shall immediately amend this Agreement, at no additional charge or fee to AASTROM, to grant AASTROM Expanded Territorial Rights.

4.3 Licensed Trademarks. IMMUNEX hereby grants AASTROM a nonexclusive

license to make, have made, use and sell products and services using the Licensed Trademarks in the Field and Territory, solely in connection with AASTROM's use, sale and distribution of Supplied Products for use in conjunction with the Systems. AASTROM's use of Licensed Trademarks shall at all times comply with all reasonable instructions and specifications provided by IMMUNEX.

4.4 Non-competition. During the term of this Agreement, neither IMMUNEX nor

any Affiliate of IMMUNEX shall directly compete with AASTROM by selling Supplied Products to AASTROM's customers for use with the Systems. AASTROM shall not sell or distribute Supplied Products to customers of IMMUNEX or customers of other companies to which IMMUNEX provides Supplied Products for use with proprietary systems of such other companies. In the event that IMMUNEX enters into any subsequent supply or license agreements with other companies for Supplied Products, IMMUNEX shall obtain a covenant from such companies that they will not sell or distribute Supplied Products to AASTROM's customers for use with the Systems.

5. FEES AND ROYALTIES

5.1 Fees. In consideration of the value of research and development

previously conducted by IMMUNEX in developing the----Supplied Products and Ancillary Materials and in assisting AASTROM with its development efforts prior to the Effective Date,

AASTROM shall pay IMMUNEX a Signing Fee of \$1,500,000, due and payable thirty (30) days following the Effective Date. In order to maintain its license and supply rights, AASTROM shall pay IMMUNEX an annual Fee of \$1,000,000, which shall be due and payable on each one year anniversary of the Effective Date during the Term. If any such Annual Fee is not paid when due, IMMUNEX shall have the right to terminate this Agreement for material breach, upon notice to AASTROM as provided in Section 8.2(a) hereof.

5.2 Royalties. AASTROM shall have no obligation to pay royalties to IMMUNEX

in respect of the licenses granted to AASTROM under Section 4 hereof, or otherwise in respect of the use or sale of Supplied Products that are supplied by IMMUNEX. In the event that AASTROM or its designee manufactures any Cytokine that is subject to Licensed Patent Rights or is manufactured using Licensed Technology transferred by IMMUNEX to AASTROM or AASTROM's designee as provided in Section 3.19 hereof, AASTROM shall pay IMMUNEX royalties in respect of the net sales value of such Cytokine, as well as pay any royalties to Third Parties that IMMUNEX would have been obligated to pay in respect of the net sales value of such Cytokine. The royalties payable to IMMUNEX by AASTROM, as well as all other terms applicable to the reporting any payment of such royalties, shall be determined by good-faith negotiation between IMMUNEX and AASTROM, taking into account the value of the Licensed Technology, customary commercial practices in the U.S. biotechnology, pharmaceutical and medical device industries, and other relevant factors.

5.3 Records. AASTROM shall keep and maintain, in accordance with generally

accepted accounting principles, proper and complete records and books of account documenting all sales or other dispositions of Supplied Products as well as sales or other dispositions of the Systems that include Supplied Products. At IMMUNEX's request and expense, AASTROM shall permit an independent public accounting firm selected by IMMUNEX to have access, not more than once in any consecutive four Calendar Quarters, to such books and records for the sole purpose of verifying sales reported by AASTROM to IMMUNEX for purposes of Exhibit B, or for calculating any royalties due IMMUNEX.

6. INTELLECTUAL PROPERTY

6.1 Inventions. AASTROM shall inform IMMUNEX of any material Improvement

that is made by its employees, provided such Improvement has been formalized as a disclosure. Title to any invention made by an employee or employees of either party in connection with its activities under this Agreement shall vest in the employer of such employee or employees in accordance with the patent laws of the United States. Inventions made jointly by one or more employees of each party shall be jointly owned. Each party shall inform the other in the event that its employees report the making of a joint invention. Each party shall cooperate with the other in completing any patent applications to secure patent rights for inventions in which the other has an ownership interest, and in perfecting such other party's legal title thereto. If AASTROM does not itself elect to obtain patent coverage in any territory for any disclosed Improvement that is made solely by its employees, it shall provide IMMUNEX with the opportunity to prepare and file appropriate patent applications covering the disclosed Improvement. Any patent rights resulting from such patent applications will be included within the scope of Licensed Patent Rights.

6.2 Notification and Abatement of Patent Infringement. AASTROM shall notify

IMMUNEX of any infringement known to AASTROM by any Person of any Licensed Patent Rights that apply also to operations of AASTROM, and shall provide IMMUNEX with the available evidence, if any, of such infringement. If such infringement is demonstrated by AASTROM to have resulted in competitive harm, or would reasonably be

expected to result in harm to AASTROM, AASTROM shall have the right to request that IMMUNEX commence suit or otherwise abate such infringement. If, following such notice, IMMUNEX has not commenced such suit within one hundred eighty (180) days following such notice, AASTROM shall have the right to suspend payment of any annual fees or royalties payable hereunder (but not any payments for Supplied Products) until IMMUNEX commences such suit or otherwise abates the infringement by licensing or otherwise. IMMUNEX shall not be obligated to undertake any patent enforcement activities if AASTROM has not paid IMMUNEX total annual fees equal to at least \$3,500,000.

IMMUNEX shall not be obligated to enforce Licensed Patent Rights against more than one infringer at any one time.

6.3 General Obligation of Confidentiality. During the Term and for a period

of five (5) years thereafter, AASTROM and IMMUNEX shall maintain in confidence the respective Confidential Information received or obtained from the other party, and use such Confidential Information solely for the purposes contemplated and permitted by this Agreement. Each party shall maintain communications to each other in confidence. Each party acknowledges that all Confidential Information exchanged or developed hereunder shall be owned by the transferor and shall continue to be owned by the transferor following transfer.

6.4 Permitted Disclosures. Notwithstanding Section 6.3 hereof, IMMUNEX and

AASTROM shall, to the extent necessary, have the right to disclose and use Confidential Information of the other party:

(a) to prepare or supplement any Regulatory Filing applicable to the use of a Supplied Product in the Field, or otherwise to assist in securing institutional or government approval to clinically test or government approval to market a Supplied Product for use in the Field; or

(b) where the disclosure and use of the Confidential Information will be useful or necessary to the procurement of Licensed Patent Rights;

provided that the affected party shall have been notified of such disclosure and that any such disclosure shall be in confidence and subject to provisions the same, or substantially the same, as those in Section 6.3 hereof, whenever reasonably possible.

6.5 Publicity, Use of Names or Trademarks. Neither party shall originate

any press release concerning this Agreement or the subject matter hereof without the prior written approval of the other party, which approval shall not be unreasonably withheld. Except as provided in Section 4.3 hereof with respect to Licensed Trademarks, neither party shall have the right to use the name or any trade name or trademark of the other in any form of publicity, advertising, or solicitation without the prior written approval of the other party. The trademarks Immunex(R), Leukine(R), Pixykine(R) and Cell Software(TM) are the exclusive property of IMMUNEX.

7. WARRANTIES AND REPRESENTATIONS

7.1 Warranties and Representations of IMMUNEX. IMMUNEX represents and

warrants to AASTROM that:

(a) IMMUNEX is a corporation duly organized, validly existing and in good standing under the laws of the State of Washington and has all necessary corporate power to enter into and perform its obligations under this Agreement;

(b) the execution, delivery and performance of this Agreement by IMMUNEX have been duly authorized and approved by all necessary corporate action, and that the Agreement is binding upon and enforceable against IMMUNEX in accordance with its terms (subject to bankruptcy and similar laws affecting the rights of creditors generally);

(c) IMMUNEX is the owner of the Licensed Patent Rights, Licensed Technology and Licensed Trademarks, and has the right to grant AASTROM the licenses granted hereunder, subject to any dominating patent rights of third parties (for example, IL-3 or GM-CSF patents owned or controlled by Genetics Institute, Inc. or Sandoz AG) and the rights of AHP under applicable agreements with IMMUNEX;

(d) IMMUNEX is not aware of any special or unusual hazards that would arise as a result of AASTROM's use of Licensed Technology as permitted hereunder;

(e) Each lot of each Supplied Product delivered to AASTROM hereunder shall be manufactured, tested and released in material compliance with current GMP and the applicable Manufacturing Regulatory Documentation; and

(f) Any documentation provided to AASTROM by IMMUNEX concerning any Supplied Product or Drug Master File shall be accurate in all material respects.

7.2 Warranties and Representations of AASTROM. AASTROM represents and warrants to IMMUNEX that:

(a) AASTROM is a corporation duly organized, validly existing and in good standing under the laws of the State of Michigan and has all necessary corporate power to enter into and perform its obligations under this Agreement;

(b) the execution, delivery and performance of this Agreement by AASTROM have been duly authorized and approved by all necessary corporate action, and that the Agreement is binding upon and enforceable against AASTROM in accordance with its terms (subject to bankruptcy and similar laws affecting the rights of creditors generally); and

(c) AASTROM shall use the Licensed Technology in compliance with all applicable federal, state and local laws and regulations.

7.3 Limitation of Liability. IMMUNEX has no knowledge or awareness of or control over the manner in which AASTROM intends to use the Licensed Technology. IMMUNEX shall not be liable to AASTROM for any losses, damages, costs or expenses of any nature incurred or suffered by AASTROM or by a Third Party, arising out of any dispute or other claims or proceedings made by or brought against AASTROM, (including, without limitation, product liability claims and claims by a Third Party alleging infringement of its intellectual property rights by the use or sale of any Supplied Product or System), nor shall IMMUNEX be responsible in any way for dealing with any such disputes, claims or proceedings, except to the extent that any such dispute, claim or proceeding arises from (a) a breach by IMMUNEX of any warranty set forth in Section 7.1 hereof, or (b) any failure by IMMUNEX to manufacture, test, document or release any Supplied Product in material compliance with current GMP and the applicable Manufacturing Regulatory Documentation. IMMUNEX shall not be responsible to AASTROM for any interruption in supply that is caused by Force Majeure. EXCEPT AS SET FORTH IN SECTION 7.1(e) HEREOF, IMMUNEX MAKES NO PRODUCT WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. IMMUNEX

SHALL NOT BE LIABLE FOR ANY USE OF LICENSED TECHNOLOGY BY AASTROM OR FOR ANY LOSS, CLAIM, DAMAGE, OR LIABILITY, OF ANY KIND OR NATURE, WHICH MAY ARISE FROM OR IN CONNECTION WITH THIS AGREEMENT OR FROM THE USE, HANDLING OR STORAGE OF THE SUPPLIED PRODUCTS OR ANCILLARY MATERIALS. NEITHER PARTY TO THIS AGREEMENT SHALL BE ENTITLED TO RECOVER FROM THE OTHER ANY SPECIAL, INCIDENTAL, CONSEQUENTIAL OR PUNITIVE DAMAGES.

7.4 AASTROM's Right to Indemnification. IMMUNEX shall indemnify each of

AASTROM, its successors and assigns, and the directors, officers, employees, agents and counsel thereof (the "AASTROM Indemnitees"), pay on demand and protect, defend, save and hold each AASTROM Indemnatee harmless from and against, on an after-tax basis, any and all liabilities, damages, losses, settlements, claims, actions, suits, penalties, fines, costs or expenses (including, without limitation, reasonable attorneys' fees) (any of the foregoing, a "Claim") incurred by or asserted against any AASTROM Indemnatee of whatever kind or nature, including, without limitation, any claim or liability based upon negligence, warranty, strict liability, violation of government regulation or infringement of patent or other proprietary rights, arising from or occurring as a result of (a) the use of any Licensed Technology by IMMUNEX or any Affiliate, agent or Third Party licensee of IMMUNEX (other than AASTROM) or (b) any breach of this Agreement by IMMUNEX, (including (i) any breach by IMMUNEX of any warranty set forth in Section 7.1 hereof, or (ii) any failure by IMMUNEX to manufacture, test, document or release any Supplied Product in material compliance with current GMP and the applicable Manufacturing Regulatory Documentation) except in any case claims resulting from the gross negligence or willful misconduct of AASTROM. AASTROM shall promptly notify IMMUNEX of any Claim, upon becoming aware thereof, and permit IMMUNEX at IMMUNEX's cost to defend against such Claim and shall cooperate in the defense thereof. Neither IMMUNEX nor AASTROM shall enter into, or permit, any settlement of any such Claim without the express written consent of the other party. AASTROM may, at its option and expense, have its own counsel participate in any proceeding that is under the direction of IMMUNEX and will cooperate with IMMUNEX or its insurer in the disposition of any such matter.

7.5 IMMUNEX Right to Indemnification. AASTROM shall indemnify each of

IMMUNEX, its successors and assigns, and the directors, officers, employees, agents and counsel thereof (the "IMMUNEX Indemnitees"), pay on demand and protect, defend, save and hold each IMMUNEX Indemnatee harmless from and against, on an after-tax basis, any and all Claims incurred by or asserted against any IMMUNEX Indemnatee of whatever kind or nature, including, without limitation, any claim or liability based upon negligence, warranty, strict liability or violation of government regulation, arising from or occurring as a result of (a) the use of any Supplied Product, Licensed Technology or Licensed Patent Rights by AASTROM or any Affiliate, agent or employee of AASTROM, (b) any breach of this Agreement by AASTROM, or (c) infringement of patent or other proprietary rights of a Third Party, except in any case claims resulting from the gross negligence or willful misconduct of IMMUNEX. IMMUNEX shall promptly notify AASTROM of any Claim, upon becoming aware thereof, and permit AASTROM at AASTROM's cost to defend against such Claim and shall cooperate in the defense thereof. Neither IMMUNEX nor AASTROM shall enter into, or permit, any settlement of any such Claim without the express written consent of the other party. IMMUNEX may, at its option and expense, have its own counsel participate in any proceeding that is under the direction of AASTROM and will cooperate with AASTROM or its insurer in the disposition of any such matter.

8. TERM AND TERMINATION

8.1 Normal Termination. Unless terminated early or renewed as provided

hereunder, this Agreement shall commence on the Effective Date and shall terminate upon the fifth (5th) anniversary of the Effective Date (the "Term").

8.2 Termination by IMMUNEX. IMMUNEX shall have the right to terminate this

Agreement, including the licenses granted pursuant to Sections 4.1 and 4.2 hereof, effective immediately upon written notice of termination to AASTROM in the event that:

(a) AASTROM fails to perform or observe or otherwise breaches any of its material obligations under this Agreement and such failure or breach continues unremedied for a period of sixty (60) days after receipt by AASTROM of written notice thereof from IMMUNEX;

(b) a proceeding or case shall be commenced without the application or consent of AASTROM and such proceeding or case shall continue undismissed, or an order, judgment or decree approving or ordering any of the following shall be entered and continue unstayed and in effect, for a period of forty-five (45) days from and after the date service of process is effected upon AASTROM, seeking (i) AASTROM's liquidation, reorganization, dissolution or winding-up, or the composition or readjustment of its debts, (ii) the appointment of a trustee, receiver, custodian, liquidation or the like of AASTROM or of all or any substantial part of its assets, or (iii) similar relief in respect of AASTROM under any law relating to bankruptcy, insolvency, reorganization, winding-up or the composition or readjustment of debts.

8.3 Termination by AASTROM for Cause other than Material Breach by IMMUNEX.

Subject to Section 8.4 hereof, AASTROM shall have the right to terminate this Agreement at any time, effective immediately upon written notice of termination to IMMUNEX.

8.4 Liquidated Damages upon Early Termination. Following the Effective Date,

Immunex will commit personnel, incur expenses and devote its resources to develop specialized formulations or vial sizes for the Supplied Products. In the event that AASTROM terminates this Agreement pursuant to Section 8.3 hereof prior to the payment to IMMUNEX of Annual Fees under Section 5.1 hereof equal to * AASTROM shall pay IMMUNEX liquidated damages that are equal to *

Such liquidated damages shall be paid by AASTROM to IMMUNEX within thirty (30) days following receipt of an invoice detailing the calculation thereof.

8.5 Termination by AASTROM for Material Breach. AASTROM shall have the right

to terminate this Agreement, including the licenses granted pursuant to Sections 4.1 and 4.2 hereof, effective immediately upon written notice of termination to IMMUNEX in the event that:

(a) IMMUNEX fails to perform or observe or otherwise breaches any of its material obligations under this Agreement and such failure or breach continues unremedied

*CONFIDENTIAL PORTION REDACTED AND FILED SEPARATELY WITH THE COMMISSION

for a period of sixty (60) days after receipt by IMMUNEX of written notice thereof from AASTROM;

(b) a proceeding or case shall be commenced without the application or consent of IMMUNEX and such proceeding or case shall continue undismissed, or an order, judgment or decree approving or ordering any of the following shall be entered and continue unstayed and in effect, for a period of forty-five (45) days from and after the date service of process is effected upon IMMUNEX, seeking (i) IMMUNEX's liquidation, reorganization, dissolution or winding-up, or the composition or readjustment of its debts, (ii) the appointment of a trustee, receiver, custodian, liquidation or the like of IMMUNEX or of all or any substantial part of its assets, or (iii) similar relief in respect of IMMUNEX under any law relating to bankruptcy, insolvency, reorganization, winding-up or the composition or readjustment of debts.

8.6 Effect of Termination. In the event of any termination of this

Agreement, all amounts previously invoiced and unpaid, or any accrued royalties due IMMUNEX, shall be due and payable as of the time of termination, except for any liquidated damages due pursuant to Section 8.4 which shall be paid as provided therein. Upon termination, all rights and licenses granted pursuant to Section 4.1 and 4.2 hereof shall immediately terminate, but the provisions of Sections 6.3 and 6.4 hereof relating to Confidential Information and AASTROM shall cease use of all IMMUNEX trademarks. The liability and indemnification provisions of Sections 7.3, 7.4 and 7.5 hereof shall survive termination or expiration of this Agreement only with respect to Claims that arose from acts or circumstances that occurred prior to termination.

8.7 Renewal. Subject to the provisions set forth below and in Sections 3.19

and 5.2, Immunex hereby grants AASTROM an option to renew this Agreement, or any amendment or renewal thereof, for an additional five (5) year term to commence upon expiration of the Term, provided that AASTROM notifies IMMUNEX of its intent to renew at least one year prior to the fifth (5th) anniversary of the Effective Date. AASTROM and IMMUNEX will negotiate the Supply Price applicable to the Supplied Product for the Renewal Term in good faith, said Supply Price to reflect any reasonable changes in manufacturing costs incurred by IMMUNEX that would cause a decreased profit margin to IMMUNEX in comparison with that attained during the initial term of the Agreement, AASTROM's profit margin on sales of the Systems, or any increases or decreases in the price charged by AASTROM or its licensees to customers for the Systems. If IMMUNEX elects to not renew the Agreement, then IMMUNEX will continue to supply AASTROM with Licensed Technology for two additional years from the date of written notification to AASTROM of IMMUNEX's intent not to renew, during which period IMMUNEX shall grant the licenses and transfer to AASTROM or its designee the Licensed Technology (apart from facilities, equipment or commercially available supplies) that is necessary or useful to manufacture Supplied Product in an alternative facility as provided in Section 3.19.

9. MISCELLANEOUS PROVISIONS

9.1 No Implied Waivers; Rights Cumulative. No failure on the part of IMMUNEX

or AASTROM to exercise and no delay in exercising any right, power, remedy or privilege under this Agreement, or provided by statute or at law or in equity or otherwise, including, without limitation, the right or power to terminate this Agreement, shall impair, prejudice or constitute a waiver of any such right, power, remedy or privilege or be construed as a waiver of any breach of this Agreement or as an acquiescence therein, nor shall any single or partial exercise of any such right, power, remedy or privilege preclude any other or further exercise thereof or the exercise of any other right, power, remedy or privilege.

9.2 Survival. All agreements, covenants, representations, warranties and

indemnities set forth in this Agreement shall survive the execution and delivery
of this Agreement.

9.3 Notices. All notices, requests and other communications to IMMUNEX or

AASTROM hereunder shall be in writing (including telecopy or similar electronic
transmissions), shall refer specifically to this Agreement and shall be
personally delivered or sent by telecopy (fax) or other electronic facsimile
transmission or by registered mail, or certified mail, return receipt requested,
postage prepaid, in each case to the respective address specified below (or to
such address as may be specified in writing to the other party hereto):

Immunex Corporation
51 University Street
Seattle, Washington 98101
Attention: General Counsel
FAX: (206) 233-0644

Aastrom Biosciences, Inc.
Lobby L, Domino's Farms
Ann Arbor, Michigan 48106
Attention: President
FAX: (313) 665-0485

9.4 Further Assurances. Each of IMMUNEX and AASTROM agrees to duly execute

and deliver, or cause to be duly executed and delivered, such further
instruments and do and cause to be done such further acts and things, including,
without limitation, the filing of such additional assignments, agreements,
documents and instruments, that may be necessary or as the other party hereto
may at any time and from time to time reasonably request in connection with this
Agreement or to carry out more effectively the provisions and purposes of, or to
better assure and confirm unto such other party its rights and remedies under,
this Agreement.

9.5 Successors and Assigns. The terms and provisions of this Agreement shall

inure to the benefit of, and be binding upon, IMMUNEX, AASTROM, and their
respective successors and permitted assigns as provided in this Section. IMMUNEX
shall have the right to assign or otherwise transfer any of its rights and
interests, or delegate any of its obligations, to an Affiliate of IMMUNEX
provided that such Affiliate agrees in writing to carry out in full any
obligations to AASTROM that are assigned to it. Either party shall have the
right to assign all of its rights and interests and delegate all of its
obligations under this Agreement to any Person that is the successor in interest
to the assigning party in any merger, consolidation or sale involving
substantially all of the business and assets of the assigning party. Any other
assignment or delegation shall only be valid and effective if the other party
has provided its prior express written consent. Any attempt to assign or
delegate any portion of this Agreement in violation of this Section shall be
null and void. Subject to the foregoing, any reference to IMMUNEX or AASTROM
hereunder shall be deemed to include the successors thereto and assigns thereof.

9.6 Amendments. No amendment, modification, waiver, termination or discharge

of any provision of this Agreement, nor consent to any departure by IMMUNEX or
AASTROM therefrom, shall in any event be effective unless the same shall be in
writing specifically identifying this Agreement and the provision intended to be
amended, modified, waived, terminated or discharged and signed by IMMUNEX and
AASTROM,

and each such amendment, modification, waiver, termination or discharge shall be effective only in the specific instance and for the specific purpose for which given. No provision of this Agreement shall be varied, contradicted or explained by any oral agreement, course of dealing or performance or any other matter not set forth in an agreement in writing and signed by IMMUNEX and AASTROM.

9.7 Governing Law. This Agreement shall in all respects, including all

matters of construction, validity and performance, be governed by, and construed and enforced in accordance with, the laws of the state of Washington applicable to contracts entered into in that state between citizens of that state and to be performed wholly within that state without reference to any rules governing conflicts of laws.

9.8 Severability. If any provision hereof should be held invalid, illegal

or unenforceable in any respect in any jurisdiction, then, to the fullest extent permitted by law, (a) all other provisions hereof shall remain in full force and effect in such jurisdiction and shall be liberally construed in order to carry out the intentions of the parties hereto as nearly as may be possible and (b) such invalidity, illegality or unenforceability shall not affect the validity, legality or enforceability of such provision in any other jurisdiction. To the extent permitted by applicable law, IMMUNEX and AASTROM hereby waive any provision of law that would render any provision hereof prohibited or unenforceable in any respect.

9.9 Headings. Headings used herein are for convenience only and shall not

in any way affect the construction of, or be taken into consideration in interpreting, this Agreement.

9.10 Execution in Counterparts. This Agreement may be executed in any number

of counterparts, each of which counterparts, when so executed and delivered, shall be deemed to be an original, and all of which counterparts, taken together, shall constitute one and the same instrument.

9.11 Entire Agreement. This Agreement constitutes, on and as of the date

hereof, the entire agreement of IMMUNEX and AASTROM with respect to the subject matter hereof, and all prior or contemporaneous understandings or agreements, whether written or oral, between IMMUNEX and AASTROM with respect to such subject matter are hereby superseded in their entireties.

IN WITNESS WHEREOF, the parties have caused this Agreement to be executed by their duly authorized officers as of the date first written above.

IMMUNEX CORPORATION

AASTROM BIOSCIENCES, INC.

By /s/ Scott G. Hallquist

By /s/ R. Douglas Armstrong

Title Senior Vice President

Title President/CEO

EXHIBIT A: LICENSED PATENT RIGHTS

NOTE: LICENSE TO INTERNATIONAL RIGHTS IS SUBJECT TO PRIOR CONSENT OF AMERICAN HOME PRODUCTS CORPORATION

Technology	Country	(Application SN) Patent Number	Filing Date (Priority Date)	
PIXYKINE(R) rh GM-CSF/IL-3 fusion protein	United States	5,073,627	8/14/90	(8/22/89)
		5,108,910	3/22/91	(8/22/89)
	Australia	632372	8/14/90	(8/22/89)
	Canada	(2,054,608)	10/31/91	(8/22/89)
	Germany	DD297,188	8/22/90	(8/22/89)
	Europe	0489116	8/14/90	(8/22/89)
	Austria	0489116	8/14/90	(8/22/89)
	Belgium	0489116	8/14/90	(8/22/89)
	Denmark	0489116	8/14/90	(8/22/89)
	France	0489116	8/14/90	(8/22/89)
	Italy	0489116	8/14/90	(8/22/89)
	Germany	0489116	8/14/90	(8/22/89)
	Luxembourg	0489116	8/14/90	(8/22/89)
	Liechtenstein	0489116	8/14/90	(8/22/89)
	Netherlands	0489116	8/14/90	(8/22/89)
	Spain	0489116	8/14/90	(8/22/89)
	Sweden	0489116	8/14/90	(8/22/89)
	Switzerland	0489116	8/14/90	(8/22/89)
	United Kingdom	0489116	8/14/90	(8/22/89)
	Finland	(920764)	8/14/90	(8/22/89)
	Ireland	64202	8/21/90	(8/22/89)
	Japan	(513381/90)	8/14/90	(8/22/89)
	Mexico	(92 03426)	6/25/92	(8/22/89)
	Malaysia	(PI9102157)	11/22/91	(8/22/89)
	Norway	(920703)	8/14/90	(8/22/89)
	Philippines	(44030)	3/11/92	(8/22/89)
	PCT	(PCT/US90/04599)	8/14/90	(8/22/89)

rh Flt3L	United States	(08/243,545)	5/11/94	(5/24/93)
		(08/444,626)	5/19/95	(5/24/93)
		(08/444,632)	5/19/95	(5/24/93)
		(08/444,625)	5/19/95	(5/24/93)
		(08/444,627)	5/19/95	(5/24/93)
	Australia	69877/94	5/12/94	
	Canada		5/12/94	
	Europe	(94303575.8)	5/19/95	(5/24/93)
	Finland	955646	5/12/94	
	Israel	(109677)	5/18/94	(5/24/93)
	Japan	500715/95	5/12/94	
	Korea	705236/1995	5/12/94	
	Mexico	(943806)	5/23/94	(5/24/93)
	Malaysia	(PI 9401321)	5/24/94	(5/24/93)
	Norway	954735	5/12/94	
	New Zealand	267541	5/12/94	
	South Africa	94/3490	5/20/94	(5/24/93)
	Thailand	(022529)	5/23/94	(5/24/93)
	Taiwan	(83105225)	6/8/94	(6/8/94)
	Taiwan	(83110743)	11/18/94	(11/18/94)
	PCT	(PCT/US94/05365)	5/12/94	(5/24/93)
Method for Improving Autologous Transplantation	United States	5,199,942	9/26/91	(6/7/91)
	Australia	(21793/92)	6/5/92	(6/7/91)
	Canada	(2,109,699)	6/5/92	(6/7/91)
	Europe	(92913333.8)	6/5/92	(6/7/91)
	Japan	(500649/93)	6/5/92	(6/7/91)
Extracorporeal Cell Culture and Transplantation Kits	PCT	(PCT/US92/04686)	6/5/92	(6/7/91)
LEUKINE(R) rh GM-CSF	United States	5,391,485	8/6/85	
		5,229,496	10/6/88	
		5,393,870	5/27/93	
	Canada	(514,337)	7/22/86	

EXHIBIT B: PRICE OF SUPPLIED PRODUCT

*

*CONFIDENTIAL PORTION REDACTED AND FILED
SEPARATELY WITH THE COMMISSION

LEASE

THIS LEASE is made as of this 18 day of May, 1992, between the following parties:

LANDLORD:

Domino's Farms Holding
Limited Partnership
(a Michigan corporation)
24 Frank Lloyd Wright Drive
Ann Arbor, MI 48105

TENANT

AASTROM Biosciences, Inc.
Post Office Box 130469
Ann Arbor, Michigan 48113-0469

LEASE OF PREMISES:

- -----

In consideration of the rents to be paid and the covenants and agreements to be performed hereunder, Landlord hereby leases to TENANT and TENANT hereby leases from Landlord the PREMISES (defined below).

SUMMARY OF LEASE TERMS:

The following is intended to summarize certain basic terms of this Lease, and is not intended to be exhaustive. In the event anything set forth in this Summary of Lease Terms ("SUMMARY") conflicts with the other specific provisions of this Lease contained in the Standard Lease Terms, the latter shall be deemed to control.

A. BUILDING:

The office building known as Phase 5 of the Domino's Farms Prairie House Office Complex and located at 24 Frank Lloyd Wright Drive, Ann Arbor, MI 48105.

B. PREMISES:

OFFICE/LABORATORY SQUARE FOOTAGE:

Approximately 4,592 of usable square feet of space.

Location: Office and laboratory space located between column lines 25 and 29, and A and C, on Level 2 of Phase 5. Perimeters of premises are as defined by BOMA (Building Owners & Managers Association) standards, and are as shown on Rider A-1.

Address: 24 Frank Lloyd Wright Drive
Ann Arbor, MI 48105

C. TERM:

COMMENCEMENT DATE: 1. _____, 19____
(check one) -----

XX 2. See Section 3.03

EXPIRATION DATE: Two years and eight months after Commencement Date, subject to renewal as set forth in Rider D.

D. RENT:

Months 1 and 2 The monthly rental charge will be equal to \$2.31 per square foot for utilities, or \$883.96.

Months 3-32 The monthly rental charge will be \$8,919.96. This amount is equal to \$107,039.52 annually, based upon a gross amount of \$23.31 per square foot (\$21.00 per square foot for rent plus \$2.31 per square foot for utilities).

- E. PERMITTED USES: Office and laboratory
- F. SECURITY DEPOSIT: \$8,919.96
- G. TENANT'S PROPORTIONATE SHARE: Not applicable
- H. LANDLORD'S AGENT: Domino's Farms Corporation
- I. MAILING ADDRESS: Domino's Farms Corporation
 24 Frank Lloyd Wright Drive
 P.O. Box 445
 Ann Arbor, MI 48105

RIDERS ATTACHED:
- - - - -

- RIDER A Floor Plan of Building
 Layout of Space Site Plan
- RIDER B Work Agreement
- RIDER C Rules and Regulations
- RIDER D Addendum to Lease
- RIDER E Right of First Refusal
- RIDER F Attornment
- RIDER G Hazardous Materials
- RIDER H To Be Attached at Lease Commencement:
 - Construction Documents
 - Specifications
 - Warranties and Manuals
 - List of Tenant-owned Equipment
 - Financial Compilation

STANDARD LEASE TERMS

SECTION 1

DEFINITIONS

1.01 Definitions: In addition to words and phrases defined in these

Standard Lease Terms, the words and phrases in the Summary of Lease Terms shall have the meanings set forth therein.

SECTION 2

AMENITIES AND COMMON AREA

2.01 Amenities: Tenant's lease of the Premises shall include the

nonexclusive right to the use of such building amenities as are generally made available to tenants of the Building.* The use and the availability of all such amenities shall be subject to the reasonable rules and regulations established by Landlord or the respective proprietor or operator of such amenities and subject to such prices or fees as may be established from time to time for the use of availability of any amenity. In addition, Tenant shall be entitled to unreserved parking spaces in the parking area provided for the Building, together with the nonexclusive right to use the walkways and other means of ingress and egress over the land surrounding the Building, and all other rights of ingress and egress provided for use in common by all owners and tenants of the Building.

2.02 Common Area: The term "Common Area" means that part of the Building

intended by Landlord for the common use of all tenants, including, but not limited to, lobbies, public entrances, restrooms, stairways, elevators, corridors, parking areas and walkways. Tenant, and its employees and licensees, shall have the nonexclusive right to use the Common Area with other tenants and other persons permitted by Landlord to use the same. Tenant shall not take any action which would interfere with the rights of other persons to use the Common Area.

SECTION 3

THE TERM

3.01 Term: The Term of this Lease and the payment of rent hereunder, shall

commence on the Commencement Date and shall end on the Expiration Date.

3.02 Commencement Date - Date Certain: If item C1 of the Summary of Lease

Terms is checked and a date inserted, the Commencement Date shall be such date. In that case Landlord agrees to substantially complete the improvements to the Building listed on the Work Agreement executed by Tenant and Landlord and attached as Rider B (the "Work Agreement") before the Commencement Date.

3.03 Commence Date - Substantial Completion: If item C2 of the Summary

Lease Terms is checked or if neither item C1 nor item C2 are checked, the Commencement Date shall be as set forth in this Section 3.03.

A. Notice of Substantial Completion. Landlord shall give Tenant ten (10)

business days prior written notice of the anticipated date of substantial completion of the work to be performed by Landlord in the Premises pursuant to the provisions of the Work Agreement, which is attached hereto as Rider B (the "Work Agreement") and incorporated herein.

*See Rider D

The Premises shall be deemed substantially complete when Landlord has substantially completed the work required to be performed by Landlord for Tenant as provided in the Work Agreement.

B. Delays. If there is a delay in the substantial completion of the

Premises, or any portion thereof, due to (a) any act or omission of the Tenant, its architects, space designers, agents, or employees, as set forth in the Work Agreement including, without limitation, delays due to changes in the "Work" (as defined in the Work Agreement), or any other work to be done by the Landlord, or delays in submission of information, approving working drawings or estimates or giving authorizations or approvals, (b) any additional time for completion of such Work which may be required because of the inclusion in the Work of any work which may hereinafter be referred to in this Lease or the Work Agreement as "Additional Work" or (c) the noncompletion by the Landlord of any Work, whether in connection with the layout or finish of the Premises or otherwise, which the Landlord is not required to do by the terms hereof until after the Commencement Date; then, the Premises, or such portion, shall be deemed substantially complete and available for occupancy on the date when the Premises or such portion would have been available but for such delay, even though the Work or Additional Work to be done by Landlord has not been commenced or completed. Any reasonable and necessary additional cost to Landlord to complete the Premises occasioned by such delay shall be paid as additional rent upon demand. For the purposes of the preceding sentence, "additional cost to Landlord" shall mean the total cost incurred in excess of the aggregate cost which the Landlord would have incurred to complete the Premises if there had been no such delay. With respect to delays occasioned by the inclusion of "Additional Work" referred to in (b) above, Landlord shall advise Tenant in writing of the approximate number of days the Work will delay the substantial completion of the Premises.

C. Termination. In the event the Premises shall not have been

substantially completed by Landlord on or prior to three months after the date of this Lease, as such date may be extended by reason of strikes, lockout, civil commotion, warlike operation, invasion, rebellion, hostilities, governmental regulations or controls, inability to obtain labor or materials despite reasonable diligence, Acts of God, or other similar causes beyond Landlord's control, then and in that event either Landlord or Tenant shall be entitled to cancel this Lease by written notice to the other and upon such cancellation, neither party shall have any further liability to the other hereunder.

3.04 Taking of Possession: The taking of possession of the Premises shall be

deemed an acceptance of the same by Tenant, and shall be deemed in any event substantial completion by Landlord of all of the improvements listed on the Work Agreement. For the purposes of this Section, the work to be done by Landlord shall be deemed substantially complete even though minor details or adjustments which shall not materially interfere with Tenant's use and occupancy of the Premises may not then have been completed, but which work Landlord agrees will thereafter be promptly completed.

3.05 Waivers: Tenant expressly waives any right to rescind this Lease and

further expressly waives the right to recover any damages, direct or indirect, which may result from Landlord's failure to deliver possession of the Premises on the Commencement

Date. The Commencement Date shall not be postponed or delayed by reason of or arising out of delays occasioned by Tenant.

3.06 Confirmation of Lease Term: Promptly after the Commencement Date,

Landlord and Tenant will execute an agreement in recordable form, hereafter referred to as the "Commencement Date Agreement", stating, among other things, the Commencement Date and Expiration Date of the Term of this Lease. Tenant's failure or refusal to sign the same shall in no event affect Landlord's designation of the Commencement Date.

SECTION 4

THE BASE RENT

4.01 Base Annual Rental: Tenant agrees to pay to Landlord the Base Annual

Rental for the original Term of this Lease without right of set-off or abatement (except as specifically provided in Section 9 or 11).

4.02 Base Monthly Rental: The Base Annual Rental shall be payable in monthly

installments equal to the Base Monthly Rental, in advance, without any set-offs or deductions (except as specifically provided in Section 9 or 11), on the first day of each month (the "Rent Day") during the Term of this Lease at the address shown in Paragraph I of the Summary, or at such other place as Landlord from time to time may designate in writing. In the event the Commencement Date is other than the first day of a calendar month, the rental for the first and last partial months shall be prorated based on the actual number of days of such months included within the Lease Term and based upon the amount of the Base Monthly Rental.

SECTION 5

LATE CHARGES AND INTEREST

5.01 Late Charges: Any rent or other sums payable by Tenant to Landlord

under this Lease which are not paid by Tenant and received and accepted by Landlord within seven (7) days after they are due will be subject to a onetime late charge of five percent (5%) of the amount due. Such late charges will be due and payable as additional rent on or before the next Rent Day.

5.02 Interest: Any rent, late charges or other sums, if any, payable by

Tenant to Landlord under this Lease not paid within thirty (30) days after the same are due will bear interest at a per annum rate of eleven (11%) percent; provided however, if such rate exceeds the maximum rate of interest permitted by law under such encumbrances, then such rate shall be reduced to the maximum permissible rate. Such interest will be due and payable as additional rent on or before the next Rent Day, and will accrue from the date that such rent, late charges or other sums are first payable under the provisions of this Lease until actually paid by Tenant.

5.03 Default: Any default in the payment of rent, late charges or other sums

will not be considered cured unless and until the late charges and interest due hereunder are paid by Tenant to Landlord. If Tenant defaults in paying such late charges and/or interest, Landlord will have the same remedies as on default in the payment of rent. The obligation hereunder to pay late charges and interest exists in addition to, and not in the place of, the other default provisions of this Lease.

SECTION 6

TAXES, ASSESSMENTS, UTILITIES, SERVICES

6.01 Personal Property Taxes: Tenant shall be responsible for and pay all

personal property taxes assessed against Tenant's fixtures, equipment and other
property of Tenant located on the Premises.

6.02 Taxes and Assessments:

6.03 Utilities:

A. Utilities to be Furnished: So long as Tenant is not in default

under the terms of this Lease, Landlord shall furnish the following
utilities ("Utilities"):

(1). Electricity

(2). Air conditioning and heat during the appropriate season, as
provided in the Rules and Regulations attached as Rider C; and

(3). Hot and cold water for lavatory purposes.

B. Tenant's Utilities Share: Tenant agrees to pay to Landlord, as

Additional Rent for the Premises, \$2.31 per square foot for utility
charges.

6.04 Telecommunications: Tenant shall arrange and pay for its own telephone

or other telecommunications services, subject to Landlord's prior written
approval of the means of installation of such service(s).

SECTION 7

USE OF PREMISES

7.01 Permitted Uses: The Premises will be used and occupied by Tenant for

the Permitted Uses and for no other purpose without prior written consent of
Landlord. Tenant agrees that it will not use or permit any person to use the
Premises or any part thereof for any use or purposes in violation of the laws of
the United States, the laws, ordinances or other regulations of the State and
municipality in which the Premises are located, or of any other lawful
authorities. During the Term or any extension, Tenant will keep the Premises and
every part thereof in a clean and wholesome condition and will comply with all
lawful health and police regulations and with the Rules and Regulations attached
as Rider C.

7.02 Rules and Regulations: The Landlord may, from time to time, establish

reasonable rules and regulations ("Rules and Regulations") for use of the
Premises, the Building and the Common Areas by Tenant and all other persons.
Those Rules and Regulations in effect on the date of this Lease are attached as
Rider C. All such rules and regulations may be amended or replaced, at
Landlord's option, upon written notice to Tenant (sent by mail or otherwise
delivered to the Premises). All such amendments or replacements shall be deemed
to automatically amend and replace those Rules and Regulations set forth in
Rider C.

SECTION 8

INSURANCE

8.01 Liability Insurance: Tenant shall obtain, at its own expense,

comprehensive general liability insurance coverage, including blanket
contractual coverage, against claims for or arising out of bodily injury, death
or property damage occurring in, on or about the Premises, which policy or
policies shall name Landlord as an additional insured. The policy may be either
a dual limit policy in the amounts of \$1,000,000 per person and \$1,000,000 per
occurrence for bodily injury and \$1,000,000 per occurrence for property damage
or a single limit policy in the amount of \$1,000,000. Landlord may require that
the limits of such insurance be increased in reasonably appropriate amounts as

may be determined by Landlord or any mortgagee of the Building; provided, however, that the amount of coverage will not be increased more frequently than at one (1) year intervals. Such policy shall be issued by an insurance company acceptable to Landlord. The policy procured by Tenant under this Subsection 8.01 must provide for at least thirty (30) days' written notice to Landlord of any cancellation. On or before the Commencement Date, Tenant shall deliver to Landlord, at Landlord's option, a certificate of insurance or a certified copy of the original policy, together with receipts evidencing payment of the premiums therefor. Tenant will deliver certificates of renewal for such policies to Landlord at least thirty (30) days prior to the expiration dates thereof. The insurance provided by Tenant under this Subsection 8.01 may be in the form of a blanket insurance policy covering other properties as well as the Premises; provided, however, that Tenant must furnish Landlord with a written statement from the insurer(s) under such policy or policies which statement shall (i) specify the policy limits of the policy or policies, (ii) state that the Premises and this Lease are covered by such policy or policies and (iii) state the amount of total insurance allocated to the Premises; provided, further, that any such policy or policies of blanket insurance must, as to the Premises, otherwise comply as to insurance amounts, endorsements, notice of cancellation and coverage with the other provisions of this Subsection 8.01.

8.02 Insurance for Leasehold Improvements: Tenant shall obtain, at its

own expense, a policy to insure the leasehold improvements to be made to the Premises and any other fixtures or equipment of Tenant which will remain the property of Landlord under Section 18 of this Lease. The policy shall name Landlord as an additional insured for full replacement cost against loss by fire, with standard extended risk coverage, vandalism, malicious mischief, sprinkler leakage and all other risk perils.

8.03 Replacement Cost: Tenant may, at his or her option, maintain

insurance for full replacement cost of property of Tenant located in or about the Premises. Landlord shall not be responsible for any damage or loss to property of the tenant located in or about the premises.

DAMAGE

9.01 Damage: If the Premises are damaged or destroyed in whole or in part

by any fire or other casualty during the Term hereof, Landlord, to the extent insurance proceeds are available to Landlord, will repair and restore the same to good tenantable condition with reasonable dispatch, and that the rent herein provided for shall abate entirely in case the entire Premises are untenable and pro rata on an equitable basis for the portion rendered untenable,

in case a part only is untenable, until the same shall be restored to a tenantable condition. The foregoing shall be subject to all of the following: (i) if Tenant shall fail to adjust its own insurance or to remove its damaged goods, wares, equipment or property within a reasonable time, and as a result thereof the repairing and restoration is delayed, there shall be no abatement of rental during the period of such resulting delay; (ii) that there shall be no abatement of rental if such fire or other cause damaging or destroying the Premises shall result from the negligence or willful act of Tenant, its agents, servants, visitors, licensees, invitees or employees; (iii) that if Tenant shall use any part of the Building other than the Premises for storage, during the period of repair, a reasonable charge shall be made therefor against Tenant; (iv) that in case the Premises or the Building shall be destroyed to the extent of more than one-half (1/2) of the value thereof, Landlord may at its option terminate this Lease

forthwith by a written notice to Tenant stating the date upon which this Lease will terminate.

SECTION 10

MAINTENANCE AND REPAIRS

10.01 Maintenance and Repairs: Landlord will maintain, repair and keep

all structural, electrical, mechanical and plumbing systems of the Building (other than such systems installed by Tenant) and any other improvements on the land which serve the entire Building, including the parking lot, at all times, in good appearance and repair except for reasonable and normal wear and tear. Landlord will also maintain the grounds, sidewalks, driveways and parking areas. Landlord assumes the responsibility for the operation, security, management, maintenance and repair of the Common Area.

10.02 Cost of Repairs. From and after the date Tenant takes possession

of the Premises, and excluding and items described in the Work Agreement as Landlord's Work and those items subject to the preceding Section 10.01, any repairs, additions or alterations to the Building including any of its systems (e.g., plumbing, electrical, mechanical) structural or nonstructural, or to the Premises, which are required by any law, statute, ordinance, rule, regulation or governmental authority or insurance carrier, including, without limitation, OSHA, arising out of Tenant's use or occupancy of the Premises, will be made by Landlord at Tenant's expense including, without limitation, those which require the making of any structural, unforeseen or extraordinary changes. The foregoing shall not apply to any such repairs that are required because of Landlord's use of the Building generally as an office building. Tenant agrees to pay the total costs incurred by Landlord for repairs made under this Subsection 10.02 within thirty (30) days after the delivery of an invoice for same. All amounts payable under this Section 10.02 will be additional rental and failure by Tenant to pay them when due will be a default under this Lease and, in addition to any other remedies provided in this Lease upon default, will result in the assessment of late charges and interest as set forth in Section 5.

10.03 Maintenance: Tenant agrees at its own expense to maintain the Premises

and all improvements thereto, including any improvements made by Tenant, at all times in good appearance and repair except for reasonable and normal wear and tear.

10.04 Janitorial Services: Landlord will provide janitorial services to the

Premises. Tenant is responsible for the removal of any and all hazardous materials, to be handled in accordance with Rider G of this lease.

SECTION 11

INTERRUPTION OF SERVICES OR UTILITIES

11.01 Interruption of Utilities: Interruption or curtailment of any Utility

for any reason or interruption or curtailment of any service maintained in the Building, if caused by strikes, mechanical difficulties, or any causes or acts beyond Landlord's control, whether similar or dissimilar to those enumerated, shall not entitle Tenant to any claim against Landlord or to any abatement in rent, nor shall the same constitute constructive or partial eviction, unless Landlord fails to take such measures as may be reasonable in the circumstances to restore the service or Utility without undue delay. In the event that the Tenant would elect to bring in portable generators or other similar equipment, Landlord will cooperate with installation of If the Premises are rendered untenable in whole or in part for a period of over three (3) full business days, by the making of repairs, replacements or additions, other than those made at Tenant's request or caused by misuse or neglect by Tenant or Tenant's agents, servants,

visitors, invitees, licensees or employees or those required by any governmental authority due to the nature of Tenant's use of the Premises, there shall be a proportionate abatement of rent during the period of such untenability.

SECTION 12

PAYMENT FOR SERVICES RENDERED BY LANDLORD

12.01 Payment for Services: If Landlord at any time (i) does any work

or performs any service in connection with the Premises, or (ii) supplies any materials to the Premises, and the cost of such services, work or materials is Tenant's responsibility under the provisions of this Lease, Landlord will invoice Tenant for the reasonable cost, payable on the next Rent Day or within ten (10) days after delivery of the invoice, whichever is later. This Section 12.01 will apply to any such work, service or materials, whether furnished at Tenant's request or on its behalf and whether furnished or caused to be furnished by Landlord, its agents, employees or contractors. All amounts payable under this Section 12.01 will be additional rental and failure by Tenant to pay them when due will be a default under this Lease and, in addition to any other remedies provided in this Lease upon default, will result in the assessment of late charges and interest under Section 5. This Section 12.01 shall not apply to Total Tax Assessments as defined in Section 6 nor to Utility Expenses as defined in Section 19.01.

SECTION 13

ALTERATIONS

13.01 Alterations: Landlord will make any structural alterations, additions,

or improvements, exterior or interior, to the Premises including alterations made at the request of Tenant and which have been approved by Landlord. Landlord's consent for any interior improvements will not be unreasonably withheld; provided that Landlord's consent to exterior improvements may be withheld in Landlord's sole and absolute discretion. Any modification of the Premises other than as specifically set forth in the Work Agreement as Landlord's expense will be at the expense of Tenant.

13.02 Restoration of Premises: All alterations, additions and improvements

made by either of the parties hereto on the Premises will be the property of Landlord and will remain on and be surrendered with the Premises at the termination of this Lease provided, however, that Tenant shall remove, at Landlord's option, all alterations, additions or improvements to the Premises made for Tenant and Tenant shall pay to Landlord to restore the Premises to the conditions stated in the Work Agreement, (Rider B), if notified in writing by Landlord.

SECTION 14

LIENS

14.01 Liens: After the Commencement Date, Tenant will keep the Building,

Premises and surrounding land free of liens of any sort attributable to the acts of Tenant and will hold Landlord harmless from any liens which may be placed on the Building, Premises or surrounding land except those attributable to the acts of Landlord or other tenants.

SECTION 15

EMINENT DOMAIN

15.01 Eminent Domain: If the Premises or any part thereof are taken by any

public authority under power of eminent domain, or by private

sale in lieu of eminent domain, this Lease will terminate as of the date of such taking or sale, and Tenant may receive a pro rata refund of any rents, deposits or other sums paid in advance. Landlord reserves the right, however, to elect to demolish, rebuild or reconstruct the Building if any portion of the Building is so taken, and if Landlord so elects, whether or not the Premises are involved in the taking, this Lease may be terminated by Landlord on 90 days written notice to Tenant and the rent will be adjusted to the date Tenant's possession of the Premises is terminated.

15.02 Condemnation Award: The whole of any award or compensation for any

portion of the Premises taken, condemned or conveyed in lieu of taking or condemnation shall be solely the property of and payable to Landlord. Nothing herein contained shall be deemed to preclude Tenant from seeking at its own cost and expense, an award from the condemning authority for loss of its business, the value of any trade fixtures or other personal property of Tenant in the Premises or moving expenses, provided that the award for such claim or claims shall not be in diminution of the award made to Landlord.

SECTION 16

ASSIGNMENT OR SUBLETTING

16.01 Assignment or Subletting: Tenant agrees not to assign or in any manner

transfer this Lease or any interest in this Lease without the previous written consent of Landlord, and not to sublet the Premises or any part of the Premises or allow anyone to use or to come in, with, through or under it without like consent, which consent, in each case, will not be unreasonably withheld. Upon any attempted unconsented to assignment or sublease, Landlord shall have the right to terminate this Lease. One such consent will not be deemed a consent to any subsequent assignment, subletting, occupation or use by any other person. Any sublease on the Premises executed by Tenant and a third party must terminate when the Term of this Lease expires. The acceptance of rent from an assignee, subtenant or occupant will not constitute a release of Tenant from the further performance of the obligations of Tenant contained in this Lease. In the event of any such assignment or sublease of all or any portion of the Premises where the rental or other consideration reserved in the sublease or by the assignment exceeds the rental or pro rata portion of the rental, as the case may be, for such space reserved in this Lease, Tenant agrees to pay Landlord monthly, as additional rent, on the Rent Day, the excess of the rental net of recovery of Tenant-paid improvement costs or other consideration reserved in the sublease or assignment over the rental reserved in this Lease applicable to the subleased/assigned space.

SECTION 17

INSPECTION AND ALTERATION OF PUBLIC PORTIONS

17.01 Inspection: Tenant agrees to permit Landlord and the authorized

representatives of Landlord to enter the Premises at all times for the purpose of inspecting the same, subject to confidentiality agreements if requested by Tenant.

17.02 Right to Enter and Alter Premises: Upon notice from Landlord, Tenant

shall permit Landlord to erect, use and maintain pipes and conduits in and through the Premises. Landlord or its agents or designees shall have the right to enter the Premises, for the purpose of making such repairs or alterations as Landlord shall be required or shall have the right to make by the provisions of this Lease and, subject to the foregoing, shall also have the right to enter the Premises for the purpose of exhibiting them to prospective purchasers or lessees of the Building or to prospective mortgages or to prospective assignees

of any such mortgages. Landlord shall be allowed to take all material into and upon the Premises that may be required for the repairs or alterations above mentioned without the same constituting an eviction of Tenant in whole or in part, and the rent reserved shall in no wise abate, except as otherwise provided in this Lease, while said repairs or alterations are being made.

17.03 Right to Show Premises: During the three (3) months prior to the

expiration of the Term of this Lease, Landlord may exhibit the Premises to prospective tenants during normal business hours.

17.04 Right to Alter Public Portions of Buildings: Landlord shall have the

right at any time without thereby creating an actual or constructive eviction or incurring any liability to Tenant therefore, to change the arrangement or location of entrances, passageways, doors, and doorways, corridors, stairs, toilets and other like public service portions of the Building. Tenant shall at all times be provided with an entrance to the Premises.

17.05 Name of Building: Landlord shall have the right at any time to name the

Building for any person(s) or tenant(s) and to change any and all such names at any time thereafter.

SECTION 18

FIXTURES AND EQUIPMENT

18.01 Landlord's Property: All fixtures and equipment paid for by Landlord

and all improvements, fixtures and equipment which may be paid for and placed on the Premises by Tenant from time to time but which are so incorporated and affixed to the Premises that their removal would involve damage or structural change to the Premises, will be and remain the property of Landlord, excepting those items specifically listed in the Work Agreement. Tenant will be responsible for the cost of repair due to removal of specified items.

18.02 Tenant's Property: All improvements, furnishings, equipment and

fixtures other than those specified in Subsection 18.01, which are paid for and placed on the Premises by Tenant from time to time will remain the property of Tenant and be removed by Tenant at the expiration of the Lease.

SECTION 19

UTILITY EXPENSES

19.01 Definitions:

(i) "Utility Expenses" means any and all charges for heat, air conditioning, ventilating, and steam, gas, electricity, water or other fuels made against the Entire Premises and all labor services and materials related thereto which are delivered or provided to or with respect to the Entire Premises.

(ii) "Tenant's Proportionate Share of Utilities" means Utility Expenses multiplied by the percentage set forth in Paragraph G of the Summary.

(iii) "Utility Expense Statements" means written statements, certified by Landlord, showing the amounts of Utility Expenses for each calendar year which includes any portion of the Term or any renewal or extension thereof.

19.02 Utility Expenses: Tenant will pay to Landlord as Additional Rent \$2.31

per square foot for Utility Expenses.

Payments due pursuant to this Section will be due at the time specified in Section 6.03.

19.03 Utility Expense Statement: Any Utility Expense Statement sent to

Tenant shall be conclusively binding upon Tenant unless, within thirty (30) days after such statement is sent, Tenant shall send a written notice to Landlord objecting to such statement and specifying the respects in which such statement is claimed to be incorrect. If such notice is sent, either party may refer the decision of the issues raised by such notice to Arthur Andersen & Co., or any successor firm, or other reputable independent firm of certified public accountants selected by Landlord, and the decision of such accountants shall be conclusively binding upon the parties. The fees and expenses involved in such decision shall be borne by the unsuccessful party (and if both parties are partially unsuccessful, the accountants shall apportion such fees and expenses between the parties, based on the degree of success of each party).

SECTION 20

NOTICES OR DEMANDS

20.01 Notices or Demands. All bills, notices, statements, communications

or demands (collectively, "notices or demands") upon Landlord or Tenant desired or required to be given under any of the provisions hereof must be in writing. Any such notices or demands from Landlord to Tenant will be deemed to have been duly and sufficiently given if a copy thereof has been personally delivered or mailed by United States mail in an envelope properly stamped and addressed to Tenant at the address of the Premises or at such other address as Tenant may have last furnished in writing to Landlord for such purpose. Any such notices or demands from Tenant to Landlord will be deemed to have been duly and sufficiently given if personally delivered to Landlord or mailed by United States mail in an envelope properly stamped and addressed to Landlord at the address set forth in this Lease. The effective date of such notice or demand will be deemed to be the time when personally delivered or mailed as herein provided.

SECTION 21

BREACH; INSOLVENCY; RE-ENTRY

21.01 Default: If any rental payable by Tenant to Landlord remains unpaid

for more than seven (7) days after written notice to Tenant of nonpayment, or if Tenant violates or defaults in the performance of any of its obligations in this Lease and the

violation or default continues for a period of ten (10) days after written notice, then Landlord may (but will not be required to) declare this Lease forfeited and the Term ended, or re-enter the Premises, or may exercise all other remedies available under Michigan law. Landlord will not be liable for damages to person or property by reason of any legitimate re-entry or forfeiture, and Landlord will be aided and assisted by Tenant, its agents, representatives and employees. Tenant, by the execution of this Lease, waives notice of re-entry by Landlord. In the event of re-entry by Landlord without declaration of forfeiture, the liability of Tenant for the rent provided herein will not be relinquished or extinguished for the balance of the Term, and any rentals prepaid may be retained by Landlord and applied against the costs of re-entry, or the costs of enforcement of this Lease, including the cost of any proceeding under the Federal Bankruptcy Code.

21.02 Bankruptcy: If Tenant is adjudged bankrupt or insolvent, files or

consents to the filing of a petition in bankruptcy under Federal or State law, applies for or consents to the appointment of a receiver for all or substantially all of its assets, or makes a general assignment for the benefit of its creditors, then Tenant shall be in default under this Lease and, to the extent from time to time permitted by applicable law, including but not limited to the Federal Bankruptcy Code, Landlord shall be entitled to exercise all remedies set forth in Section 21.01. In a reorganization under Chapter 11 of the Federal Bankruptcy Code, the debtor or trustee must assume this Lease or assign it within sixty (60) days from the filing of the proceeding, or he shall be deemed to have rejected and terminated this Lease. Tenant acknowledges that its selection to be the tenant hereunder was premised in material part on Landlord's determination of Tenant's creditworthiness and the character of its occupancy and use of the Premises would be compatible with the nature of the Premises and other adjacent properties and tenants of Landlord. Therefore, if Tenant, as debtor, or its trustee elects to assume this Lease, in addition to complying with all other requirements for assumption under the Federal Bankruptcy Code, then Tenant, as debtor, or its trustee or assignee, as the case may be, must also provide the adequate assurance of future performance, including but not limited to a deposit, the amount of which shall be reasonably determined based on the duration of time remaining in the Term, the physical condition of the Premises at the time the proceeding was filed, and such damages as may be reasonably anticipated after reinstatement of the Lease.

21.03 Re-Leasing of Premises: In the event of declaration of forfeiture

at or after the time of re-entry, Landlord may re-lease the Premises or any portion(s) of the Premises for a term or terms and at a rent which may be less than or exceed the balance of the term of and the rent reserved under this Lease. In such event Tenant will pay Landlord as liquidated damages for Tenant's default any deficiency between the total rent reserved and the net amount, if any, of the rents collected on account of the lease or leases of the Premises which otherwise would have constituted the balance of the term of this Lease. In computing such liquidated damages, there will be added to the deficiency reasonable expenses which Landlord may incur in connection with re-leasing, such as legal expenses, attorney's fees, brokerage fees and expenses, advertising and for keeping the Premises in good order or for preparing the Premises for re-leasing. Any such liquidated damages will be paid in monthly installments by Tenant on the Rent Day and any such suit brought to collect the deficiency for any month will not prejudice Landlord's right to collect the deficiency for any subsequent month by a similar proceeding. In lieu of the foregoing computation of liquidated damages, Landlord may elect, at its sole option, to receive

liquidated damages in one payment equal to any deficiency between the total rent reserved hereunder and the fair and reasonable rental of the Premises, both discounted at five (5%) percent per annum to present value at the time of declaration of forfeiture.

21.04 Failure to Re-Lease Premises: Whether or not forfeiture has been

declared, Landlord will attempt to re-lease the Premises, however, Landlord will not be responsible in any way for failure to re-lease the Premises, or in the event that the Premises are re-leased, for failure to collect the rent under such re-leasing. The failure of Landlord to re-lease all or any part of the Premises will not release or affect Tenant's liability for rent or damages.

SECTION 22

SURRENDER OF PREMISES ON TERMINATION

22.01 Condition of Premises Upon Termination: At the expiration (or earlier

termination) of the Term, Tenant will surrender the Premises broom clean and in as good condition and repair as they were at the time Tenant took possession, reasonable wear and tear excepted, and promptly upon surrender will deliver all keys and building security cards for the Premises to Landlord at the place then fixed for payment of rent. All reasonable costs and expenses incurred by Landlord in connection with repairing or restoring the Premises to the condition called for herein, together with the costs, if any, of removing from the Premises any property of Tenant left therein, together with liquidated damages in an amount equal to the amount of minimum net rental plus all other charges which would have been payable by Tenant under this Lease if the term of this Lease had been extended for the period of time reasonably required for Landlord to repair or restore the Premises to the condition called for herein, shall be invoiced to Tenant and shall be payable within ten (10) days of the date of such invoice.

22.02 Storage of Tenant's Property: If Tenant fails to remove all its

property (or property of others in its possession) from the Premises on termination of this Lease (for any cause), Landlord at its option may remove the property in any manner that it chooses and may store the property without liability to Tenant for loss, whether based on contract, tort or otherwise. Tenant agrees to pay Landlord on demand any and all expenses incurred in such removal, including court costs, attorneys' fees and storage charges on the property for any length of time it is in Landlord's possession. Tenant will indemnify and hold Landlord harmless from any claim by third parties with respect to property owned or claimed by them, left in the Premises by Tenant, and removed by Landlord pursuant to this paragraph. Under no circumstances will Landlord be obligated to retain any property left on the Premises or in Landlord's possession longer than two (2) months after termination of this Lease (for any cause) and Landlord may after two (2) months dispose of the property in any manner it deems appropriate, including public or private sale or by destruction, discard or abandonment and the proceeds of any such sale will be applied against any sums due Landlord under this Lease.

SECTION 23

PERFORMANCE BY LANDLORD OF THE COVENANTS OF TENANT

23.01 Tenant's Failure to Perform: If Tenant fails to pay any sum of money,

other than rental, required to be paid hereunder or fails to perform any act on its part to be performed hereunder and such failure shall continue for a period of ten (10) days (or a reasonable period of less than ten (10) days when life, person or property is in jeopardy), Landlord may (but shall

not be required to), and without waiving or releasing Tenant from any of Tenant's obligations, make any such payment or perform any such other act. All sums paid by Landlord and all reasonable incidental costs, including without limitation the cost of repair, maintenance or restoration of the Premises if so performed by Landlord hereunder, shall be deemed additional rental and, together with interest thereon at the rate set forth in Section 5.02 from the date of payment by Landlord until the date of repayment by Tenant to Landlord, shall be payable to Landlord within fifteen (15) days after receipt of invoice by Tenant. On default in such payment, Landlord shall have the same remedies as on default in payment of rent. The rights and remedies granted to Landlord under this Section 23 shall be in addition to and not in lieu of all other remedies, if any, available to Landlord under this Lease or otherwise, and nothing herein contained shall be construed to limit such other remedies of Landlord with respect to any matters covered herein.

SECTION 24

SUBORDINATION; ESTOPPEL CERTIFICATES

24.01 Subordination: Tenant agrees, that at Landlord's option, this Lease may

be either subordinate or paramount to any construction loans, mortgages, trust deeds and ground or underlying leases now or hereafter affecting the Premises and to any and all advances to be made thereunder, and to the interest and charge thereon, and all renewals, replacements and extensions thereon, provided the mortgagee, lessor or trustee named in any such mortgages, trust deeds or leases agrees to recognize the lease of Tenant in the event of foreclosure or other enforcement of such instruments (and, if requested by Tenant, shall enter into a non-disturbance agreement with Tenant) if Tenant is not in default. This section shall be self-operative and no further instrument shall be required. However, Tenant will execute promptly any instrument or certificate that Landlord may reasonably request confirm such subordination or superior status, subject to Tenant's receipt of a non-disturbance agreement, if so requested, and hereby irrevocably appoints Landlord as Tenant's attorney-in-fact to execute such instrument or certificate on its behalf.

SECTION 25

SUBSTITUTE SPACE

SECTION 26

QUIET ENJOYMENT

26.01 Quiet Enjoyment: Landlord agrees that at all times when Tenant

is not in default under the provisions and during the Term of this Lease, Tenant's quiet and peaceable enjoyment of the Premises will not be disturbed or interfered with by Landlord or any person claiming by, through, or under Landlord.

SECTION 27

HOLDING OVER

27.01 Holding Over: If Tenant remains in possession of the Premises after

expiration of this Lease without executing a new lease, it will be deemed to be occupying the Premises as a tenant from month-to-month, subject to all the provisions of this Lease to the extent that they can be applicable to a month-to-month tenancy, except that the minimum rental for each month will be one hundred percent (100%) of the Base Monthly Rental.

SECTION 28

REMEDIES NOT EXCLUSIVE; WAIVER

28.01 Remedies: Each and every of the rights, remedies and benefits provided

by this Lease are cumulative and are not exclusive of any other of said rights, remedies and benefits, or of any other rights, remedies and benefits allowed by law.

28.02 Waiver of Covenant: One or more waivers of any covenant or condition by

Landlord will not be construed as a waiver of a further or subsequent breach of the same covenant or condition, and the consent or approval by Landlord to or of any act by Tenant requiring Landlord's consent or approval will not be deemed to waive or render unnecessary Landlord's consent to or approval of any subsequent similar act by Tenant.

SECTION 29

WAIVER OF SUBROGATION

29.01 Waiver of Subrogation: Landlord and Tenant shall obtain permission

from each insurer to, and to the extent so permitted, hereby waive any and all right of recovery against each other for any loss or damage caused by fire or any of the risks covered by standard fire and extended coverage, vandalism and malicious mischief insurance policies.

SECTION 30

INDEMNIFICATION

30.01 Indemnification: Tenant at its expense will defend, indemnify and save

Landlord and its licensees, servants, agents, employees and contractors, harmless from any claim or condition of the Premises, the use or misuse thereof by Tenant or any other person, the acts or omissions of Tenant, its clients, customers, invitees, licensees, servants, agents, employees or contractors, the failure of Tenant to comply with any provision of this Lease, or any other event occurring on the Premises, whatever the cause; provided, however, that nothing herein shall be construed to require Tenant to indemnify Landlord or its licensees, servants, agents, employees, and contractors against Landlord's or its licensees' servants' agents', employees' and contractors' own acts, omissions or neglect.

SECTION 31

ASSIGNMENT BY LANDLORD

31.01 Assignment by Landlord: The term "Landlord" as used in this Lease so

far as covenants, agreements, stipulations or obligations on the part of the Landlord are concerned is limited to mean and include only the owner or owners of fee title (or of a ground leasehold interest or land contract vendee's interest) to the Premises at the time in question, and in the event of any transfer or transfers of the title to such fee the Landlord herein named (and in case of any subsequent transfers or conveyances the then grantor) will automatically be freed and relieved from and after the date of such transfer or conveyance of all liability for the performance of any covenants or obligations on the part of the Landlord contained in this Lease thereafter to be performed.

31.02 Landlord's Default: If Landlord fails to perform any provision of this

Lease upon Landlord's part to be performed, and if as a consequence of such default Tenant recovers a money judgment against Landlord, such judgment may be satisfied only out of the proceeds of sale received upon execution of such judgment and levied thereon against the right, title and interest of Landlord in the Premises and out of rents or other income from such property receivable by Landlord and Landlord shall not be personally liable for any deficiency.

SECTION 32

SECURITY DEPOSIT

32.01 Security Deposit: Landlord hereby acknowledges the receipt of the

Security Deposit. If Tenant defaults in any of the provisions of this Lease, Landlord may use, apply or retain all or any part of the Security Deposit for the payment of rents and/or other charges which are the obligation of Tenant under this Lease in default or for any other sum which Landlord may expend by reasons of Tenant's default, including any damages or deficiency in the releasing of the Premises. If Tenant fully complies with all the provisions of this Lease, the Security Deposit, or balance thereof, will be returned to Tenant without interest after (i) the termination of this Lease, (ii) the removal of Tenant, and (iii) the surrender of possession of the Premises to Landlord. Unless Landlord is shown evidence satisfactory to it that the right to receive the Security Deposit has been assigned, Landlord may return the Security Deposit to the original Tenant regardless of one or more assignments of the Lease itself.

SECTION 33

MOVEMENT OF TENANT'S PROPERTY

33.01 Moving Tenant's Property: All activities of Tenant in connection with

(a) Tenant's move into the Premises at the commencement of this Lease, (b) the movement of equipment, furniture or other bulky items into, out of or within the Premises during the Term, or (c) Tenant's move out of the Premises at any time (whether or not on the termination of this Lease) will be subject to the following:

- A. Designated Access. All furniture, equipment and all other

items of personal property being moved or transferred will enter and leave the Building solely through and by way of such area or entrance as may be designated from time to time by Landlord for such purposes;
- B. Tenant Responsible. Tenant will be responsible for the active

supervision (on-site) of all workmen and others

performing the move, and will indemnify and hold harmless Landlord against and from all liability for damage to property (whether belonging to landlord, other tenants or any other person) and injuries to persons in connection with the move and the actions, or failure to act, or by those performing the move;

C. Damage. Tenant will be responsible for any damage to the Building,

the Common Areas, the Premises, or the premises and property of other tenants, caused by or incurred in connection with the move or the activities connected therewith. Landlord will perform such inspection(s) as Landlord in its sole discretion determines to be appropriate, and will invoice Tenant for the costs of repair of all such damage or the replacement, if necessary, of damaged items. All determinations of the extent of damage and the costs of repair or replacement will be made by Landlord in the exercise of its reasonable discretion. The invoiced sums will constitute amounts included within and payable under Section 12, above.

SECTION 34

NON-TERMINABILITY, COMPLIANCE WITH LAWS, COSTS, SEVERABILITY

34.01 Non-Terminability: Except as otherwise specifically provided in

this Lease, this Lease shall neither terminate nor shall Tenant have any right to terminate this Lease or to be released, relieved or discharged from any obligations or liabilities hereunder for any reason whatsoever, including, without limitation:

A. Damage. Any damage to, or destruction of, the Premises or any

portion thereof.

B. Condemnation. Any condemnation, confiscation, requisition or

other taking or sale of the possession, use, occupancy or title to the Premises or any portion thereof;

C. Omission. Any action, omission or breach on the part of Landlord

under this Lease or under any other agreement at the time existing between Landlord and Tenant.

D. Other Claims. Any claim as a result of any other business

dealings of Landlord and Tenant.

E. Impossibility. The impossibility or illegality of performance by

Landlord or Tenant or both.

F. Force Majeure. Force majeure.

G. Governmental Action. Any action or threatened or pending action

of any court, administrative agency or other governmental authority.

Except as otherwise specifically provided in this Lease, Tenant shall remain obligated under this Lease in accordance with its terms, and will not take any action to terminate, rescind or avoid this Lease for any reason, notwithstanding any bankruptcy, insolvency, reorganization, composition, readjustment, liquidation, dissolution or other proceeding affecting Landlord or any assignee of Landlord or any action with respect to this Lease which may be taken by any receiver, trustee or liquidator (or other similar official) or by any court. All payments by Tenant hereunder shall be final and Tenant will not seek to recover any such payment or any part thereof for any reason. Tenant waives all rights now or hereafter conferred by statute or otherwise to

quit, terminated or surrender this Lease, or to any abatement, suspension, deferment, diminution or reduction of rent, additional rent or other amounts payable by Tenant hereunder, or for damage, loss, cost or expense suffered by Tenant, on account of any of the reasons referred to herein or otherwise.

SECTION 35

ENTIRE AGREEMENT

35.01 Entire Agreement: This Lease and the Riders attached hereto and forming

a part hereof, set forth all of the covenants, agreements, stipulations, promises, conditions and understandings between Landlord and Tenant concerning the Premises and there are no covenants, agreements, stipulations, promises, conditions or understandings, either oral or written, between them concerning the Premises other than herein set forth.

SECTION 36

RECORDING

36.01 Recording: This Lease shall not be recorded by Tenant nor shall Tenant

file or record a memorandum of lease or affidavit of claim with respect to this Lease or the Premises. At Landlord's option, Landlord may record this Lease. Upon Landlord's request, Tenant shall execute and deliver to Landlord a memorandum of lease or affidavit of claim for recording by Landlord.

SECTION 37

GENERAL

37.01 General Terms: Many references in this Lease to persons, entities and

items have been generalized for ease of reading. Therefore, reference to a single person, entity or item will also mean more than one person, entity or thing whenever such usage is appropriate. Similarly, pronouns of any gender should be considered interchangeable with pronouns of other genders.

37.02 Joint and Several: All agreements and obligations of Tenant and

Landlord under this Lease are joint and several in nature.

37.03 Captions: Captions to sections and paragraphs are provided solely for

the sake of convenience and shall have no substantive effect whatsoever.

37.04 Amendments: This lease can be modified or amended only by a written

agreement signed by Landlord and Tenant.

37.05 Binding Lease: All provisions of this Lease are and will be binding on

the heirs, executors, administrators, personal representatives successors and assigns of Landlord and Tenant.

37.06 Governing Law: The laws of the State of Michigan will control in the
construction and enforcement of this Lease.

IN WITNESS WHEREOF, the parties hereto have executed this Lease as of the day and year first above written.

WITNESSES:

DOMINO'S FARMS HOLDING
LIMITED PARTNERSHIP
(a Michigan Corporation)

/s/ MARGARET T. PARKINSON

By: /s/ _____

Its: SENIOR VICE PRESIDENT

For: Landlord

AASTROM BIOSCIENCES, INC.

/s/ PATRICIA A. POWELL

By: /s/ R. DOUGLAS ARMSTRONG

Its: President/CEO

For: Tenant

RIDER A-1

FLOOR PLAN

RIDER A-2

LAYOUT OF SPACE

RIDER A-3

SITE PLAN

RIDER B

WORK AGREEMENT

The terms and conditions of this Work Agreement shall govern Landlord and Tenant's participation in the design, construction and installation of improvements to the Premises in accordance with the Final Plans (as defined below) and the terms hereof (the "Work"). Tenant acknowledges that it has had an opportunity to inspect the Premises prior to the execution and delivery of this Work Agreement. Tenant further acknowledges and agrees that all construction or improvements to the Premises to be completed at Landlord's expense have been completed and are accepted by Tenant in an "As Is" condition except for work to be performed by Landlord pursuant to the Work Agreement. All additional improvements to the Premises and services incidental or related thereto are referred to as "Work" and shall be paid for by Landlord and Tenant as set forth herein.

A. PRE-LEASE WORK

1. Preliminary Drawings. Landlord and Tenant acknowledge that they have

agreed on preliminary drawings prepared by H. Scott Diels, Architect, at Tenant's direction and containing general design and technical information for the Work to be performed on the Premises (the "Preliminary Drawings"), copies of which are attached to this Lease as Rider A-2, May 4, 1992. The Preliminary Drawings have been or will be submitted to the Architect and Engineer for preparation of the Formal Drawings (as defined below).
2. Contractor. Landlord and Tenant acknowledge that the Contractor will

be selected with the approval of Tenant and Landlord.
3. Transition of Administration. Tenant shall inform the Architect,

Engineer and Contractor that Landlord will assume responsibility for administration and coordination of the Work after execution of the Lease and that Landlord will be, and perform the obligations of the "Owner" under the Architect Agreement, the Engineer Agreement and the Construction Agreement. Tenant shall cooperate with Landlord and assist in the transition of responsibility for administration and coordination of the Work. Landlord and Tenant agree that all communications with, and instructions or directions to, the Architect, Engineer and Contractor after transition of the Work to the Landlord will go through Landlord.

B. PROJECT REPRESENTATIVES/FIELD CHANGE ORDERS

1. Landlord's Representative. Landlord's representative in connection

with administration of the Work shall be Larry McGonigal unless otherwise directed in writing by Landlord ("Landlord's Representative"). All instructions, requests, or directives from Tenant to the Landlord, Architect, Engineer or Contractor in connection with the construction of the Work will be given or communicated to Landlord's Representative who will in turn contact or notify the appropriate party.
2. Tenant's Representative. Tenant's representative in connection with

the Work shall be R. Douglas Armstrong unless otherwise directed in writing by Tenant ("Tenant's Representative"). All requests, notification, directives, inquiries or information intended for Tenant shall be given or communicated by Landlord or Landlord's Representative to Tenant's Representative. Tenant's Representative shall have access to the Work at all reasonable times for the purpose of making inspections, taking measurements and observing the Work and may inspect, copy, and discuss with Landlord's Representative or other appropriate personnel of Landlord from time to time the Work and all invoices and documentation in connection with the Work. Tenant's Representative shall be requested to attend all regularly scheduled progress meetings related to the Work.
3. Field Change Orders. Tenant's Representative shall have the right to

request Field Change Orders in writing. For purposes of this section, "Field Change Orders" shall mean: (a) a "Change Order" or "Field Work Order" (as defined in the Contractor Agreement) or similar request for changes or modifications in the Work; or (b) revisions to the Final Plans or other work-related documents or materials requested by Tenant.
4. Approval of Field Change Orders. All Field Change Orders shall be

approved in writing by both Landlord and Tenant and shall be acceptable to

Landlord and Tenant in all respects. The cost of any Field Change Order shall be an additional Work Cost. Tenant's Representative shall approve all Field Change Orders, changes or modifications to the Final Plans and any design changes to the Work. Tenant's Representative, on behalf of Tenant, and Landlord's Representative, on behalf of Landlord, will promptly respond to any requests or inquiries of Landlord or Tenant, as the case may be, including those relating to Field Change Orders, so as not to interfere with the orderly progress of the Work. Landlord shall have the right to reject any Field Change Order requested by Tenant which, individually or in the aggregate, would delay the Commencement Date of the term of this Lease in excess of fourteen (14) days, unless in conjunction therewith, Tenant agrees to pay rental for the Premises as of the date the Commencement Date would have occurred but for the completion of the Field Change Order. The Landlord's and Tenant's reasonable judgement as to whether delay may ensue as a result of Tenant requested Field Change Orders shall be conclusive.

5. Other Tenant Employee's. Officers, employees or agents of Tenant

other than Tenant's Representatives shall have access to the Work provided that Tenant notifies Landlord's Representative in advance and Tenant's Representative or his designee in writing accompanies such parties during such access. Landlord may deny access to such parties excluding Tenant's Representative (but access by Tenant's Representative shall nevertheless be subject to the delay provisions in Section 3.03 of the Lease) in the event that their presence materially hampers, interferes with or prevents Landlord, Architect, Engineer or Contractor from proceeding with the completion of the Work. Any entry on the Premises by Tenant's Representative and other officers, agents, employees, representatives, licensees or invitees of Tenant shall be at their sole risk. Tenant hereby agrees to indemnify, defend and hold Landlord harmless from and against any loss, expense, claim, demand, action or proceeding arising out of or relating to such access to the Premises other than such losses, expenses, claims, demands, actions, proceedings caused by the negligence, gross negligence or willful misconduct of Landlord or its directors, officers, employees, agents, servants, representatives, invitees or licensees other than any party performing services under the Contractor Agreement, Architect Agreement or Engineer Agreement.

6. Consultation/Cooperation. Landlord shall advise Tenant of, and

consult with Tenant regarding, all material matters relating to the Work, including, without limitation, the design, construction and engineering of the Work, as well as the services performed or to be performed by the Architect, Engineer and Contractor. Tenant shall reasonably cooperate with Landlord with respect to such consultations and shall not act or fail to act in a manner which will delay the design or construction of the Work. Landlord agrees to use reasonable efforts to cause Architect, Engineer, Contractor and all other persons working on or in connection with the Work to perform and comply with terms of this Agreement and any other applicable agreement (including, without limitation, pursuing any applicable legal recourse against such persons). If any one or more Architect, Engineer or Contractor breach their respective contracts with Landlord described herein, Landlord may, but shall not be obligated to, commence civil proceedings to obtain specific enforcement of such breached contract and/or for any other remedies or damages available to Landlord. In the event of such a breach and if Landlord fails or refuses to commence such legal proceedings against the breaching party for sixty (60) days, Tenant may commence civil proceedings, at Tenant's sole expense, for specific enforcement of the breached contract or any other remedies or damages available to Tenant, and to the extent necessary to permit and prosecute such proceedings Landlord will assign its rights under the breached contract or contracts to Tenant and reasonably cooperate with Tenant in connection therewith.

C. RETENTION OF ARCHITECT, ENGINEER AND CONTRACTOR

1. Retention of Architect

(a) Architect Agreement. Landlord shall retain the Architect to

prepare formal design drawings and working drawings and specifications (collectively the "Formal Drawings"). The Formal Drawings shall contain design, technical and engineering specifications for the Work based on the Preliminary Drawings. Landlord shall negotiate and execute, as Owner, the written agreement with the Architect governing Architect's participation in the Work (the "Architect Agreement"). All Preliminary Services performed by the Architect shall be included in and made a part of and subject to the terms and conditions of the Architect Agreement. Landlord shall provide, upon request, Tenant with a copy of the proposed Architect Agreement and

shall consult with, and include reasonable suggestions of, Tenant with respect to the terms and conditions of the Architect Agreement prior to execution thereof. Landlord shall be, and perform the obligations of, the Owner under the Architect Agreement.

(b) Formal Design and Working Drawings. Landlord shall

submit the Preliminary Drawing to the Architect for preparation of the Formal Drawings. Landlord and Tenant shall each have a period of seven (7) days after receipt of the Formal Drawings to 1) approve such drawings in writing, or 2) send written notice to the other party describing any objections to the Formal Drawings. In the event either Landlord or Tenant sends a notice of objections to the formal Drawings, Landlord and Tenant will meet within seven (7) days after such notice is sent to discuss and resolve those matters objectionable to Landlord or Tenant. Either Landlord or Tenant may request the presence of the Architect at such meeting. Landlord and Tenant agree to use their good faith efforts in negotiating and preparing revised Formal Drawings, but the Formal Drawings must be acceptable to both Landlord and Tenant in all respects. The Architect shall revise the Formal Drawings in accordance with those modifications which are approved by Landlord and Tenant at such meeting. The revised Formal Drawings shall reflect the agreed to modifications and shall be given to Tenant and Landlord for final approval. Tenant and Landlord shall give final approval of the Formal Drawings in writing within seven (7) days after receipt of satisfactory Formal Drawings which reflect the agreed to modifications (the Formal Drawings, once so approved, are referred to as "Final Plans").

(c) Landlord's Insurer. The Final Plans, once completed,

shall be sent to Factory Mutual Insurance Company, the Landlord's Insurer, ("Insurer") for review and approval. In the event that Insurer has any objections to the Final Plans, such Final Plans shall be revised by the Architect, as expeditiously as possible, in a manner satisfactory to Insurer, Landlord and Tenant.

(d) Cost of Architectural Services. Landlord and Tenant

acknowledge that Architect has agreed to perform the services under the Architectural Agreement. Landlord shall not agree to any increase in fees or authorize any additional services other than those set forth in the Architect Agreement, or any change to the Final Plans, without the prior written consent of Tenant or Tenant's Representative.

2. Retention of Engineer

(a) Engineer Agreement. Landlord shall retain the Engineer

to prepare designs and specifications with respect to mechanical engineering and technical aspects of the Formal Drawings, the Final Plans and the Work and to the connection and interfacing of the Work with existing systems or equipment of Landlord (the "Engineering Report"). Landlord shall negotiate and execute, as Owner, the written agreement with the Engineer governing the Engineer's participation in the Work (the "Engineer Agreement"). All Preliminary Services and the cost of all Preliminary Services performed by the Engineer shall be included in and be made a part hereof and subject to the terms and conditions of the Engineer Agreement. Landlord shall provide Tenant with a copy of the proposed Engineer Agreement and shall consult with Tenant, and include the reasonable suggestions of, with respect to the terms and conditions of the Engineer Agreement prior to execution thereof. Landlord shall be, and perform the obligations of, the Owner under the Engineer Agreement.

(b) Cost of Engineering Services. Landlord and Tenant

acknowledge that Engineer has agreed to perform the service under the Engineer Agreement. Landlord shall not agree to any increase in fees or authorize any additional services other than those set forth in the Engineer Agreement, or any change to the Engineering Report, without the prior written consent of Tenant or Tenant's Representative.

3. Retention of Contractor

(a) Contractor Agreement. Landlord shall retain the

services of the Contractor to construct the Work

according to the Final Plans. Landlord shall negotiate and execute as Owner, the written agreement with the Contractor governing construction of the Work

according to the Final Plans (the "Contractor Agreement"). Landlord shall provide Tenant with a copy of the proposed Contractor Agreement and shall consult with Tenant with respect to the terms and conditions of the Contractor Agreement prior to execution thereof. Landlord shall be, and perform the obligations of, the Owner under the Contractor Agreement. The Contractor Agreement shall include a completion date satisfactory to Tenant (which date shall not be changed or modified except by an amendment to the Contractor Agreement with prior written consent of both landlord and Tenant). Landlord shall not have any liability whatsoever to Tenant for any cost, expense, lost profits, damage or other liability suffered or incurred by Tenant by reason of the Contractor's failure to complete the Work on or before the completion date contained in the Contractor Agreement. Landlord shall use its reasonable best efforts to cause the Contractor to complete the Work on or before the Completion Date contained in the Contractor Agreement, and in any event as soon as possible.

(b) Cost of Construction. Landlord and Tenant acknowledge

that Contractor has agreed to perform the services under the Contractor Agreement. Landlord shall not agree to any increase in fees, or authorize any additional services other than those set forth in the Contractor Agreement, or any Field Change Orders, without the prior written consent of Tenant or Tenant's Representative.

4. Responsibility for Contents of Plans and Drawings.

Notwithstanding anything herein to the contrary, Landlord shall not be responsible for the accuracy, efficacy or sufficiency of any drawings, plans or specifications to be provided by any person herein (including without limitation, those plans, drawings or specifications to be furnished by Tenant, the Engineer or the Architect) except (i) those portions of the plans, drawings, and specification provided by Landlord and (ii) Landlord agrees that the Work as described in the Final Plans and any Field Change Orders is sufficient for Landlord's purposes and will meet Landlord's needs and requirements for improvements to the Building. The Architect, Engineer and/or Contractor shall be otherwise responsible for all plans, drawings and specifications including, without limitation, the Final Plans and any Field Change Orders, all technical and other examination of the Premises and shall be exclusively responsible with respect to verification of actual field conditions and actual field measurements and a full review of all technical and engineering requirements with respect to the Premises and Work to be performed hereunder. In addition, Tenant shall be exclusively responsible for determining whether the plans, specifications and drawings including, without limitation, the Final Plans and any Field Change Orders and the systems and equipment described therein, meet the needs of the Tenant.

5. Compliance. Landlord will insure that the Final Plans and all

Work shall comply with and conform to the Building plans and with all the rules, regulations and other requirements of any governmental department or agency having jurisdiction over the construction of the Work. Landlord, Architect or Contractor shall file all necessary architectural plans, together with any mechanical plans and specifications, and any and all other filings necessary to complete the Work in such form as may be necessary, with the appropriate governmental and other agencies and obtain those governmental and other approvals or consents necessary to authorize completion of the Work, including required permits and zoning approvals. Any changes required by any governmental or other agency affecting the construction of the Premises shall be complied with by Landlord in completing the Work at Tenant's expense and shall not be deemed to be a violation of the Final Plans or any provisions of this Work Agreement, and shall be deemed automatically accepted and approved by Tenant. Landlord shall cause the Work to be constructed and completed in accordance with the prevailing and customary construction standards in accordance with the Final Drawings and all applicable laws, rules, regulations, ordinances and codes and shall ensure that safety standards acceptable in the industry are employed. Landlord shall maintain appropriate insurance with respect to the work. Tenant shall reasonably cooperate with the Owner in complying with the foregoing requirements and Owner shall keep Tenant advised of the progress in connection with such requirements.

D. WORK COST

1. Work Cost. "Work Cost" shall mean contracted amount with

architect, engineer and contractor, except as adjusted by Field Change Orders, and all the following:

- (a) All filing fees and permit costs incurred in connection with the Work to the extent not included in contracts above, and Landlord shall provide receipts for payment of the same upon Tenant's request.
- (b) Legal fees, as mutually agreed upon in writing, in connection with obtaining governmental approvals of the Work and Tenant's uses of the Premises.
- (c) Litigation costs in connection with the Work Agreement as mutually agreed upon in writing.
- (d) All other costs of the Work mutually agreed upon in writing.

E. PAYMENT OF WORK COST

Tenant shall pay the Work Cost in the following manner:

1. Payment of Work Cost

- (a) Payment - General. Tenant will make a deposit to the Landlord based on construction estimates (per Rider D). Landlord will utilize said deposit to pay all construction related invoices.
- (b) Change Orders. Authorized change orders are to be accompanied with a check from the Tenant to cover said amount.
- (c) Final Payment. After project is complete and within fifteen (15) days after billing is received by Landlord, a reconciliation will be provided showing total costs. Tenant will provide final check for the total amount of the improvements less any previous payments and the Landlord's contribution when:
 - (1) Tenant, Architect and Landlord shall have inspected the Work and determined that the Work is complete and that all items comprising the Punch List prepared pursuant to Section 3.03 of this Lease shall have been completed or corrected. In the event of any dispute regarding completion, the Architect's determination shall be final;
 - (2) Landlord shall have removed or have caused to be removed, at its expense, from the site of the Work all material, equipment and structures which are not part of the Work and shall have made the site of the Work clean and ready for use; and
 - (3) Landlord shall have caused to be executed and copies delivered to Tenant of lien waivers executed by all persons, firms, and companies who have provided labor or furnished materials in connection with the Work including a general release and specific lien waiver from Contractor both in form and substance reasonably satisfactory to Tenant.

2. Continuing Obligations. Nothing herein shall be construed to

relieve Tenant from any liability for unpaid Work Costs due and payable pursuant to the terms of this Work Agreement.

F. WARRANTIES

Landlord warrants to Tenant that the Work will be performed in a workmanlike manner and in accordance with the Final Plans and any approved changes or modifications thereto and shall comply with all applicable codes, laws, and regulations. Landlord will obtain from the Contractor under the terms of the Construction Agreement such warranties as the Contractor generally provides in connection with its services. Landlord will use reasonable efforts to have all such warranties include a provision that they may be assigned to Tenant at Landlord's option. Upon the completion of the Work, Landlord shall assign to Tenant those warranties and manuals with respect to those items described in Rider H to this Lease and such other items as Tenant is required to maintain or repair pursuant to the terms of this Lease or otherwise, procured by Landlord from the Contractor, the Architect, Engineer, or others in connection with the performance of the Work or and any material or equipment installed upon the Premises as part of the Work. Landlord shall retain all other warranties and manuals. If such warranties are not assignable, Landlord shall pursue and, if possible, obtain coverage as requested by Tenant for and on behalf of Tenant, under such warranties (at Tenant's cost and expense). LANDLORD HEREBY DISCLAIMS ANY AND ALL OTHER

WARRANTIES OF ANY KIND IN CONNECTION WITH THE WORK INCLUDING WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE.

G. INDEMNIFICATION BY TENANT

To the fullest extent permitted by law, Tenant agrees to defend, indemnify and hold Landlord, its partners, employees, officers, and agents, and their legal successors and assigns (herein the "Landlord Indemnitees"), free and harmless of and from any and all liability, damages, all losses, costs and expenses, including, without limitation, all Work Cost and attorney fees, (collectively "Losses") incurred, suffered or required to be paid by Landlord Indemnitees to the extent that such losses result from or are attributable to (a) Tenant's failure to pay the Work Cost due and payable pursuant to this Work Agreement or (b) Landlord's Indemnitees' reliance on orders, instructions, directives or requests of Tenant in connection with the construction of the Work and the preparation of the Final Plans or (c) any negligent or grossly negligent acts, or omissions and/or intentional malfeasance, of Tenant, its employees, agents, guests or invitees prior to final completion of the Work, provided however, that notwithstanding anything herein to the contrary, the foregoing obligation to indemnify, hold harmless and defend shall not apply to any liability, damages, losses, costs or expenses attributable to the Landlord's Indemnitees. If any claim is made by a third party against any Landlord Indemnitees for which the Landlord Indemnitee seeks indemnification from Tenant hereunder, Landlord shall give prompt notice to Tenant who shall have the right at Tenant's sole expense to participate in or control the defense of such claim at its own expense and through counsel of its own choice. If after such notice Tenant does not so participate, Tenant shall nevertheless be bound by the results obtained by Landlord insofar as the claim against any Landlord Indemnitee is concerned.

H. INDEMNITY BY LANDLORD

Landlord shall defend, indemnify and hold harmless Tenant, its affiliates, and any of their respective directors, officers, employees, agents, servants and representatives ("Tenant Indemnitees") from and against any and all liability, damages, all losses, costs and expenses, including reasonable attorney fees, incurred, suffered or required to be paid by Tenant Indemnitee, resulting from or caused by or arising out of any action, omission or operation (i) under this Agreement or in connection with the Work attributable to Landlord, (ii) under the Architect Agreement, the Engineer Agreement, the Contractor Agreement or any other construction related document attributable to Landlord or the performance of any obligation of Landlord under such agreements or documents, or (iii) relating to any claim against Tenant arising under the Architect Agreement, the Engineer Agreement, the Contractor Agreement or any Work related document provided, however, that the foregoing obligation by the Landlord to defend, indemnify and hold harmless shall not apply to (x) any liability, damages, losses, costs or expenses, attributable to the negligence, gross negligence or willful misconduct of any Tenant Indemnitee, (y) the breach of any obligation of Tenant hereunder or (z) those matters for which Tenant is obligated to indemnify Landlord pursuant to Section B(5) of this Work Agreement. If any claim is made by a third party against any Tenant Indemnitee for which the Tenant Indemnitee seeks indemnification from Landlord hereunder, the Tenant Indemnitee shall give prompt notice to Landlord who shall have the right, at its sole option, to participate in or control the defense of such claim at its own expense and through counsel of its own choice. If after such notice Landlord does not so participate, Landlord shall nevertheless be bound by the results obtained by Tenant Indemnitee insofar as the claim against Tenant Indemnitee is concerned.

I. OWNERSHIP OF DOCUMENTS, CONFIDENTIALITY

Landlord and Tenant shall both be furnished copies of, and own, all drawings, specifications, manuals for equipment described on Rider H, design analyses, shop drawings, as-built record prints, calculations, renderings and any other related documents or materials prepared in connection with the Work.

J. MISCELLANEOUS

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1. Approvals, Notices. All prints, drawing information and other material to be furnished by Tenant to Landlord or by Landlord to Tenant for approval as required herein shall be addressed to Landlord or Tenant, as the case may be, at the addresses set forth in the Summary of Lease Terms. Approvals of such documents shall be sent in accordance with Section 20 of the Lease relating to notices.
 2. Relationship. Landlord and Tenant agree that Landlord is not the employee or agent of Tenant and with respect to this Work Agreement is an independent contractor. It is expressly agreed that all persons engaged in the

performance of the Work hired by Landlord or by any contractor of Landlord as between Landlord and Tenant shall be conclusively deemed to be employees or contractors of Landlord and not Tenant. This Agreement shall not constitute Landlord or any contractor as the agent, partner, or legal representative of Tenant, and Tenant shall not be responsible in any way for any obligations or liability incurred or assumed by Landlord or any contractor (the foregoing shall not in any manner limit the liability of obligations of Tenant to Landlord hereunder). Landlord shall contract only in its own name and only for its own account. Each such contract shall expressly state that the contractor recognizes that, to the extent permitted by law, it does not have a right to make any claim for payment directly from Tenant, since the contract has been made exclusively with Landlord and that, upon the request of Landlord, the contractor shall provide Landlord with a sworn statement regarding the contractor's right to receive payments for work or materials provided to the Work.

3. Confidentiality of Work and Plans. Landlord agrees that Landlord will

maintain the confidentiality of, and not disclose to third persons or parties, any of the Final Plans, Field Change Orders or other plans or specifications relating the Work except as Landlord may require for the construction of the Work, maintenance, operation, financing, insuring, sale of other conveyance of the Building or as may be required by any governmental authority, department or agency.

RIDER C

RULES AND REGULATIONS

The Landlord, or the Agent of the Landlord, as the case may be, reserves the right to make such other further and reasonable rules and regulations as in its judgment may from time to time be necessary or desirable for the safety and preservation of good order and prestige therein.

Wherever the word "Tenant" occurs, it is understood and agreed that it shall mean Tenant's employees, agents, clerks, servants and visitors. Wherever the word "Landlord" occurs, it is understood and agreed that it shall mean Landlord's assigns, agents, clerks, servants and visitors.

1. No sign, picture, lettering, notice or advertisement of any kind shall be painted, taped or displayed on or from the windows, doors, roof or outside wall of the premises. Landlord shall have the right to approve all signs, exhibits and displays to be made by Tenant in and from common areas of the building. All of Tenant's interior sign painting or lettering shall be approved by Landlord and the cost thereof shall be paid by Tenant. (See footnote #1)
2. No electric or other wires for any purpose shall be brought into the premises without Landlord's written permission specifying the manner in which same may be done. This shall prohibit use of hot plates (cooking) and only approved electric percolators or coffee makers shall be permitted. No boring, cutting or stringing of wire shall be done without Landlord's prior written consent. Tenant shall not disturb or in any way interfere with the electric light fixtures, and all work upon or alterations to the same shall be done by persons authorized by Landlord.
3. Water closets and other toilet fixtures shall not be used for any purposes other than that for which the same is intended, and any damage resulting to same from Tenant's misuse shall be paid for by Tenant. No person shall waste water by interfering or tampering with the faucets or otherwise.
4. No person shall disturb the occupants of this or adjoining buildings or premises by the use of radios, television sets, loud speakers, or musical instruments, or by making loud or disturbing noises.
5. No bicycle or other vehicle and no pets shall be allowed in offices, hall, corridors or elsewhere in the building.
6. No floor load exceeding an average rate of 60 pounds of live load per square foot of floor area can be allowed. Tenant's business machines and mechanical equipment which cause vibration or noise that may be transmitted to the building structure or to any other leased space in the building shall be placed and maintained by Tenant in settings of cork, rubber, spring or other types of vibration eliminators sufficient to eliminate such vibration or noise.
7. Any safe, vault, heavy equipment, furniture, or machinery moved in or out of the premises shall be moved in such manner and at such times as Landlord shall in each instance approve.

May 20, 1991

8. No additional lock or locks shall be placed on any door in the building without Landlord's prior written consent. Upon the termination of this Lease, the Tenant shall surrender to Landlord all keys to the premises.
9. Tenant shall not install or operate any steam or gas engine or boiler or carry on any mechanical business on said premises or use oil burning fluids, or gasoline for heating or lighting or for any other purpose. (See Rider G.)
10. The premises shall not be used for lodging or sleeping or for any immoral or illegal purposes.
11. Any newspaper, magazine or other advertising done from the said premises or referring to the said premises, Domino's Farms or Prairie House, which in the opinion of the Landlord is objectionable, shall be immediately discontinued upon notice from the Landlord.
12. The sidewalk, entry, passage hall and stairway shall not be obstructed or used for any purpose other than those of ingress and egress without the express written consent of the Landlord.
13. Window coverings other than those which may be provided by Landlord, either inside or outside of the windows, may only be installed with the Landlord's prior written consent, and must be furnished, installed and maintained at the expense of the Tenant and at Tenant's risk, and must be of such shape, color, material, quality and design as may be prescribed by the Landlord. Tenant shall exercise reasonable care in placing furniture, equipment, etc. in such a position as to not obstruct the windows.
14. Tenant will exercise reasonable discretion with regards to thermostat settings within the tenant space. Acceptable temperatures for heating will not exceed 72 degrees or fall below 68 degrees for cooling.
15. Tenant will be responsible for vending service located within the tenant premises. Landlord will designate approved vending contractors within the building. Tenant will coordinate vending installation with Landlord.
16. Domino's Farms Prairie House is a smoke free building; smoking of cigars, pipes and cigarettes is not allowed inside the building.
17. Subject to the terms of the Lease between Tenant and Landlord, Landlord will provide normal heating, ventilation and air conditioning as reasonably required by prevailing weather conditions to the leased premises on the following days (except legal holidays):

Monday - Friday from 8:00 a.m. to 6:00 p.m.
Saturday from 8:00 a.m. to 12:00 p.m.

Footnotes: #1 - Tenant will be permitted to provide signage for door leading from lobby into tenant space. Such signage must be reviewed and approved by Landlord.

RIDER D

ADDENDUM TO LEASE

TENANT IMPROVEMENT ALLOWANCE

- - - - -

The tenant improvement allowance shall equal \$29.25 per square foot. Any costs in excess of this allowance, based upon construction estimates, shall be paid by the Tenant to the Landlord according to the following payment schedule:

Fifty percent (50%) shall be deposited by Tenant with Landlord prior to commencement of work.

Forty percent (40%) shall be paid when the project is approximately fifty percent complete, based upon projected project costs.

The remaining ten percent (10%) shall be held until project completion, and until a project costs compilation is prepared. At such time, the ten percent plus any overages or minus any amount under budget will be paid to Landlord.

The Landlord shall provide cold water and sanitary to the leased space. The cost of internal routing will be a portion of the tenant build improvements.

OPTION FOR RENEWAL

- - - - -

The Tenant will have an option to renew the lease for an additional period of up to five (5) years, at a rate equal to \$21.00 per square foot plus an adjustment based upon the Consumers Price Index. Once per year for each year during the renewal term, the rate will be adjusted based upon the Consumers Price Index. Such increases shall not be less than three (3) percent nor more than seven (7) percent in any one year.

If Tenant exercises said option to renew, Landlord may elect to install, at Landlord's expense, a meter for electrical service to the Premises. In such event, Tenant will then become responsible for monthly electrical charges based upon actual meter readings. In the event Landlord elects not to install a meter, then Tenant will be assessed a monthly pro rata share of electrical charges for Phase 5.

TEMPORARY SPACE

- - - - -

Landlord will provide temporary office space and associated utility costs to the Tenant at no charge, upon signing of lease, and until Commencement Date of lease. Said space shall be approximately 1,000 square feet, and location in building will be at discretion of Landlord based upon availability of space. Tenant shall be responsible for telephone, furniture, post office box, moving charges, and all other associated costs.

AMENITITES

- - - - -

As of the Commencement Date of this Lease, the following amenities were available to tenants in the building. Landlord does not guarantee that all will be available at all times, and amenities are subject to change at the discretion of the Landlord.

- | | |
|--------------------------------|---------------------|
| Ample, free parking | Travel Agency |
| 24 hour on-site security staff | Fitness center |
| 24 hour access | Auto rental agency |
| A variety of restaurants | Dry cleaners |
| Catering services | Clothier & tailor |
| Conference and Meeting Rooms | Sundry shop |
| Automated teller machine | U.S. Post Office |
| Hair salon | Child care facility |

During the Initial Term and Renewal Term, if any, of this Lease, Tenant shall have a First Right of Refusal ("Right of Refusal") to lease certain additional space in the Building, under the following terms and conditions:

A. Space. Tenant's Right of Refusal shall apply to the approximately 2,306 square feet of rentable space on the second floor of Phase 5 of the Building, which is located adjacent to the Premises leased hereunder, and which is outlined on the attached floor plan.

To the greatest extent possible, Landlord will endeavor to locate alternative space for any leasing prospects interested in approximately 2,300 square feet.

B. Exercise by Tenant. Tenant shall have the right to exercise its Right of Refusal in the following manner: If at any time after the date hereof, the space is vacant, and Landlord intends to let such vacant space, as evidenced by a written proposal from Landlord (Landlord's Proposal) to a proposed lessee, then Landlord shall give Tenant written notice of such intention (Notice of Intent to Lease). Tenant shall have a period of ten (10) business days from the date of receipt of such Notice of Intent to Lease to exercise its Right of Refusal by sending written notice to Landlord of such exercise (which notice must be received by Landlord within such ten (10) day period).

C. Refusal by Tenant. If Tenant does not exercise its Right of Refusal as to the space covered by a Landlord's Proposal, Landlord shall be free to lease the space pursuant to the Landlord's Proposal.

If Tenant does not exercise its Right of Refusal and the proposed lessee does not accept the Landlord's Proposal, Tenant's Right of Refusal with respect to such space shall be reinstated as set forth above, including, without limitation, the right to exercise its Right of Refusal as to any subsequent proposals to lease the space as set forth above.

D. Notices. All notices hereunder shall be sent in compliance with Section 20 of the Lease.

E. Same Lease Terms. Under the exercise of Tenant's Right of Refusal, the space affected thereby shall be subject to all of the same terms and conditions of this Lease (including, without limitation, the Renewal Option set forth above and the Expiration Date) except that (i) additional rent with respect to such space shall commence ninety (90) days after the exercise of Tenant's Right of Refusal relating to such space, or upon taking possession of such space, if sooner; and (ii) Base Annual Rent and Base Monthly Rent for the additional space taken by Tenant shall be at the same rate in effect for the Premises at the time of exercise of Tenant's Right of Refusal; and (iii) an allowance for Tenant's build out of such space shall be given by Landlord at the rate of \$28 per square foot.

RIDER E

RIGHT OF REFUSAL

[CRC]

RIDER F

ATTORNMENMENT

1. Attornment. Tenant covenants and agrees that, if by reason of default

under any mortgage which may now or hereafter affect the Premises, including, without limitation, the Mortgage and Security Agreement dated as of March 29, 1990, between the owner of the Premises hereunder or a successor in title or interest, as Mortgagor, and Kansallis-Osake-Pankki, New York Branch, as Mortgagee, and any amendments, supplements or modifications thereof (the "Mortgage"), the mortgagee thereunder enters into and becomes possessed of the mortgaged property of which the Premises form a part either through possession or foreclosure action or proceeding, or in the event of the sale of the said action or proceeding, or in the event of the sale of the said mortgaged property as a result of any action or proceeding to foreclose said mortgage or as a result of a conveyance in lieu of foreclosure, the Tenant will attorn to the mortgagee or such then owner as its Landlord under this Lease, unless the mortgagee or such then owner shall elect to terminate this Lease and the rights of the Tenant hereunder. The Tenant agrees to execute and deliver, at any time and from time to time, upon the request of the mortgagee or the then owner of the mortgaged property, any instrument which may be necessary or appropriate to evidence such attornment and the Tenant hereby appoints the mortgagee or the then owner of the Premises the attorney-in-fact, irrevocable, of the Tenant to execute and deliver for and on behalf of the Tenant any such instrument. The Tenant further waives the provision of any statute or rule of law now or hereafter in effect which may terminate this Lease or to surrender possession of the Premises in the event of foreclosure or any proceeding is brought by the mortgagee under any such mortgage to terminate the same, and agrees that unless and until the mortgagee, in connection with any such proceeding, shall elect to terminate this Lease and the rights of the Tenant hereunder, this Lease shall not be affected in any way whatsoever by any such proceeding.

2. Nondisturbance. Notwithstanding the provisions of Paragraph 1 above:

(a) The mortgagee or the then owner, as the case may be, shall not disturb Tenant's use and possession of the Premises nor terminate the Lease so long as Tenant is not in default of the terms of this Lease.

(b) In addition, the mortgagee or the then owner, as the case may be, shall at all times during Tenant's attornment hereunder, be bound to Tenant as Landlord under all the terms and conditions of this Lease, provided, however, that the mortgagee or the then owner, as the case may be, shall not be (i) liable for the act or omission of any prior landlord under the Lease (including Landlord); (ii) subject to any offsets or defenses which Tenant might have against any prior landlord under the Lease (including Landlord); (iii) bound by any rent or additional rent which Tenant might have paid for more than the current month to any prior landlord under the Lease (including Landlord) unless such rent or additional rent has been delivered to mortgagee or such then owner; (iv) responsible for any security deposit which Tenant may have paid to any landlord (including Landlord), unless such deposit has been delivered to the mortgagee or such then owner, or (v) bound by any modification, amendment, surrender or cancellation of the Lease made without the prior written consent of mortgagee or the then owner.

3. No Release of Landlord. This Agreement shall not relieve Domino's Farms

Holding Limited Partnership of any obligation as Landlord under the Lease.

RIDER G

HAZARDOUS MATERIALS

HAZARDOUS MATERIALS/TENANTS OBLIGATIONS

A. Definitions: As used in this Section, "Environmental Law" and

"Hazardous Materials" shall have the following meanings:

1. "Environmental Law" means any applicable federal, state or local

government law, rule, ordinance or regulation in effect from time
to time relating to the environment, pollution, toxic substances,
Hazardous Materials or solid and/or toxic waste disposal, including,
without limitation, the following statutes and the regulations
promulgated thereunder:

(a) Michigan Solid Waste Management Act, MCLA Section 299.401 et seq.;

(b) Michigan Hazardous Waste Management Act, MCLA Section 299.501
et seq.;

(c) Federal Resource Conservation and Recovery Act of 1976;
(d) Federal Comprehensive Environmental Response, Compensation and
Liability Act of 1980; and
(e) Federal Superfund Amendments and Reauthorization Act of 1986.
2. "Hazardous Materials" means "Hazardous Waste" or "Hazardous Substance"

as those terms are currently defined in the Resource Conservation and
Recovery Act of 1976, the Comprehensive Environmental Response,
Compensation Liability Act of 1980 and the Superfund Amendments and
Reauthorization Act of 1986.

B. Use of Premises. Tenant shall not cause or permit the Premises to be used

to generate, manufacture, refine, transport, treat, store, handle, dispose
of, transfer, produce or process Hazardous Materials in violation of any
Environmental Law. At all times Tenant shall use and dispose of Hazardous
Materials in compliance with all applicable Environmental Law and all
requirements and guidelines of the United States Nuclear Regulatory
Commission. Tenant shall not cause or permit, as a result of any
intentional or unintentional act or omission on the part of Tenant, a
release of Hazardous Materials onto the Premises, the Building or any area
comprising part of the Domino's Farms Prairie House Office Complex in
violation of Environmental Law. Landlord and Tenant will promptly deliver
to the other copies of all notices received from any federal, state or local
authority regarding environmental problems affecting the Premises. The
provisions hereof shall be in addition to any and all other obligations
and liabilities Tenant may have to the Landlord at law or in equity
regarding Tenant's violation of Environmental Law and shall survive
termination of this Lease and the satisfaction of all other obligations
of Tenant hereunder.

C. Presence of Hazardous Materials/Indemnity. If Hazardous Materials are

present on or under the Premises in amounts, concentrations or in a manner
in violation of Environmental Law by reason of the acts or omissions of
Tenant or its agents, representatives, contractors, officers, directors,
employees, licensees or invitees, Tenant shall: (i) conduct and complete all
investigations, studies, sampling and testing, and all remedial, removal and
other actions necessary to clean up and remove all such Hazardous Materials
on, under, from or affecting the Premises in accordance with all applicable
Environmental Law; (ii) defend, indemnify and hold harmless Landlord, its
employees, agents, officers and directors from and against any claims,
demands, penalties, fines, liabilities, settlements, damages, costs or
expenses (including attorney's fees) of whatever kind or nature, known or
unknown, contingent or otherwise, arising out of or in any way related
to: (A) the presence, disposal, release or threatened release of any such
Hazardous Materials on, over, under, from or affecting the Premises or the
soil, water, vegetation, buildings, personal property, persons or animals
on, in, over or under the Premises; (B) any personal injury (including
wrongful death) or

property damage (real or personal) arising out of or related to such Hazardous Materials; (C) any lawsuit brought or threatened, settlement reached or government order relating to such Hazardous Material; and/or (D) any violation of laws, orders, regulations, requirements or demands of government authorities, or any reasonable policies or requirements of Landlord (and in the case Landlord's requirements of which Tenant was provided prior written notice), which are based upon or in any way related to such Hazardous Materials, including, without limitation, reasonable attorney's and reasonable consultant's fees, investigation and laboratory fees, court costs and out-of-pocket litigation expenses. In no event shall Tenant have any liability for: (i) conditions not in existence on the day Landlord, its successors or assigns, takes possession of the Premises from Tenant, (ii) conditions existing prior to the date Tenant takes possession of the Premises, or (iii) conditions aggravated or worsened (but only to the extent so aggravated or worsened) by Landlord, or its successors, assigns or any third party, after the date Landlord or its successors and assigns takes such possession of the Premises. Landlord shall give Tenant prompt notice of any claim or information of which Landlord has knowledge that is likely to give rise to a claim for defense, indemnity or hold harmless under this Section, and shall permit Tenant's involvement in the defense of any such claim as reasonably requested by Tenant. Neither Landlord nor Tenant shall settle or pay any third party claim with respect to any claim hereunder, except upon the written approval of both Landlord and Tenant. The provisions hereof shall be in addition to any and all other obligations and liabilities Tenant may have to the Landlord at law or in equity and shall survive termination of this Lease and the satisfaction of all other obligations of Tenant hereunder.

D. Right of Inspection. Landlord, its successors and assigns shall have the -----

right to inspect the Premises at any reasonable time and from time to time upon not less than two (2) hours advance notice in order to determine whether Hazardous Materials are being used in violation of Environmental Law and whether Tenant is in full compliance with the terms of this Section, but Landlord shall have no obligation to conduct such inspections. All such inspections, including, without limitation, investigation, studies, sampling and testing, shall be at Tenant's expense if the Premises are not in compliance with this Section, otherwise they shall be at Landlord's expense. Tenant is authorized to install its own security system for access to the Premises using so-called security card devices. Tenant shall immediately release any such security system upon notice from Landlord's security personnel that an emergency exists requiring access to the Premises. Inspections by Landlord under this paragraph shall not unreasonably interfere with the operation of Tenant's business and Landlord shall comply with Tenant's Confidentiality Requirements (as defined in Section 17.01 of this Lease) and Tenant's reasonable requests, provided, however, these provisions are subject to any actions reasonably necessary to meet or ameliorate any emergency threatening serious bodily injury or property damage.

E. Effect on Insurance. Notwithstanding anything in this Section to the -----

contrary, Tenant shall not use or occupy or permit the Premises to be used or occupied, nor do or permit anything to be done in or on the Premises, in a manner which will in any way make void or voidable any insurance customary for buildings or property similar to the Premises (containing terms and conditions customary for insuring buildings or property similar to the Premises) then in force with respect thereto, or which will make it unreasonably difficult or impossible to obtain fire or other insurance (containing terms and conditions customary for insuring buildings or property similar to the Premises) carried by Landlord with respect to the property of which the Premises is a part. If Tenant's failure to comply with the provisions of this Section causes any insurance premium to be higher than it would otherwise be, Tenant shall reimburse Landlord, as additional rent, for that part of all insurance premiums thereafter paid by Landlord which have been changed because of Tenant's failure.

F. Reports. At reasonable intervals, and at least annually, Tenant shall -----

provide to Landlord, at Landlord's request, a list of all Hazardous Materials at any time used, stored, placed or brought onto the Premises since the date of the last report furnished to Landlord with respect to Hazardous Materials. In addition, Tenant shall provide to Landlord such reasonable documentation as Landlord may request to review the methods and procedures used by the Tenant in handling and disposing of any Hazardous Materials. If Landlord determines in its reasonable judgment that any Hazardous Material as it is being used by Tenant (taking into account the nature of the Hazardous

Material, the manner of its use and the quantities on the Premises) presents an unreasonable hazard to, or unreasonably endangers the health, safety or welfare of, the Building's Tenants, or any of them, Tenant shall, as appropriate, upon written notice from Landlord cease using any such Hazardous Material on the Premises and immediately dispose of such Hazardous Material in compliance with all Environmental Law or appropriately modify its use thereof so as to not render such use unreasonably hazardous or dangerous. In the event that Tenant disputes Landlord's assessment or designation of any prohibited Hazardous Material, the matter shall be referred to an Environmental Engineer for decision. The decision of such Environmental Engineer shall be conclusive on the parties (except the extent that such decision is overridden by any governmental authority enforcing any Environmental Law). The fees of such Environmental Engineer shall be paid by the unsuccessful party and if both parties are partially unsuccessful, the Environmental Engineer shall apportion such fees and expenses between the parties, based on the degree of success of each party.

HAZARDOUS MATERIALS/LANDLORD'S OBLIGATION

A. Representations

In addition, Landlord represents, warrants and covenants to Tenant that:

1. Landlord has not, and, to Landlord's knowledge no prior owner of the Building, tenant or prior tenant, occupant or prior occupant of the Building has, used or permitted the release of any Hazardous Materials on, from or affecting the Premises in any manner which violates Environmental Law.
2. Landlord has never received any summons, citation, directive, letter, notice or other communication, written or oral, regarding any violation of Environmental Law affecting the Premises, and there have been no actions commenced to Landlord's knowledge threatened by any party for noncompliance therewith.
3. Any and all plumbing, sewer and disposal systems, and pipelines and tanks, located upon or beneath or servicing the Premises will be maintained in good and safe operating condition and repair and to Landlord's knowledge are in good and safe operating condition and repair.

If it is determined during or following the termination or expiration of the Lease that there is a violation of Environmental Law associated with the leased premises and the violation was not created by Tenant, its agents, representatives, contractors, officers, directors, employees, licensees or invitees in violation of Environmental Law then Landlord agrees to comply with all federal, state and local laws, ordinances, rules, regulations, and policies pertaining to such violation that are binding upon Landlord and to take whatever safety precautions and measures are required or prescribed, at the Landlord's expense. Landlord also agrees to defend and indemnify Tenant and its affiliates and their respective agents, representatives, contractors, officers, directors, employees, licensees and invitees, from and against all obligations, liabilities, loss, costs, damages, settlement or expenses of whatsoever kind or nature, known or unknown, contingent or otherwise, directly or indirectly arising out of or in any way related to any of the following caused solely by Landlord, its agents, representatives, contractors, officers, directors, employees, licensees or invitees: (i) the presence, disposal, release or threatened release of any Hazardous Materials on, over, under, from or affecting the Premises or the soil, water, vegetation, buildings, personal property, persons or animals thereon; (ii) any personal injury (including wrongful death) or property damage (real or personal) arising out of or related to such Hazardous Materials; (iii) any lawsuit brought or threatened, settlement reached or government order relating to such Hazardous Materials; and/or (iv) any violations of laws, regulations, requirements or demands of government authorities which are based upon or are in any way related to Hazardous Materials, including, without limitation and in each of the foregoing cases, reasonable attorney and consultant fees, investigation and laboratory fees, court costs and litigation expenses. Landlord will notify Tenant in writing immediately of any condition of which Landlord has knowledge and which involves Hazardous Materials or violation of Environmental Law which might affect the Premises.

FIRST AMENDMENT TO LEASE

This Amendment to Lease is made the 26th day of February, 1993, by and between

Domino's Farms Holding Limited Partnership, a Michigan Corporation, having
offices at 24 Frank Lloyd Wright Drive, Ann Arbor, Michigan 48105 ("Landlord"),
and AASTROM Biosciences, Inc., having offices at 24 Frank Lloyd Wright Drive,
Ann Arbor, Michigan 48105 ("Tenant").

WHEREAS, Landlord and Tenant entered into a Lease commencing October 1, 1992
(the "Lease") for approximately 4,592 of usable square feet of office space in
the building commonly known as Domino's Farms Prairie House; and

WHEREAS, Tenant desires modifications to be made to the original lease; and

WHEREAS, Landlord agrees to the modifications proposed by Tenant;

NOW, THEREFORE, in consideration of the mutual covenants contained in this
First Amendment to Lease, the parties agree to the following changes:

Tenant expanded into an additional 191 square feet of usable space.
Construction of said expansion was complete and rent became effective
January 1, 1993.

Per the terms of the original Lease, Landlord will contribute Five
Thousand Three Hundred Forty Eight Dollars (\$5,348) towards the
construction costs for said expansion.

The total monthly charge for rent will now be Nine Thousand Two Hundred
Ninety Dollars and Ninety Eight Cents (\$9,290.98).

Per the original Lease, Tenant was to pay Landlord a Security Deposit in
the amount of \$8,919.96. Said deposit was not paid as of the date of
this Amendment, and Landlord hereby waives requirement for said deposit.

IN WITNESS WHEREOF, this Amendment to Lease is executed on the 26th day of
February, 1993.

DOMINO'S FARMS HOLDING
LIMITED PARTNERSHIP
(A Michigan Corporation)

By: /s/ THOMAS R. MINICK

Thomas R. Minick

Its:

AASTROM BIOSCIENCES, INC.
(A Michigan Corporation)

By: /s/ R. Douglas Armstrong

R. Douglas Armstrong, Ph.D.
Its: President and C.E.O.

[CRC]

SECOND AMENDMENT TO LEASE

This Amendment to Lease is made the third day of October, 1994, by and between DOMINO'S FARMS HOLDING LIMITED PARTNERSHIP, a Michigan Corporation, having offices at 24 Frank Lloyd Wright Drive, Ann Arbor, Michigan 48106 ("Landlord"), and AASTROM BIOSCIENCES, INC. having offices at 24 Frank Lloyd Wright Drive, Ann Arbor, Michigan 48106 ("Tenant").

WHEREAS, Landlord and Tenant entered into a Lease commencing October 1, 1992 (the "Lease") for approximately 4,592 of usable square feet of office space in the building commonly known as Domino's Farms Prairie House; and

WHEREAS, modifications were made to the original lease on February 26, 1993 which increased the total usable square feet to 4,783 with a corresponding increase in rent charge; and

WHEREAS, Tenant desired further modifications to be made to the original lease and subsequent First Amendment; and

WHEREAS, Landlord agreed to the modifications proposed by Tenant;

NOW, THEREFORE, in consideration of the mutual covenants contained in this Second Amendment to Lease, the parties agree to the following changes:

1. Tenant expanded into the former Allstate Insurance Company suite, effective July 12, 1993. Said suite is 750 square feet, and is further identified on the attached floor plan. Tenant accepted space in current configuration; Landlord painted suite, provided an allowance of \$1,200 for carpet replacement (to be arranged by Tenant), and provided an allowance of \$806.30 for installation of soffit lighting (to be arranged by Tenant). No further contribution was made by Landlord, and no further modifications to space were made by Tenant. Based upon the necessity of relocation of Allstate Insurance Company to allow for said expansion, Tenant agreed to pay a pro-rated share of the unamortized tenant improvement costs initially paid by the Landlord. A surcharge of \$228.45 will be assessed each month through May 1995 (initial term covered by this Lease agreement).
2. Tenant expanded into an additional 2,115 square feet of usable space, located between the leased premises and the expansion space described in Item #1 above. Construction of said space was complete and rent became effective September 20, 1993.

Per the terms of the original Lease, Landlord contributed Fifty Nine Thousand, Two Hundred Twenty Dollars (\$59,220.00) towards the construction costs for said expansion. Tenant contracted for and managed construction, with approval of Landlord.

3. Tenant agreed to lease a storage room located on Level 1 of the Building. Said room is 868 square feet, of which 728 square feet is usable by Tenant, and is further identified on the attached floor plan. Tenant agrees to at all times maintain a five foot (5') clear aisle to doors entering building mechanical room east of leased storage room. Landlord agrees to provide an allowance of \$600 for installation of electrical power to said room. Tenant, at its expense, may elect to make additional modifications to room, and same will be coordinated with Landlord. Rent for said room will be calculated based upon 728 square feet, at a rate of \$8.00 per square foot, and will equal \$485.33 per month.

4. Based upon the changes described in Item #1 and #2 above, the total monthly charge for rent will now be based upon a total of 7,648 usable square feet, and will equal \$14,856.24. With the surcharge described in Item #1 above, total monthly rent due for office and lab space will equal \$15,084.69. Total rent due for storage space described in Item #3 above will equal \$485.33.
5. The terms and conditions of the Lease shall remain in full force and effect except as specifically modified herein.

IN WITNESS WHEREOF, this Second Amendment to Lease is executed on the date set forth above.

AASTROM BIOSCIENCES, INC.
(A Michigan Corporation)

By: /s/ R. DOUGLAS ARMSTRONG

R. Douglas Armstrong, Ph.D.
Its: President & C.E.O.

DOMINO'S FARMS HOLDING
LIMITED PARTNERSHIP
(A Michigan Corporation)

By: /s/ THOMAS R. MINICK

Thomas R. Minick
Its: Vice President of Services

[CRC]

[CRC]

THIRD AMENDMENT TO LEASE

This Amendment to Lease is made the 16th day of November, 1994, by and

between DOMINO'S FARMS HOLDING LIMITED PARTNERSHIP, a Michigan Corporation, having offices at 24 Frank Lloyd Wright Drive, Ann Arbor, Michigan 48106 ("Landlord"), and AASTROM BIOSCIENCES, INC., having offices at 24 Frank Lloyd Wright Drive, Ann Arbor, Michigan 48106 ("Tenant").

WHEREAS, Landlord and Tenant entered into a Lease commencing October 1, 1992 (the "Lease") for approximately 4,592 of usable square feet of office space in the building commonly known as Domino's Farms Prairie House; and

WHEREAS, modifications were made to the original lease on February 26, 1993 which increased the total usable square feet to 4,783 with a corresponding increase in rent charge (First Amendment); and further modifications were made to the original lease on October 3, 1994 which increased the total usable square feet to 7,648 and provided for rental of a storage room of 728 square feet, with corresponding increases in rent charge (Second Amendment); and

WHEREAS, Tenant desires further modifications to be made to the original lease and subsequent First and Second Amendments; and

WHEREAS, Landlord agrees to the modifications proposed by Tenant;

NOW, THEREFORE, in consideration of the mutual covenants contained in this Third Amendment to Lease, the parties agree to the following changes:

1. Tenant will expand into 6,723 usable square feet located across the corridor from the existing premises, and further identified on Attachment A.
2. Modifications will be made to the expansion suite. Tenant will be responsible for development of plans and all aspects of the construction process. However, plans must be submitted to and approved by Landlord prior to construction start-up.
3. \$188,244 will be contributed by the Landlord to the cost of the tenant improvements. This sum is equal to \$28.00 per square foot. Further, Landlord will bear responsibility for certain work, to include floor leveling (cement work), installation of a fire damper, relocation of an alarm panel, construction of the demising wall along the East wall of the expansion suite, and installation of a major air supply duct. Upon completion of the project, as-built drawings and a financial summary will be provided to Landlord to detail the total scope of the project. Said improvements are projected to be completed by November 15, 1994.
4. On or before January 1, 1995, Tenant will vacate and be released of all responsibility for the 750 usable square feet acquired by Tenant on July 12, 1993. Said space is required by Landlord for installation of a mechanical room. A corresponding reduction in rent will be applied, and the monthly surcharge for said space will be discontinued.
5. For the period of November 16, 1994 through March 15, 1995, Tenant will pay no rent for the expansion suite. However, during this time period, Tenant will pay \$7.35 per square foot (\$4,117.84 per month) to be applied to the cost of utilities, maintenance, taxes, grounds, and housekeeping for the expansion suite.

For the period from March 16, 1995 through May 31, 1995, Tenant will pay rent for the expansion suite at the same rate provided in the initial lease (\$21.00 per square foot plus \$2.31 for a utility charge).

6. The Lease will expire on May 31, 1995, and via this Third Amendment, will be extended for an additional three year term (June 1, 1995 through May 31, 1998). From June 1, 1995 forward, the rental rate will be considered a gross rate.
7. Effective June 1, 1995, an annual increase of three percent (3%) will be applied to the rates for this Lease. Said rates and rents due are detailed on Attachment B to this Amendment (Rent Payment Schedule).
8. Tenant shall have a right to terminate the Lease during the three year extension period, in the event of any one of the following:
 - a.) Landlord is unable to provide acceptable space for further expansion of the Tenant; or
 - b.) AASTROM Biosciences, Inc. is acquired by another company and the company is relocated to a non-Michigan site; or
 - c.) Zoning or other governmental restrictions limit the Tenant from conducting business at Domino's Farms.

In the event the Tenant elects to terminate the Lease based upon one of the stated factors, the following shall apply:

- i) Tenant shall provide Landlord with twelve (12) month written notice of any intent to terminate.
- ii) To the extent reasonable, Tenant will assist with location of a replacement tenant. Subject to Section 16 of the Lease, Tenant may sub-lease the Premises.
- iii) Tenant will re-pay the unamortized tenant improvements stated above (\$188,244.00) based upon a three year amortization schedule. Such re-payment of unamortized tenant improvements will be made only if Tenant is unable to find a sub-tenant and/or Landlord is unable to lease the premises essentially "as is" within ninety (90) days following the early termination date of Lease.
- iv) The four month rent abatement will be re-paid if notice to terminate is given within the initial eighteen months of the three year lease extension period.

9. Tenant shall have a Second Right of Refusal for the approximately 7,590 square feet located North of and contiguous to the expansion suite. (As of the date of this Amendment, Parke-Davis has a First Right of Refusal for said suite.) Tenant shall have a First Right of Refusal for the approximately 5,000 square feet located North of and contiguous to the suite covered by the Second Right of Refusal. Said suites are further identified on Attachment A.

Under the exercise of either Right of Refusal stated above, the terms and conditions shall be as provided in Rider E of the Lease, with the exception of paragraph E(iii). For any space previously unoccupied by a Tenant and in an unfinished status, an allowance in the set amount of \$28.00 per square foot shall be provided. For any space built out and occupied by another tenant, the Landlord would be responsible for any negotiated

relocation and associated costs. An allowance to Tenant would be provided in the amount of \$8.00 per square foot for any alterations resulting in office space, and \$12.00 per square foot for any alterations resulting in laboratory space.

10. Tenant shall have one option to extend the lease for a term up to five (5) years. Tenant shall notify Landlord in writing of intent to extend at lease one hundred eighty days (180) prior to lease expiration. Rent for such extension shall be at a rate equivalent to the rate in effect during the last year of the lease prior to such proposed extension, with an adjustment of three percent (3%) applied during the first and each subsequent year of the extension.
11. The terms and conditions of the Lease shall remain in full force and effect except as specifically modified herein.

IN WITNESS WHEREOF, this Third Amendment to Lease is executed on the date set forth above.

AASTROM BIOSCIENCES, INC.
(A Michigan Corporation)

By: /s/ R. DOUGLAS ARMSTRONG

R. Douglas Armstrong, Ph.D.
Its: President and C.E.O.

DOMINO'S FARMS HOLDING
LIMITED PARTNERSHIP
(A Michigan Corporation)

By: /s/ THOMAS R. MINICK

Thomas R. Minick
Its: Vice President of Services

[CRC]

DOMINO'S FARMS PRAIRIE HOUSE
RENT PAYMENT SCHEDULE

AASTROM BIOSCIENCES - PHASE V

- - - - -

	OFFICE RENT (6,898 SQ.FT.)	STORAGE CAGE (64 SQ.Ft.)	STOREROOM (728 SQ.FT.)	1994 EXPANSION (6,723 SQ.FT)	TOTAL RENT
=====					
10/01/94 - 10/31/94	15,084.69 *	64.00	485.33	N/A	15,634.02
11/01/94 - 11/30/94	15,084.69 *	64.00	485.33	2,058.92 **	17,692.94
12/01/94 - 12/31/94	15,084.69 *	64.00	485.33	4,117.84 **	19,751.86
01/01/95 - 01/31/95	13,399.37	64.00	485.33	4,117.84 **	18,066.54
02/01/95 - 02/28/95	13,399.37	64.00	485.33	4,117.84 **	18,066.54
03/01/95 - 03/31/95	13,399.37	64.00	485.33	8,935.26 ***	22,883.96
04/01/95 - 04/30/95	13,399.37	64.00	485.33	13,059.43	27,008.12
05/01/95 - 05/31/95	13,399.37	64.00	485.33	13,059.43	27,008.12
06/01/95 - 06/30/95	13,801.75	64.00	499.89	13,451.60	27,817.24
07/01/95 - 07/31/95	13,801.75	64.00	499.89	13,451.60	27,817.24
08/01/95 - 08/31/95	13,801.75	64.00	499.89	13,451.60	27,817.24
09/01/95 - 09/30/95	13,801.75	64.00	499.89	13,451.60	27,817.24
10/01/95 - 10/31/95	13,801.75	64.00	499.89	13,451.60	27,817.24
11/01/95 - 11/30/95	13,801.75	64.00	499.89	13,451.60	27,817.24
12/01/95 - 12/31/95	13,801.75	64.00	499.89	13,451.60	27,817.24
01/01/96 - 01/31/96	13,801.75	64.00	499.89	13,451.60	27,817.24
02/01/96 - 02/28/96	13,801.75	64.00	499.89	13,451.60	27,817.24
03/01/96 - 03/31/96	13,801.75	64.00	499.89	13,451.60	27,817.24
04/01/96 - 04/30/96	13,801.75	64.00	499.89	13,451.60	27,817.24
05/01/96 - 05/31/96	13,801.75	64.00	499.89	13,451.60	27,817.24
06/01/96 - 06/30/96	14,215.63	64.00	515.06	13,854.98	28,649.67
07/01/96 - 07/31/96	14,215.63	64.00	515.06	13,854.98	28,649.67
08/01/96 - 08/31/96	14,215.63	64.00	515.06	13,854.98	28,649.67
09/01/96 - 09/30/96	14,215.63	64.00	515.06	13,854.98	28,649.67
10/01/96 - 10/31/96	14,215.63	64.00	515.06	13,854.98	28,649.67
11/01/96 - 11/30/96	14,215.63	64.00	515.06	13,854.98	28,649.67
12/01/96 - 12/31/96	14,215.63	64.00	515.06	13,854.98	28,649.67
01/01/97 - 01/31/97	14,215.63	64.00	515.06	13,854.98	28,649.67
02/01/97 - 02/28/97	14,215.63	64.00	515.06	13,854.98	28,649.67
03/01/97 - 03/31/97	14,215.63	64.00	515.06	13,854.98	28,649.67
04/01/97 - 04/30/97	14,215.63	64.00	515.06	13,854.98	28,649.67
05/01/97 - 05/31/97	14,215.63	64.00	515.06	13,854.98	28,649.67
06/01/97 - 06/30/97	14,641.01	64.00	530.23	14,269.57	29,504.80
07/01/97 - 07/31/97	14,641.01	64.00	530.23	14,269.57	29,504.80
08/01/97 - 08/31/97	14,641.01	64.00	530.23	14,269.57	29,504.80
09/01/97 - 09/30/97	14,641.01	64.00	530.23	14,269.57	29,504.80
10/01/97 - 10/31/97	14,641.01	64.00	530.23	14,269.57	29,504.80
11/01/97 - 11/30/97	14,641.01	64.00	530.23	14,269.57	29,504.80
12/01/97 - 12/31/97	14,641.01	64.00	530.23	14,269.57	29,504.80
01/01/98 - 01/31/98	14,641.01	64.00	530.23	14,269.57	29,504.80
02/01/98 - 02/28/98	14,641.01	64.00	530.23	14,269.57	29,504.80
03/01/98 - 03/31/98	14,641.01	64.00	530.23	14,269.57	29,504.80
04/01/98 - 04/30/98	14,641.01	64.00	530.23	14,269.57	29,504.80
05/01/98 - 05/31/98	14,641.01	64.00	530.23	14,269.57	29,504.80
=====					

* 1994 OFFICE RENT BASED ON 7,648 SQ. FT. AND INCLUDES THE
ALLSTATE SURCHARGE OF \$228.00.

** CAM EXPENSES ONLY - EFFECTIVE 11/16/94

*** CAM EXPENSES AND RENT PRO-RATED TO REFLECT CHANGE EFFECTIVE
ON THE 16TH.

RENTAL AGREEMENT FOR STORAGE SPACE

1. AASTROM BIOSCIENCES, INC. agrees to rent Storage Unit #13, located on Level 1 of Prairie House, effective March 15, 1993. It is understood that rental is on a monthly basis, and can be terminated by either Landlord or Tenant with thirty (30) days written notice.

2. Rent for the period from March 15 through March 31, 1993 is \$32.00. Rent for a full calendar month is \$64. Rate is \$12 per square foot, based upon 64 square feet (8' x 8'). The Tenant will be invoiced on a monthly basis, and rent shall be due on the first day of each month.

3. No security deposit is required, and a key request form must be submitted to the Control Center for access to the unit. Responsibility for any keys issued is solely the responsibility of the tenant.

4. The unit will be used only for the storage of property, and will not be used to store any edible, flammable, explosive, toxic or dangerous materials. However, Landlord acknowledges that Tenant may store hazardous materials in said unit, and Tenant agrees that any hazardous materials shall at all times be stored in appropriate containers. The unit will never be intentionally damaged, and rubbish will be disposed of in appropriate containers. Access will be only during normal business hours. No alterations will be made to the unit.

5. Signature below indicates an understanding that Landlord is only renting space, and will bear no responsibility for damage or loss to personal property contained within said space. It is an option for the Tenant to secure and purchase property insurance through an independent agent.

6. This rental agreement is independent and separate from any other lease the undersigned may have with respect to other space at the Domino's Farms complex.

/s/ R. DOUGLAS ARMSTRONG

For Tenant

/s/ MARGARET PARKINSON

For Landlord

FOURTH AMENDMENT TO LEASE

This Amendment to Lease is made this 29th day of July, 1996, by and between DOMINO'S FARMS HOLDING LIMITED PARTNERSHIP, a Michigan Corporation, having offices at 24 Frank Lloyd Wright Drive, Ann Arbor, Michigan 48106 ("Landlord"), and AASTROM BIOSCIENCES, INC., a Michigan Corporation, having offices at 24 Frank Lloyd Wright Drive, Ann Arbor, Michigan 48106 ("Tenant").

WHEREAS, Landlord and Tenant entered into a Lease commencing October 1, 1992 (the "Lease") for approximately 4,592 of usable square feet of office space in the building commonly known as Domino's Farms Prairie House; and

WHEREAS, modifications were made to the original lease on February 26, 1993 which increased the total usable square feet to 4,783 with a corresponding increase in rent charge (First Amendment); and further modifications were made to the original lease on October 3, 1994 which increased the total usable square feet to 7,648 and provided for rental of a storage room of 728 square feet, with corresponding increases in rent charge (Second Amendment); and further modifications were made to the original lease on November 16, 1994 which increased the total usable square feet to 14,371 with a corresponding increase in rent charge (Third Amendment); and

WHEREAS, Tenant desires further modifications to be made to the original lease and subsequent First, Second and Third Amendments; and

WHEREAS, Landlord agrees to the modifications proposed by Tenant;

NOW, THEREFORE, in consideration of the mutual covenants contained in this Fourth Amendment to Lease, the parties agree to the following changes:

1. Tenant will expand into 5,510 usable square feet, which is further identified on Attachment A.
2. Modification will be made to the expansion suite. Tenant will be responsible for development of plans and all aspects of the construction process. However, plans must be submitted to and approved by Landlord prior to construction start-up. Upon project completion, Tenant must furnish Landlord with complete set of "as-built" drawings and a financial summary which details the total scope of the project.
3. \$66,668.00 will be contributed by the Landlord to the cost of the tenant improvements. Further, Landlord will bear responsibility for certain work, to include floor leveling (cement work), installation of two fire dampers, construction of the

demising wall along the North wall of the expansion suite, removal of storm conductor, removal of double doors on West wall and installation of glass to match building standard, and upgrade of patio area on West side of suite.

The tenant improvement allowance provided by the Landlord shall be calculated as follows:

2,550 square feet	\$17.60 per square foot	\$44,880.00
1,568 square feet	\$ 9.43 per square foot	\$14,786.24
1,392 square feet	\$ 5.03 per square foot	\$ 7,001.76
-----		-----
5,510 square feet		\$66,668.00

4. Rent will commence on August 1, 1996 and shall run current with existing Lease term which will expire on May 31, 1998.
5. An annual increase of three percent (3%) will be applied to the rates for this Lease. Said rates are as follows:

8/1/96 to 5/31/97	\$24.73 per square foot
6/1/97 to 5/31/98	\$25.47 per square foot

A portion of the proposed expansion space is considered to be somewhat less desirable than usual, due to interior location or lower than normal ceiling height. Such areas amount to 2,808 square feet, and are further defined on Attachment B. Rental rate for same shall be as follows:

8/1/96 to 5/31/97	\$18.00 per square foot
6/1/97 to 5/31/98	\$18.54 per square foot

Tenant currently occupies two (2) storage cages located on Level One in close proximity to the dock. Rental rate for same shall remain at a flat rate of \$12.00 per square foot.

Cage #1	\$ 64.00 per month
Cage #2	\$336.00 per month

Tenant currently occupies a 728 square foot storage room located on Level One of the building. Rental rate for same shall increase at a rate of three percent (3%) per year as follows:

8/1/96 to 5/31/97	\$8.49 per square foot
6/1/97 to 5/31/98	\$8.74 per square foot

6. Tenant shall have a right to terminate the Lease during the remaining lease term, in the event of any one of the following:

- a) Landlord is unable to provide reasonably acceptable space for further expansion of the Tenant; or
- b) AASTROM Biosciences, Inc. is acquired by another company and the company is relocated to a non-Michigan site; or
- c) Zoning or other governmental restrictions limit Tenant from conducting business at Domino' Farms.

In the event the Tenant elects to terminate the Lease based upon one of the above stated factors, the following shall apply:

- i) Tenant shall provide Landlord with twelve (12) month written notice of any intent to terminate.
- ii) To the extent reasonable, Tenant will assist with location of a replacement tenant. Subject to Section 16 the Lease, Tenant may sub-lease the Premises.
- iii) In addition to the financial obligation defined in 8(iii) of the Third Amendment to Lease, the tenant will re-pay the unamortized tenant improvements stated above (\$66,668.00) based upon a two year amortization schedule. Such repayment of unamortized tenant improvements will be made only if Tenant is unable to find a subtenant and/or Landlord is unable to lease the premises essentially "as is" within ninety (90) days following the early termination date of Lease.

7. Tenant shall have a First Right of Refusal for the approximately 10,000 square feet located North of and contiguous to the suite covered by this amendment.

Under the exercise of the Right of Refusal stated above, the terms and conditions shall be as provided in Rider E of the Lease, with the exception of paragraph E(iii). For any space previously unoccupied by a Tenant and in an unfinished status, an allowance in the set amount of \$28.00 per square foot shall be provided. For any space built out and occupied by another tenant, the Landlord would be responsible for any negotiated relocation and associated costs. An allowance to Tenant would be

provided in the amount of \$8.00 per square foot for any alterations resulting in office space, and \$12.00 per square foot for any alterations resulting in laboratory space. All such allowances are based upon a five (5) year lease term.

Additionally, Tenant shall have a First Right of Refusal for the suite located on Level 3, between Lobby K and Lobby L, and directly above Tenant's premises. Any Tenant improvement allowance would depend on the proposed alterations to the suite and length of lease term.

8. Tenant shall retain one option to extend the Lease for a term up to five (5) years, in whole or in part. Tenant shall notify Landlord in writing of intent to extend at least one hundred eighty (180) days prior to Lease expiration. Rent for such extension shall be at a rate equivalent to the rate in effect during the last year of the Lease prior to such proposed extension, with an adjustment of three percent (3%) applied during the first and each subsequent year of the extension.
9. The terms and conditions of the Lease shall remain in full force and effect except as specifically modified herein.

IN WITNESS WHEREOF, this Fourth Amendment to Lease is executed on the date set forth above.

AASTROM BIOSCIENCES, INC.
(A Michigan Corporation)

By: /s/ Todd E. Simpson

Its: Vice President - Financial
Administrator, Chief Financial
Officer

DOMINO'S FARMS HOLDING LIMITED
PARTNERSHIP
(A Michigan Corporation)

By: /s/

Its:

[ATTACHMENT A BLUEPRINT APPEARS HERE]

[ATTACHMENT B BLUEPRINT APPEARS HERE]

DOMINO'S FARMS PRAIRIE HOUSE
RENT PAYMENT SCHEUDLE

	OFFICE RENT (6,695 sq. ft)	STORAGE CAGE (64 sq. ft.)	STORE ROOM (728 sq. ft.)	1994 EXPANSION (6,723 sq. ft.)	1994 EXPANSION (5,510 sq. ft)	TOTAL RENT
=====						
10/01/94 - 10/31/94	15,084.69*	64.00	485.33	--	--	15,834.02
11/01/94 - 11/30/94	15,084.60*	64.00	485.33	2,058.92**	--	17,692.94
12/01/94 - 12/31/94	15,084.89*	64.00	485.33	4,117.84**	--	19,751.88
01/01/95 - 01/31/95	13,399.87	64.00	485.33	4,117.84**	--	18,066.54
02/01/95 - 02/28/95	13,389.37	64.00	485.33	4,117.84**	--	18,066.54
03/01/95 - 03/31/95	13,399.87	64.00	485.33	8,838.26***	--	22,883.98
04/01/95 - 04/30/95	13,399.87	64.00	485.33	13,059.49	--	27,006.18
05/01/95 - 05/31/95	13,399.87	64.00	485.33	13,059.43	--	27,006.13
06/01/95 - 06/30/95	13,001.75	64.00	499.89	13,451.60	--	27,817.24
		-----	-----	-----	-----	-----
		576.00	4,382.53	62,916.16	--	193,929.36
07/01/95 - 07/31/95	13,801.75	64.00	499.89	13,451.60	--	27,817.24
08/01/95 - 08/31/95	13,801.75	64.00	499.89	13,451.60	--	27,817.24
09/01/95 - 09/30/95	13,801.75	64.00	499.89	13,451.60	--	27,817.24
10/01/95 - 10/31/95	13,801.75	64.00	499.89	13,451.60	--	27,817.24
11/01/95 - 11/30/95	13,801.75	64.00	499.89	13,451.60	--	27,817.24
12/01/95 - 12/31/95	13,801.75	64.00	499.89	13,451.60	--	27,817.24
01/01/96 - 01/31/96	13,801.75	64.00	499.89	13,451.60	--	27,817.24
02/01/96 - 02/29/96	13,801.75	64.00	499.89	13,451.60	--	27,817.24
03/01/96 - 03/31/96	13,801.75	64.00	499.89	13,451.60	--	27,817.24
04/01/96 - 04/30/96	13,801.75	64.00	499.89	13,451.60	--	27,817.24
05/01/96 - 05/31/96	13,801.75	64.00	499.89	13,451.60	--	27,817.24
06/01/96 - 06/30/96	14,215.83	64.00	515.06	13,854.98	--	28,849.87
		-----	-----	-----	-----	-----
		768.00	6,013.85	161,822.58	--	334,639.31
07/01/96 - 07/31/96	14,215.63	64.00	515.06	13,854.98	--	28,649.67
08/01/96 - 08/31/96	14,215.63	64.00	515.06	13,854.98	9,780.37	38,430.04
09/01/96 - 09/30/96	14,215.63	64.00	515.06	13,854.98	9,780.37	38,430.04
10/01/96 - 10/31/96	14,215.63	64.00	515.06	13,854.98	9,780.37	38,430.04
11/01/96 - 11/30/96	14,215.63	64.00	515.06	13,854.98	9,780.37	38,430.04
12/01/96 - 12/31/96	14,215.63	64.00	515.06	13,854.98	9,780.37	38,430.04
01/01/97 - 01/31/97	14,215.63	64.00	515.06	13,854.98	9,780.37	38,430.04
02/01/97 - 02/28/97	14,215.63	64.00	515.06	13,854.98	9,780.37	38,430.04
03/01/97 - 03/31/97	14,215.63	64.00	515.06	13,854.98	9,780.37	38,430.04
04/01/97 - 04/30/97	14,215.63	64.00	515.06	13,854.98	9,780.37	38,430.04
05/01/97 - 05/31/97	14,215.63	64.00	515.06	13,854.98	9,780.37	38,430.04
06/01/97 - 06/30/97	14,641.01	64.00	530.23	14,269.57	10,073.35	39,578.16
		-----	-----	-----	-----	-----
		768.00	6,195.89	166,874.35	107,877.05	452,528.23
07/01/97 - 07/31/97	14,641.01	64.00	530.23	14,269.57	10,073.35	39,578.16
08/01/97 - 08/31/97	14,641.01	64.00	530.23	14,269.57	10,073.35	39,578.16
09/01/97 - 09/30/97	14,641.01	64.00	530.23	14,269.57	10,073.35	39,578.16
10/01/97 - 10/31/97	14,641.01	64.00	530.23	14,269.57	10,073.35	39,578.16
11/01/97 - 11/30/97	14,641.01	64.00	530.23	14,269.57	10,073.35	39,578.16
12/01/97 - 12/31/97	14,641.01	64.00	530.23	14,269.57	10,073.35	39,578.16
01/01/98 - 01/31/98	14,641.01	64.00	530.23	14,269.57	10,073.35	39,578.16
02/01/98 - 02/28/98	14,641.01	64.00	530.23	14,269.57	10,073.35	39,578.16
03/01/98 - 03/31/98	14,641.01	64.00	530.23	14,269.57	10,073.35	39,578.16
04/01/98 - 04/30/98	14,641.01	64.00	530.23	14,269.57	10,073.35	39,578.16
05/01/98 - 05/31/98	14,641.01	64.00	530.23	14,269.57	10,073.35	39,578.16
		-----	-----	-----	-----	-----
		704.00	5,892.83	186,988.27	110,806.85	436,359.76

* 1994 Office Rental based on 7,648 sq. ft. and includes the Allstate surcharge of \$228.00

** CAM expenses only - Effective 11/16/94

*** CAM expenses and rent pro-rated to reflect change effective on the 16th.

CLINICAL TRIAL AGREEMENT

This Clinical Trial Agreement ("Agreement") is entered into as of the 19 day
 of April, 1995 (the "Effective Date"), by and among Aastrom Biosciences,

Inc. ("Aastrom"), located at 24 Frank Lloyd Wright Dr., Lobby L, Ann Arbor, MI 48105, and The University of Texas M.D. Anderson Cancer Center (the "Institution"), located at 1515 Holcombe Blvd., Houston, TX 77030. Definitions shall have the meaning as set forth in Exhibit A.

RECITALS

WHEREAS, Aastrom is the developer, manufacturer and/or licensee of medical devices and materials, such as a Cell Production System ("CPS") device and related materials and device, which have potential medical application for use in subjects care and research;

WHEREAS, Aastrom desires to conduct a human clinical trial ("Study") of the CPS in subjects in accordance with a protocol entitled "Feasibility Study of Expanded Progenitor Cells for Hematopoietic Engraftment in Patients with Breast Cancer" ("Protocol") which is incorporated herein by reference as Exhibit B attached hereto;

WHEREAS, the Institution has research, clinical and medical facilities, technical capabilities and expertise in order to conduct the Study in accordance with the Protocol;

WHEREAS, the Study contemplated by this Agreement is of mutual interest and benefit to the Institution and to Aastrom such that the parties hereto desire to have the Institution conduct the Study under the qualified direction of Richard E. Champlin, M.D. (the "Principal Investigator"); and

WHEREAS, Aastrom and the Institution agree to conduct the Study in accordance with the terms and conditions hereinafter set forth.

AGREEMENT

I. CLINICAL TRIAL DESCRIPTION

The Institution agrees to undertake and complete the Study described in the Protocol in compliance with all applicable laws, rules and regulations relating to the Study, including without limitation, all laws, rules and regulations concerning or promulgated by the Food and Drug Administration ("FDA").

Aastrom agrees to loan the Institution the laboratory and clinical equipment listed in the Schedule of Laboratory and Clinical Equipment on Exhibit C which are reasonably necessary for the Institution to conduct the Study. Aastrom shall retain title to all such equipment which shall promptly be returned to Aastrom upon request by Aastrom.

II. FUNDING

Aastrom shall provide payment to the Institution in accordance with the terms contained in the Schedule of Clinical Trial Milestone Payments attached as Exhibit D and incorporated herein.

III. CONDUCT OF STUDY

A. Facilities

The Study shall be conducted only at the following location(s): The University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, Texas 77030. The CPS and other Study materials may not be transferred to any other location or to any third party without the prior written consent of Aastrom.

B. Investigator

The Institution agrees that the Study will be conducted under the direction of the Principal Investigator in accordance with the Protocol and the Investigator Agreement (included as Exhibit E of the Agreement) and incorporated herein by reference. The Principal Investigator may, subject to the prior written consent of Aastrom, designate a clinical coordinator and one or more subinvestigators to assist in conducting the Study. The Institution acknowledges that the Principal Investigator and subinvestigators have each executed an Investigator Agreement, copies of which are included in Exhibit E. In the event that additional subinvestigators are added to the Study, such subinvestigators must execute and deliver an Investigator Agreement which shall be deemed incorporated by reference into this Agreement. In the event the Principal Investigator can no longer function in such capacity, then Aastrom and the Institution shall attempt to agree on a replacement. If a mutually acceptable replacement cannot be agreed upon, this Agreement and the Study at the Institution shall terminate. The Institution agrees that it will use its best efforts to recruit qualified subjects for enrollment in the Study consistent with the guidelines contained in the Protocol and the best interest of the subjects; however, no subjects shall be enrolled in the Study if they are currently enrolled in another investigational study without the prior written consent of Aastrom.

C. Compliance with Protocol

Any changes to the Protocol may only be made with the prior written agreement of Aastrom; provided that during the Study, if the Principal Investigator feels that it is necessary to deviate from the Protocol in order to protect the life or physical well-being of a Study subject before written approval can be obtained, he/she may do so in accordance with the procedures detailed in the Protocol.

D. Institutional Review Board Approval and Informed Consent

The Institution will obtain: (i) the approval of the governing the Institutional Review Board ("IRB") prior to initiating the Study and thereafter as required by applicable laws, rules and regulations; and (ii) prior written informed consent of all subjects and/or their legal guardians in a form that is substantially the same as provided in the Protocol and satisfactory to both the governing IRB and Aastrom and in compliance with applicable laws, rules and regulations.

E. Adverse Events

The Institution shall immediately notify Aastrom (Dr. Thomas E. Muller at 313/930-5555 and/or by fax at 313/665-0485) of any unanticipated adverse effect, whether ascribed to the investigational device or not, in accordance with instructions provided in the Protocol.

IV. STUDY MONITORING AND ACCESS TO FACILITIES

Aastrom's designated representatives and/or authorized representatives of regulatory agencies may, at all reasonable times, visit the Institution in order to: (i) determine the adequacy of the facilities; (ii) validate case reports against original data in the subject medical records and the files of the Principal Investigator; and (iii) monitor the conduct of the Study to determine whether the Study is being conducted in compliance with the Protocol and all applicable laws, rules and regulations. The Institution agrees to obtain any required subject release(s) to allow Aastrom's designated representatives, and/or authorized representatives of regulatory agencies, to conduct such review prior to enrolling each subject in the Study.

V. REPORTS

The Institution agrees to have the Principal Investigator submit reports to Aastrom and the reviewing IRB in accordance with the Protocol and all applicable laws, rule and regulations.

VI. PROPRIETARY RIGHTS

A. Data and Materials

The Institution understands and agrees that the underlying rights to the CPS and other intellectual property and materials which are the subject of the Protocol belong to Aastrom. The parties agree that the Institution shall retain control over the CPS and Study materials, and further agree not to allow access to, disclose the existence or nature of, or transfer the CPS or Study materials to third parties without advance written approval of Aastrom. Aastrom reserves the right to distribute the CPS and Study materials to others and to use them for its own purposes. Title to the CPS and Study materials shall remain with Aastrom. Further, the Institution agrees that data and materials derived as a direct result of the Study described in the Protocol (hereinafter referred to as "Clinical Trial Information") whether generated by the

Institution, the Principal Investigator, and/or their agents or employees, either solely or jointly with others, is the property of Aastrom; provided that the Institution and the Principal Investigator may utilize the Clinical Trial Information in furtherance of academic publications authorized by this Agreement and for subject care purposes.

B. Patent Ownership and Related Matters

The Institution agrees that the Study results and any inventions or discoveries by the Institution, the Principal Investigator or their agents or employees during the Study that are modifications, improvements or new uses applicable to the CPS or that are a direct result of the performance of the Study in accordance with the detailed testing Protocol provided by Aastrom to Institution and which are dependent on, or relate to, the Study, the claims of Aastrom's patentable inventions, the use of the cells processed through the CPS or Aastrom's Confidential Information shall be the property of Aastrom. Any invention arising out of the work performed under this Study solely by the Institution and not covered in the previous sentence shall be the exclusive property of the Institution (the "Institution Invention") and shall not be considered a part of Aastrom's Confidential Information. The Institution shall promptly disclose each such Institution Invention and the terms under which the Institution would be prepared to license it. Aastrom shall have a right of first refusal to exclusively develop, license and commercialize such Institution Invention. Aastrom shall have sixty (60) days after receipt of such disclosure to exercise its right of first refusal, and if so exercised, the parties shall thereafter negotiate a mutually acceptable licensing agreement in good faith. If the Institution at any time offers such Institution Invention on terms different than those disclosed to Aastrom, the Institution shall offer such Institution Invention to Aastrom on such different terms in accordance with the first right refusal herein. The Institution and Principal Investigator shall not obtain, or attempt to obtain, patent coverage on the CPS or its use without the express written consent of Aastrom. The Institution and the Principal Investigator shall assist Aastrom in prosecuting any Aastrom patent applications and shall execute and deliver any and all instruments necessary to make, file and prosecute all such applications, divisions, continuations, continuations-in-part or reissues thereof.

VII. WARRANTIES AND REPRESENTATIONS

A. No Warranties

It is understood that the CPS is experimental in nature, has not been approved for commercial distribution and is provided hereunder for investigational purposes only. NEITHER THE INSTITUTION NOR AASTROM MAKES ANY REPRESENTATIONS OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING ANY REPRESENTATION WITH RESPECT TO SAFETY, EFFICACY, MERCHANTABILITY, FITNESS FOR ANY PURPOSE OR NON-INFRINGEMENT OF ANY INTELLECTUAL PROPERTY RIGHTS, WITH RESPECT TO THE PRODUCT OR INFORMATION PROVIDED TO THE OTHER HEREUNDER.

B. Representations of the Parties

Each party hereto represents that it has right to enter into and perform its respective obligations under this Agreement.

C. Representations by the Institution and the Principal Investigator

The Institution represents that: (i) it has adequate facilities and staff to conduct the Study in accordance with the Protocol; (ii) the governing IRB is qualified to review and approve the Study; and (iii) the Principal Investigator is qualified by education and training to conduct the Study and has not been disqualified, or otherwise limited, as a clinical investigator by the FDA or any other regulatory or administrative body. The Institution represents that the Principal Investigator and all other investigators and personnel that may perform services hereunder are its employees and shall abide by the terms and conditions of this Agreement as if each were a party hereto.

VIII. LIMITATIONS OF LIABILITY

In no event shall any party be liable to the other party hereto for any incidental, special or consequential damages.

IX. INDEMNIFICATION

A. Indemnification of Aastrom

Aastrom agrees to indemnify, defend and hold harmless the Institution, the University of Texas System, and their Regents, officers, agents and employees from and against any and all claims, suits, and liabilities (collectively "Liabilities") arising out of or resulting from the activities to be carried out pursuant to the obligations of this Agreement, including but not limited to the use by Aastrom of the results of the Study; provided that such Liabilities do not arise from:

- i. a failure to adhere to the Protocol or written instructions relative to use of the CPS or other materials utilized in the Study;
- ii. a failure to comply with any applicable law, rule or regulation relating to the Study, including without limitation, all FDA regulations or other governmental requirements; or
- iii. the negligence or willful misconduct by the regents, officers, agents or employees of the Institution or the University of Texas System.

B. Indemnification by the Institution

The Institution agrees, to the extent allowed by the Constitution and the laws of the State of Texas, to indemnify, defend and hold harmless Aastrom and its directors,

officers, agents and employees from and against any and all liabilities they may suffer in connection with the Study which arise out of the negligent acts or omissions of the Institution, its employees or agents pertaining to the activities to be carried out pursuant to the obligations of this Agreement; provided, however, that Institution shall not hold Aastrom harmless from claims arising out of the negligence or willful malfeasance of Aastrom, its directors, officers, agents or employees, or any person or entity not subject to Institution supervision or control.

C. Notification

The Institution and Aastrom each agree to notify the other in writing as soon as they become aware of a claim or action and to, subject to the statutory duties of the Texas Attorney General, cooperate with the management and defense of such claim or action. The indemnifying party agrees, at its own expense, subject to the statutory duties of the Texas Attorney General, to provide attorneys of its own selection to defend against any actions brought or filed against the indemnified party with respect to the subject of indemnity contained herein. The indemnifying party shall, subject to the statutory duties of the Texas Attorney General, control the defense of any action; however the indemnified party may, at its own expense, participate by providing attorneys of its own selection. No indemnified party shall compromise or settle any claim of action without the prior written approval of the indemnifying party.

X. RESTRICTIONS ON USE; COMPLIANCE WITH LAWS

The Institution and the Principal Investigator agree that the CPS will be used for clinical research purposes only in connection with the Study by the Principal Investigator and his/her subinvestigators at the facility(ies) described in Section III.A. under suitable containment conditions. Neither the Institution nor the Principal Investigator shall use the CPS for any commercial purposes, including screening, production or sale. The CPS will not be used in the treatment or diagnosis of human or animals except for the purpose of conducting the Study as described in the Protocol. The Institution agrees to comply with all laws, rules and regulations applicable to the Study and the handling, use and disposal of any Study materials. The CPS is to be used with caution and prudence since all of its characteristics are not known.

XI. CONFIDENTIALITY

A. Treatment of Confidential Information

The Institution agrees that it will not disclose or use Confidential Information for any purpose other than the purpose of conducting the Study, obtaining any required review of the Protocol or its conduct, or ensuring proper medical treatment of any subject or subject. The Institution agrees to limit distribution of Aastrom's Confidential Information to Institution personnel on a need-to-know basis. The Institution agrees to ensure that its personnel abide by the confidentiality obligations as set forth herein in accordance with Section VII.C. The obligations set forth in this Section XI.A. shall survive for a period of five (5) years following the termination or expiration of this Agreement.

The term "Confidential Information" shall mean any and all oral, written or tangible proprietary or confidential ideas, inventions, information, data, plans, materials and know-how or the like owned, controlled or developed by Aastrom and disclosed to Institution. Aastrom shall attempt to identify the confidential status of Confidential Information disclosed hereunder, but the failure to so mark or identify shall not destroy the confidential nature of such Confidential Information. Without limiting the generality of the foregoing, Confidential Information shall include, without limitation, all clinical trial plans, protocols, information, data analyses, proprietary equipment, and materials related to the Confidential Information. Confidential Information shall not include any information which the Institution can demonstrate:

- i. Was known to the Institution prior to receipt from Aastrom, provided that the Institution promptly notifies Aastrom in writing of the same promptly after disclosure by Aastrom;
- ii. Is or becomes part of the public domain through no act by or on behalf of the Institution;
- iii. Was lawfully received by the Institution or the Principal Investigator from a third party who had a legal right to disclose the same; or
- iv. Is required by law or regulation to be disclosed.

In the event that Confidential Information is required to be disclosed pursuant to subsection iv., the Institution will notify Aastrom to allow Aastrom to assert whatever exclusions or exemptions may be available to it under such law or regulation.

B. Publicity

No publicity, news releases, or other public announcement, written or oral, relating to the Agreement, to any amendment hereto or to performance hereunder or to the existence of an arrangement between the parties, shall be originated by either party without the prior written approval, such approval not to be unreasonably withheld, of the other party except as shall be required by law.

C. Use of Name

No Party shall use or publicly disclose the name of another party hereto without the prior written consent, such consent not to be unreasonably withheld, of such other party except that the name of a party may be disclosed to regulatory bodies such as the FDA, Securities and Exchange Commission or as required by law.

XII. PUBLICATION RIGHTS

At least thirty (30) days prior to submission for publication, the Institution agrees to provide Aastrom a final draft of any manuscript describing the results obtained by the Institution from

the Study. Aastrom shall be permitted to advise as to the implications of such manuscripts upon patentability of any inventions or the potential effects on commercialization. The Institution shall, upon Aastrom's request, delete any of Aastrom's Confidential Information and shall consider all reasonable editorial suggestions based on sound scientific and clinical judgment. Aastrom acknowledges that Institution shall have the final authority to determine the scope and content of any publication, provided that such authority shall be exercised with reasonable regard for the commercial interests of Aastrom. Subject to Aastrom's right to delete such Confidential Information and to propose mutually agreeable modification of such manuscripts, the Institution shall have the right to submit the manuscript for publication. However, if Aastrom determines that any invention disclosed therein is patentable and that a patent application should be filed on such invention, Aastrom shall so notify the Institution in writing and the Institution shall postpone publication for a period not to exceed sixty (60) days from said notice (unless otherwise mutually agreed in writing) to provide time for patent applications to be filed.

XIII. TERM AND TERMINATION

A. Term

Except as otherwise provided in this section, this Agreement shall commence on the Effective Date hereof and continue for the period necessary to satisfy the requirements of the Protocol.

B. Termination

Aastrom and the Institution shall have the right to terminate this Agreement at any time without cause upon thirty (30) days prior written notice. Any party may terminate the Study at any time if, in its option, it is in the best interest of the Study subjects.

C. Termination Obligations

Any termination of this Agreement shall not relieve any party hereto of any obligation or liability accrued hereunder prior to such termination, or rescind or give rise to any right to rescind anything done hereunder prior to the time such termination becomes effective; nor shall such termination relieve any party from any obligation which, by its nature, survives termination including the obligations set forth in Articles IV through IX, XI and XIV.D.

The parties further agree that all Study data and used and unused Study equipment, materials and supplies, including the CPS, provided to the Institution by Aastrom for the purpose of this Study will be returned to Aastrom promptly upon request by Aastrom.

XIV. MISCELLANEOUS

A. Independent Contractor

The Institution recognizes and agrees that it is operating as an independent contractor and not as an agent of Aastrom. The Agreement shall not constitute a partnership or joint venture, and no party may be bound by the other to any contract, or make any representations or warranties, express or implied, on behalf of another party, or otherwise create any liability against another party in any way for any purpose.

B. Assignment

The rights and obligations of the parties under this Agreement shall bind and inure to the benefit of the successors, assigns and transferees of the parties; provided, however, this Agreement shall not be assignable by either party without the prior written consent of other party.

C. Governing Law

This Agreement shall be construed and interpreted in accordance with and governed by the laws of the State of Texas.

D. Alternative Dispute Resolution

Any controversy or claim arising out of or relating to this Agreement or the breach thereof, including, without limitation, disputes relating to patent validity or infringement arising under this Agreement, shall be settled through use of an appropriate method of Alternative Dispute Resolution, including, without limitations, by arbitration in accordance with the rules of the American Arbitration Association, and judgment upon an award rendered may be entered in any court having jurisdiction thereof. Notwithstanding the foregoing, the parties shall be entitled to petition any court of competent jurisdiction in the event of any alleged breach of Article XI.

E. Entire Agreement; Modification

This Agreement contains the entire agreement and understanding between the parties and supersedes all prior agreements and understandings between them relating to the subject matter hereof.

F. Headings

The headings of this Agreement are to facilitate reference only, do not form a part of this Agreement and shall not effect the interpretation thereof.

G. Severability

If any provision of this Agreement or portion of this Agreement shall be construed to be a waiver of any other breach of the same or any other provision.

H. No Waiver

No waiver of a breach by a party of any provision of this Agreement shall be construed to be a waiver of any other breach of the same or any other provision.

I. No Implied License

No right or license to the CPS or to its use is granted by Aastrom or implied as result of the transmission of the CPS to the Institution under the supervision of the Principal Investigator, except to the limited extent necessary to conduct the Study. The transfer of the CPS provided for herein does not constitute a public disclosure.

J. Necessary Acts

At the request of Aastrom, the Institution and the Principal Investigator shall execute any documents and take any actions which may be necessary, in the opinion of Aastrom, or its legal counsel, to evidence or perfect any rights of Aastrom hereunder.

K. Counterparts

This Agreement may be executed in counterparts all of which together shall constitute one and the same instrument.

L. Notices

All notices and other communications permitted or required under this Agreement shall be in writing and shall be deemed to have been given when received at the addresses set forth on the signature page hereof, or at such other address as may be specified by one party in writing to the other. Said written notice may be given by mail, telecopy, rush delivery service, telegram, telex, personal delivery or any other means to the parties at the addresses as follow:

If to the Institution:

Donna S. Gilberg, CPA
Manager, Sponsored Programs
The University of Texas
M.D. Anderson Cancer Center
1515 Holcombe Blvd.
Houston, TX 77030

If to the Principal Investigator:

Richard E. Champlin, M.D.
The University of Texas
M.D. Anderson Cancer Center
1515 Holcombe Blvd.
Houston, TX 77030

If to Aastrom:

Thomas E. Muller, Ph.D.
Aastrom Biosciences, Inc.
24 Frank Lloyd Wright Drive, Lobby L
Ann Arbor, MI 48105

IN WITNESS WHEREOF, the parties hereto have caused this Agreement to be duly executed as of the date and year first above written.

INSTITUTION:

AASTROM:

THE UNIVERSITY OF TEXAS
M.D. ANDERSON CANCER CENTER

AASTROM BIOSCIENCES, INC.

By: /s/ DONNA S. GILBERG

By: /s/ R. DOUGLAS ARMSTRONG

Donna S. Gilberg, CPA
Manager, Sponsored Programs

Name:
Title: President/CEO

Date: 5/10/96

Date: 5/20/96

I have read this agreement and understand
my obligations hereunder:

By: /s/ RICHARD E. CHAMPLIN

Richard E. Champlin, M.D.
Principal Investigator
Interim Chairman, Dept. Of Hematology

By: /s/ ROBERT C. BAST

Robert C. Bast, Jr., M.D.
Head, Division of Medicine

EXHIBIT A
DEFINITIONS

1. Aastrom Aastrom shall have the meaning as set forth in the first

paragraph of this Agreement.
2. Clinical Trial Information Clinical Trial Information shall have the

meaning as set forth in Section VI.A. of this Agreement.
3. Confidential Information Confidential Information shall have the meaning

as set forth in Section XI.A.
4. CPS The CPS means the Cell Production System developed by Aastrom for the

ex vivo growth and expansion of human stem and hematopoietic progenitor
cells. The CPS consists of : (a) a disposable bioreactor where the growth
and expansion of cells takes place; (b) disposable growth medium as
required by the cell culture (to which specified growth factors and
glutamine are added); and (c) disposable harvest regents which facilitate
the removal of the expanded cells from the cell cassette.
5. Effective Date The Effective Date shall have the meaning as set forth in

the first paragraph of this Agreement.
6. FDA FDA shall have the meaning as set forth in Article 1 of this

Agreement.
7. Institution Institution shall have the meaning as set forth in the first

paragraph of this Agreement.
8. Institution Invention Institution Invention shall have the meaning set

forth in paragraph VI.B. of this Agreement.
9. Principal Investigator Principal Investigator shall have the meaning as

set forth in the Recitals on page 1 of this Agreement.
10. Protocol Protocol shall have the meaning as set forth in the Recitals on

page 1 of this Agreement.
11. Study Study shall have the meaning as set forth in the Recitals on page 1

of this Agreement.

EXHIBIT B

PROTOCOL

THE UNIVERSITY OF TEXAS
M.D. ANDERSON CANCER CENTER

DIVISION OF MEDICINE

CLINICAL FEASIBILITY STUDY OF EXPANDED PROGENITOR CELLS FOR
HEMATOPOIETIC ENGRAFTMENT IN PATIENTS WITH BREAST CANCER

- 1.0 OBJECTIVES
- 2.0 BACKGROUND
- 3.0 BACKGROUND DRUG AND DEVICE INFORMATION
- 4.0 PATIENT ELIGIBILITY
- 5.0 TREATMENT PLAN
- 6.0 PRETREATMENT EVALUATION
- 7.0 STUDY PROCEDURES AND EVALUATIONS
- 8.0 DATA COLLECTION
- 9.0 ADVERSE EVENTS
- 10.0 STATISTICAL CONSIDERATIONS AND DATA ANALYSIS
- 11.0 CLINICAL SUPPLIES
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- 13.0 INVESTIGATOR OBLIGATIONS
- 14.0 REFERENCES
- APPENDIX A: TOXICITY CRITERIA
- APPENDIX B: PATIENT EVALUATION
- APPENDIX C: ZUBROD PERFORMANCE STATUS
- APPENDIX D: INFORMED CONSENT
- APPENDIX E: CASE REPORT FORMS

STUDY CHAIRMAN:

- - - - -
Richard Champlin, M.D.

STUDY CO-CHAIRMAN:

- - - - -
Rakesh Mehra, M.D. James Gajewski, M.D.

STUDY COLLABORATORS:

----- Gabriel Hortobagyi, M.D.	----- Zia Rahman, M.D.
----- David Seong, M.D.	----- David Claxton, M.D.
----- Borje S. Andersson, M.D., Ph.D.	----- Koen van Besien, M.D.
----- Donna Przepiorka, M.D., Ph.D.	----- Martin Korbiling, M.D.

The Section of Blood and Marrow Transplantation, Departments of Hematology and Medical Breast and Gynecologic Oncology, Division of Medicine, The University of Texas, M.D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, Texas 77030. Telephone: 713-792-3611 or 713-792-2684.

PROTOCOL ABSTRACT

Protocol:

FEASIBILITY STUDY OF EXPANDED PROGENITOR CELLS FOR HEMATOPOIETIC ENGRAFTMENT IN PATIENTS WITH BREAST CANCER

Study Chairman: Richard Champlin, M.D.

OBJECTIVES:

Assess the safety of the mixture of early- mid- and late stage bone marrow derived mononuclear cells produced in the Cell Production System (CPS) (primary objective and the biologic effect on hematopoietic recovery after infusion of ex vivo expanded hematopoietic cells following high dose chemotherapy as treatment of patients with breast cancer.

RATIONALE:

High dose chemotherapy is increasingly used for treatment of malignancies. Despite infusion of autologous bone marrow or PBPC, patients experience at least one week of profound pancytopenia prior to engraftment and hematologic recovery. Recently technology for expansion of hematopoietic progenitors ex vivo has been developed and we performed a study showing no toxicity and rapid hematopoietic recovery when given in addition to autologous bone marrow. The expansion systems produces large numbers of progenitors similar to that present in full autologous marrow graft and the expansion conditions do not support the growth of malignant cells, thus the system acts to purge contaminating tumor cells from the autologous graft. Preliminary studies suggest that infusion of large numbers of expanded cells may modify the nadir of granulocytopenia and potentially reduce infectious complications. Recently, Brugger et al reported rapid engraftment and hematopoietic recovery using ex vivo expanded cells alone. This study is designed to assess hematopoietic recovery after high dose chemotherapy and infusion of cells expanded using the Aastrom expansion device.

ELIGIBILITY:

Female patients age 18- 65 years with diagnosis of Stage IV breast carcinoma who are not eligible for protocols of higher priority and who have received no more than one chemotherapy regimen for metastatic disease, with chemotherapy responsive or stable disease at the time of study entry. Zubrod performance status 0 or 1. Patients must be HIV negative and have a creatinine less than or equal to 1.5 mg/dl, SGOT, SGPT, & bilirubin less than 2 x normal, normal cardiac ejection fraction and DLCO greater than 50% of predicted. Patients must have WBC greater than 3,000/mm³. Women of childbearing potential must have a negative pregnancy test within 3 weeks of initiation of therapy. Exclusion Criteria include: History of central nervous system (CNS) disease; Concurrent involvement in any other clinical trial that affects engraftment (e.g. other hematopoietic growth factors); Previous pelvic radiotherapy; Previous treatment with mitomycin-C or carmustine (BCNU); any co-morbid conditions which, in the view of the principal investigators, renders the patient at high risk from treatment complications; bone marrow involvement with tumor at the time of marrow harvest as demonstrated by standard histopathological examination of bilateral iliac marrow biopsies.

TREATMENT PLAN:

Prior to planned marrow transplant, 2.25×10^8 mononuclear cells are inoculated into 3 Aastrom expansion devices and expanded ex vivo over the next 12 days. Patients receive the following pretransplant regimen: Cyclophosphamide 2.0 gm/m²/ IV days -7, -6, -5; Thiotepa 240 mg/m²/IV days -7, -6, -5; Benu 150 mg/m²/ days -7, -6, -5 with reinfusion of the ex vivo expanded cells on day 0. Patients with WBC less than .2 by day 12 or less than .5 by day 16 or less than 1.0 after day 21 or platelets less than 20×10^9 /l by day 28 or with later graft failure will receive backup bone marrow, harvested using standard techniques with greater than 0.5×10^6 CD34 positive cells/kg. SEE PROTOCOL FOR COMPLETE TREATMENT PLAN

STATISTICAL CONSIDERATION:

10 patients will be treated and receive infusion of ex vivo expanded cells to meet the objectives of the study, to the toxicity and biologic effects of these cells on engraftment.

PATIENT EVALUATION:

Pretreatment evaluation will consist of: complete history, physical

examination, and CBC, diff and platelet count, SMA, cardiac ejection fraction, DLCO, HIV, hepatitis panel. HTLV1, pregnancy test in women of childbearing potential, bilateral bone marrow aspirate and biopsy tumor staging (bone scan with X-ray of hot spots, CXR, CT scan of chest and abdomen, and CEA). Evaluation following high dose chemotherapy and autologous blood stem cell

transplantation: CBC, diff, platelet counts daily while hospitalized and at

least twice per week as an outpatient until WBC greater than 3000/mcl and platelets greater than 100,000/mcl. SMA twice per week while hospitalized. Tumor restaging as indicated including bone scan with X-ray of hot spots, CXR, CT scan of abdomen, and CEA at 60 days and as indicated thereafter.

ESTIMATED ACCRUAL

10 patients will be required. It is estimated that 2 patients per month will be accrued: this study accrual will be completed within 6 months.

SITE OF STUDY:

This protocol will be performed in patients both inpatients and outpatients

LENGTH OF STAY:

The total time in hospital is approximately three weeks. This does not represent an increase over the current standard of care for PBPC mobilization and transplantation.

RETURN VISITS:

Patients return to MD Anderson daily to three times per week during the granulocytopenic phase of this treatment up to 28 days post PBPC transplant. Thereafter, they are seen as per standard practice for disease reassessment and long term follow up.

HOME CARE:

None, other than outpatient care monitored at MDACC.

WHERE WILL THE STUDY BE CONDUCTED?

Only MDACC

NAME OF SPONSOR OF FUNDING SOURCE

Astrom Corporation

COMPETING PROTOCOLS

This protocol is the follow-up to DM94-127.

NAME OF RESEARCH NURSE/DATA MANAGER

Marilyn Davis, R.N.

1.0 OBJECTIVE

Assess the safety of the mixture of early-, mid-, and late-stage bone marrow-derived mononuclear cells produced in the CPS (primary objective), and the biological effect in terms of hematopoietic recovery after infusion of ex vivo-produced hematopoietic cells following high dose chemotherapy as treatment of patients with breast cancer.

2.0 BACKGROUND

Autologous bone marrow transplantation has been increasingly employed as supportive therapy for subjects undergoing high dose chemotherapy or chemoradiotherapy for malignant diseases, including lymphoma, leukemia, and breast cancer. Breast cancer is now the most frequent indication for autologous bone marrow or blood progenitor cell transplantation.

Despite the use of cytokines such as granulocyte-macrophage colony-stimulating factor (GM-CSF) and granulocyte colony-stimulating factor (G-CSF) following bone marrow reinfusion, there is an obligate period of profound pancytopenia lasting 1-3 weeks, and delayed engraftment can occur, resulting in morbidity or mortality.

The safety, comfort, and cost of stem- and progenitor cell harvest are also concerns. The standard techniques employed to harvest bone marrow involves obtaining 500-1500 mL of bone marrow from the marrow donor, usually under general anesthesia. In addition to the discomfort caused by the hundreds of marrow aspirates performed, donors are subject to the risks of general anesthesia. Finally, the bone marrow harvest procedure is expensive. Alternatively, stem - and progenitor cells can be collected from peripheral blood by apheresis, but this requires chemotherapy and/or growth factors for mobilization and multiple collections are generally necessary, which are costly.

Recently, novel technology has been developed to produce stem- and progenitor cell populations in vitro, commonly referred to as ex vivo expansion. Hematopoietic cell expansions achieved with this technology are based upon the principles of continuous perfusion culture, a bioengineered metabolic environment, augmented by hematopoietic growth factors. Through this technology, a small bone marrow or peripheral blood mononuclear cell population can be perfused ex vivo so that total cell numbers, colony forming units (CFUs) and long term culture initiating cells (LTC-ICs) increase up to 20 fold (1-17). In a preliminary study, Brugger et al

recently reported that expanded cells alone can reconstitute hematopoiesis after high dose chemotherapy (18).

Important differences exist among approaches, systems and devices used for ex vivo expansion. This study utilizes the Aastrom CPS, which includes a cell

culture device and a biological environment designed to allow the establishment of a stromal adherent layer, using constant perfusion with medium, and relatively low concentrations of hematopoietic growth factors. Preliminary studies at MD Anderson Cancer Center (DM94-127), using transplantation of ex vivo-produced cells prepared with this system, in combination with a standard autologous marrow transplant, indicate that ex vivo expansion can be performed reliably and reproducibly, and that no toxicity occurs with intravenous infusion (19). Ten patients, age 18-60 years with breast carcinoma, were entered into a study transplanting bone marrow plus ex vivo-produced cells. Bone marrow was harvested, collecting greater than 2×10^8 /nucleated cells/kg and greater than 0.5×10^6 /CD34+ cells/kg. Twelve days prior to the planned bone marrow transplant, 2.25×10^8 /mononuclear cells were inoculated into a cell culture device, part of the CPS, and continuously perfused with medium containing PIXY321 (5 ng/ml), Epo (0.1 U/ml) and hydrocortisone (5×10^{-6} M). The expansion reproducibly increased total nucleated cells, CFU-GM, and long term culture initiating cells (LTC-IC). Patients received Cyclophosphamide 2.0 g/m²/d; Thiotepa 240 mg/m²/d; BCNU 150 mg/m²/d, Days -7, -6, -5, with reinfusion of the cryopreserved bone marrow on Day 0 plus the ex vivo-produced cells four hours later. No toxicity was observed from the expanded cell infusion. Nadir WBC was less than 0.1/ul. All patients engrafted within narrow time ranges, with median recovery of WBC greater than 200/ul on Day 8 (range 7-8) granulocytes greater than 500/ul on Day 11 (range 10-13) and platelets greater than 25,000/ul on Day 16 (range 13-21) and greater than 50,000 on Day 20 (range 18-27). A median of 4 (range 1-9) platelet and 4 (range 2-9) RBC transfusions were administered. No grade greater than 2 toxicity occurred from the chemotherapy or bone marrow infusions. Four patients had infections unrelated to the infusion of the cells produced in the CPS. These data compare favorably with 29 historical controls receiving the same chemotherapy and autoBMT without cell expansion, in which granulocytes recovered to greater than 500 on Day 11 (range 7-29) and platelets to greater than 25,000 and greater than 50,000 on Days 24 (range 9-78) and 28 (range 9-147), respectively.

A potential advantage of collecting a relatively small marrow inoculum is that the number of contaminating malignant cells is reduced; additionally, growth of breast cancer cells is not stimulated under these expansion conditions (Brugger et al).

Application of this technology to autologous bone marrow and peripheral stem cell transplant offers a potentially attractive means to increase the efficacy and safety of autologous transplantation, while reducing its complexity and cost. In particular, this technology could eliminate the need for operative bone marrow harvests, produce more rapid recovery of hematopoiesis post-transplant, reduce the length of post-transplant hospitalization, and could increase the purity of the stem- and progenitor cells transfused. In addition, the inclusion of cytokine-primed progenitors could result in accelerated hematopoietic recoveries.

2.1 PREVIOUS PRE-CLINICAL RESEARCH

During hematopoietic expansion culture, total cell numbers increase 8 to 11-fold over 12 days. This includes nonadherent, loosely adherent, and tightly adherent cells. Over 80% of the nucleated cells are viable, as shown by exclusion of propidium iodine stain (4) or Trypan blue dye. These cells have the morphological distribution of normal bone marrow cells, including blast cells and maturing granulocyte precursors, maturing erythroid cells, monocytes and macrophages.

These expanded cells also show typical immunophenotype characteristics of normal granulocyte, erythroid, monocyte/macrophage megakaryocytic, and blast cells (5). Cell surface antigens identified using this technique include CD3, CD11b, CD15, CD20, CD33, CD71, and glycophorin A. While there are minor variations in staining patterns from sample to sample, the expanded cells are typically less than 3% CD3+, 20-50% CD11b+, less than 1% CD19+, and 40-70% CD71+. The frequency of mature T and B lymphocytes in the expanded cell population is significantly reduced.

As shown in the experiments summarized in the Table below, it was shown by Aastrom that varying the standard growth factor combination (IL-3+GM-CSF or PIXY321, Epo, SCF and flt3L) had a direct effect on the productivity of cells in the CPS, but the relative cell mixture composition remained substantially similar. These data were obtained in 36-well plate studies. This finding provided the original justification for selecting the growth factor combination (Epo + PIXY321 + flt3L) for this study to yield the desired relative composition and mixture of early-, mid- and late-stage cells produced in the pre-clinical experiments.

Growth Factors	Product/cm/2/			
	CellsX10/6/	CFU-GM	LTC-IC	n
None	0.58	404	yes/a/	7
Epo, GM-CSF, IL-3, SCF	2.35	4,790	48	23
Epo, GM-CSF, IL-3	1.13	2,060	yes/a/	3
Epo, PIXY, SCF	1.72	6,960	yes/a/	4
Epo, PIXY	1.31	3,140	94	13
Epo, PXY, flt3L	1.57	10,580	108	14

/a/LTC-IC were not evaluated, but in these conditions, 24 week CFU-GM producing cultures were obtained, representing an LTC-IC proxy.

Aastrom has projected, based on this pre-clinical research, that clinical-size CPSS are expected to yield a mean of 3.0×10^9 cells, 17.7×10^6 CFU-GM and 6.4×10^5 LTC-IC per patient cell yield from the CPS at 1.6×10^9 total nucleated cells and 7.0×10^6 CFU-GM. In an average 70 kg patient, this translates to a dose of 2×10^6 CFU-GM/kg. The clinically standard ABMT engrafting dose is reported to be 1×10^5 CFU-GM/kg. Therefore, using the cell dose and the CFU-GM content in the cells produced in the CPS as a key progenitor marker, along with the reliable presence of early stage cells (e.g., LTC-IC, CD34+lin-), there is an expectation that the CPS-produced cells should provide a minimum full engrafting dose for these subjects, with a greater number expected for most patients. Should the minimum cell number, 1.6×10^9 , not be attained, the cryopreserved back-up cells will be reconstituted and administered to a subject on Day 0.

It is anticipated that infusion of ex vivo-produced progenitors generated with the CPS will enhance engraftment and shorten time to recovery of granulocytes and platelets and, in so doing, reduce the incidence of infections, febrile episodes and the need for blood- and platelet transfusions.

2.2 HIGH DOSE CHEMOTHERAPY AND AUTOLOGOUS BONE MARROW TRANSPLANT FOR METASTATIC BREAST CANCER - MD ANDERSON PROGRAM

Breast cancer is responsive to initial combination chemotherapy for metastatic disease with a 50-80% response rate and a 10-20% complete response rate, but few patients are cured and median duration of response is generally less than one year (20-24). Once patients relapse, the response to second-line therapy is 20-40% with very few complete responses (CR) and a median duration of response of 2-3 months and a median survival of 12 months.

When patients with metastatic breast cancer receive high-dose chemotherapy, there is substantially higher complete response rate than that can be achieved with conventional treatment (25-38). Peters et al (39) used a regimen of Cyclophosphamide, Cisplatin, and BCNU or Melphalan in 22 ER-negative patients without prior induction chemotherapy, and reported a 54% CR rate and an overall response rate of 73% and a median duration of response of 7 months from the time of transplant. Antman et al recently reported similar results with a

combination of high-dose Carboplatin, Cyclophosphamide and Thiotepa (26); each study reported approximately 20% 5-year disease-free survival. Application of the same therapy to patients with Stage II breast cancer with greater than or equal to 10 positive nodes or Stage III disease has resulted in approximately 70% 5-year disease-free survival, substantially higher than that reported with standard adjuvant therapy in such patients.

Studies from a number of drug-resistant cell lines suggest that different alkylating agents may not be cross-resistant, particularly if they interact with

DNA at different sites, or if the alkylating agent previously used may have specific mechanisms of resistance (such as exaggerated levels of aldehyde dehydrogenase) in tumor cells resistant to Cyclophosphamide. Cyclophosphamide and Thiotepa have been shown to have synergistic activity against human breast cancer in preclinical models (40). These two agents have been used together in high dose therapy with the reported MTD being 6g/m²/ of Cyclophosphamide with 720 mg/m²/ of Thiotepa, with severe mucositis being the dose-limiting toxicity if one attempts to increase Thiotepa dose further (41,42). None of the 17 patients treated with 6000 mg/m²/ of Cyclophosphamide and Thiotepa, in doses ranging from 180 to 720 mg/m²/ developed mucositis. Mild oral pain and erythema developed in 2/3 patients treated at the 720 mg/m²/ level of Thiotepa, and at 900 mg/m²/ 3/3 had severe life-threatening but reversible oral and esophageal mucositis. Cyclophosphamide, BCNU, and Cisplatin has been a commonly used preparative regimen at other centers for ABMT for breast cancer (33). In other studies with high dose BCNU, pulmonary complications can be avoided by lowering the dose of BCNU to 450 mg/m²/, including the CBT regimen described below.

Phase I studies of the combination of Cyclophosphamide, BCNU, and Thiotepa with autologous bone marrow transplantation in high risk patients with metastatic breast cancer (DM91-031, DM92-060 and DM92-084) were recently evaluated. The maximum tolerated dose was Cyclophosphamide 6 gm/m²/, BCNU 450 mg/m²/ and Thiotepa 720 mg/m²/. The regimen produces marked myelosuppression, but with prompt recovery using autologous bone marrow transplantation. Response rates and survival with autologous bone marrow transplantation are highly dependent on patient prognostic characteristics, such as prior disease-free interval, sites and number of metastasis, and response to prior chemotherapy. This regimen has proven to be highly active. Among patients with a partial response to chemotherapy, 52% achieved a complete response with this regimen; results were from comparable to superior to other high dose programs.

3.0 BACKGROUND DRUG AND DEVICE INFORMATION

3.1 DESCRIPTION OF THE CPS

The single-use, sealed, sterile cell culture device in the Aastrom CPS consists of three rigid plastic parts separated by a gas-permeable, water-impermeable membrane. The lower cell culture chamber is continuously perfused by growth medium. The cells expand in culture on the plastic surface of the cell culture bed. The upper cell culture chamber is provided with a constant flow of gas, such that oxygenation of the cell culture bed is accomplished by diffusion across the membrane and through the culture medium. Carbon dioxide is removed by the same mechanism. The medium used to perfuse the cultured cells is stored in a closed vessel in an adjacent refrigerator at 4 degrees C whose only external connection is by medical grade tubing. A "Y" connector, attached to the effluent line, allows sampling of the cell product prior to harvest, to test for

bacterial and fungal contaminants. A detailed device description is provided in the Operator's Manual provided by Aastrom.

3.1.1 CELL CULTURE CONDITIONS

The hematopoietic cells are suspended in tissue culture medium composed of Iscove's Modified Dulbecco's Media supplemented with 10% fetal bovine serum, 10% horse serum, hydrocortisone (5 x 10⁻⁶M), PIXY321 (5 ng/ml), glutamine (4 mM), Erythropoietin (Epo 0.1 U/ml), flt3L (5 ng/ml), gentamicin sulfate (5 Fg/ml), vancomycin (20 Fg/ml), sterile water for injection, and are inoculated into the CPS. The cells are cultured in the CPS for 12 days at 37 degrees C with the tissue culture medium continuously replaced with fresh medium. Sampling of the culture medium is carried out 48 hours prior to harvest, to allow testing for bacterial and fungal contaminants.

To harvest the cells, the non-adherent fraction is removed from the cell culture device by draining the growth medium from the cell culture device into the harvest bag. The chamber is then rinsed with 50 ml of Hank's Balanced Salt solution (HBSS) by injection of the solution with a syringe via an access port. This is followed by agitation of the cell culture device and collection of the rinse into the harvest bag. The adherent layer is detached from the cell culture bed surface by injection of 50 ml of Trypsin-EDTA solution by syringe via an access port. This is also followed by agitation of the cell production device and collection of the rinse into the harvest bag. The chamber is then given a final rinse by injecting 50 ml of HBSS with a syringe via an access port. This is followed by agitation of the cell production device and collection of the rinse into the harvest bag.

Following collection, the cells are washed free of culture medium as detailed in the Operator's Manual. The final product is suspended in appropriate media for immediate infusion.

3.1.2 CELL CULTURE MEDIA INFORMATION

Studies by Aastrom and the University of Michigan have shown that, after the cell washing regimen, the added growth factors and other reagents are below detectable limits, using a very sensitive ELISA assay (R&D Systems, Minneapolis, MN, and Immunex Research Corporation, Seattle, WA). These levels are well below the level of biological activity. The horse and fetal calf sera are tested preclinically for contamination for bacteria, fungi, mycoplasma, endotoxin and viruses. The expanded cell product is washed (See Operator's Manual) prior to transfusion. Nonetheless, the human toxicities and contraindications identified for these drugs are included below:

3.1.2.1 RECOMBINANT HUMAN EPO

Recombinant Human Erythropoietin: Epoetin Alfa, Procrit, NDC 0062-7402-01
Amgen, Thousand Oaks, CA.

Human Toxicity: Toxicities have included hypertension, headache, fever, seizures, and skin rash. The majority of these subjects had chronic renal failure, and these adverse events are frequent sequelae of chronic renal failure and were not necessarily attributable to Epo.

Contraindications: Epo is contraindicated in subjects with: uncontrolled hypertension, known hypersensitivity to mammalian-derived products, and known sensitivity to human albumin.

3.1.2.2 PIXY321

PIXY321 is a fusion protein of granulocyte-macrophage colony-stimulating factor (GM-CSF) and interleukin 3 (IL-3).

3.1.2.3 RECOMBINANT GM-CSF

Human Toxicity: Specific toxicities include peripheral edema, pleural and/or pericardial effusions, fluid retention, sequestration of granulocytes in the lung, supraventricular arrhythmia, elevation of serum creatinine, and elevation of hepatic enzymes.

Contraindications: GM-CSF is contraindicated in subjects with excessive leukemic blasts in the bone marrow or peripheral blood (greater than 10%), or with known hypersensitivity to GM-CSF, yeast-derived products, or any component of the product.

3.1.2.4 FLT3 LIGAND (FLT3L)

The manufacturer of flt3L, Immunex Research and Development Corporation, Seattle, WA, has advised that a biologic Master File is in preparation for clinical, in vivo grade flt3L, and that the Master File will be submitted to the FDA in 1996, and will be available as reference for the purposes of this clinical feasibility trial (Letter, Immunex to Aastrom, December 11, 1995).

Immunex has also advised that flt3L appeared to be well tolerated when administered to mice and monkeys for 14 days, at doses up to 400 ug/kg/day. Based on the safety profile established by Immunex, including the animal data generated to-date, flt3L has no apparent toxicities, and does not stimulate the proliferation and detrimental activation of mast cells.

As indicated above, the cells produced in the CPS are washed four times, resulting in a 5-log reduction in the presence of media components, to levels

below detectable limits. An ELISA, supplied by Immunex, is used to determine residual flt3L levels subsequent to cell washing.

3.1.2.5 HORSE SERUM

Contraindications: Known hypersensitivity to horse serum.

3.1.2.6 FETAL CALF SERUM

Contraindications: Known hypersensitivity to bovine serum.

3.1.3 INTENDED USE

The intended use of the CPS is to produce human stem- and hematopoietic progenitor cells to support subjects with compromised hematopoietic systems. A per-patient cell production procedure, beginning with 225×10^6 nucleated bone marrow cells per device, will yield at least 1.6×10^9 cells. The cells will not be infused if the cell yield is below this level; the back-up cells will be infused in such a case.

3.2 CHEMOTHERAPY DRUG INFORMATION

CYCLOPHOSPHAMIDE NSC# 26271

Synonyms (Trade names, etc.): Cytoxan, Endoxan

Therapeutic Classification: Alkylating agent

Pharmaceutical Data: Oral tablets of 25 mg and 50 mg; powder for

injection in vials of 100 mg, 200 mg, and 500 mg.

Solution Preparation: Add 5 ml sterile water for injection or normal

saline for injection to 100 mg vial, 10 ml to 200 mg vial, and 25 ml to 500 mg vial. The resulting concentrations will be 20 mg/ml. For infusion, dilute further with 100-250 ml of D5W or NS and infuse over 15-60 minutes.

Stability and Storage Requirements:

Prior to mixing: Room temperature

After mixing: Stable for 24 hours at room temperature and 6 days if refrigerated.

Routes of Administration: Oral, IV Push, IV infusion

Usual Dosage Range: Up to 2000 mg/m²/ as a single dose, repeated every 3 weeks. Smaller doses may be given more frequently. Doses of up to 1.5 gm/m²/d x 4 may be used in conjunction with bone marrow transplant.

Known Side Effects and Toxicities: Myelopsuppression (leukopenia greater than

thrombocytopenia), hemorrhagic cystitis, nausea, vomiting, alopecia, and rare
amenorrhea and azoospermia.

Special Precautions: Adequate hydration with 2-3 liters of fluid daily with

copious urine output can prevent cystitis. Due to significant renal excretion,
dose reductions must be made in patients with renal insufficiency.

Status: Commercially available

Mechanism of Action: Cyclophosphamide is considered a classical bifunctional

alkylating agent, with the predominant alkylation reaction occurring at the 7
nitrogen of guanine. Cyclophosphamide must be activated by liver microsomal
enzymes in order to damage the DNA molecule. Although active throughout the cell
cycle, the agent is most active during the S phase.

Animal Tumor Data: Cyclophosphamide exerts its greatest activity against the

Walker 256 carcinoma, Yoshida ascitic and solid sarcomas, DS-Carcinosarcoma, and
Jensen sarcoma. Activity is also noted against the leukemia L1210,
adenocarcinoma 755 and sarcoma 189 tumors.

Animal Toxicity: Hypoplastic changes in the bone marrow have been noted. Other

pathologic findings include hemorrhagic areas in the gastrointestinal tract,
bladder, and lungs. Leukopenia was observed to a greater degree than
thrombocytopenia.

Human Pharmacology: Cyclophosphamide can be given orally or intravenously,

although oral absorption is incomplete (30-60% of a dose is recoverable in the
stool). Maximum plasma levels are achieved within one hour from an oral dose.
Plasma T-1/2 is 4-6.5 hours. Approximately 60% of an intravenous dose is
recovered in the urine within 24 hours, requiring dosage adjustments in
patients with renal insufficiency. The drug is activated and subsequently
deactivated by liver microsomal enzymes.

References:

Bagley, C., et al.: Clinical pharmacology of cyclophosphamide. Cancer Res.

33:226-233, 1973. Symposium (various authors): Metabolism and mechanism of
action of cyclophosphamide. Cancer Treat. Rep. 60(4):299-525, 1976. Carter,

S.K.: Cyclophosphamide in solid tumors. Cancer Treat. Rev. 2:295-322, 1975.

THIOTEPA

Chemistry: Thiotepea, an ethylenimine derivative, is a polyfunctional

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alkylating agent. The drug occurs as fine, white, crystalline flakes having a faint odor and is freely soluble in water and in alcohol. The commercially available powder for injection contains 80 mg of sodium chloride and 50 mg of sodium bicarbonate so that, following reconstitution with sterile water for injection, solutions of the drug are isotonic. Reconstituted Thiotepea solutions containing 10 mg/mL in sterile water for injection may be clear to slightly opaque and have a pH of 7.6.

Stability: Both Thiotepea powder for injection and reconstituted solutions of the

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drug should be stored at 2-8 degree C, protected from light. Reconstituted Thiotepea solutions containing 10 mg/mL in sterile water for injection are stable for at least 5 days at 2-8 degree C; however, since the solutions do not contain a preservative, the possibility of microbiologic contamination must be considered. Solutions which are grossly opaque or contain a precipitate should not be used. Although Thiotepea is reportedly unstable in acid media, the manufacturer states that reconstituted solutions of the drug may be diluted with sodium chloride, dextrose, dextrose and sodium chloride, Ringer's, or lactated Ringer's injection. The manufacturer also states that Thiotepea solutions containing 0.5 mg/mL in Ringer's injection are stable for at least 15 days at room temperature or 2-8 degree C. Reconstituted solutions of Thiotepea are compatible with 2% procaine hydrochloride injection and/or 0.1% (1:1000) epinephrine hydrochloride injection.

Pharmacology: Thiotepea, as an alkylating agent, interferes with DNA replication

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and transcription of RNA, and ultimately results in the disruption of nucleic acid function. Thiotepea also possesses some immunosuppressive activity. Following intracavitary administration, thiotepea may control malignant effusions by a direct anti-neoplastic effect.

Pharmacokinetics:

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Absorption: Thiotepea is incompletely absorbed from the GI tract. Variable absorption also occurs through serous membranes, such as the pleura and bladder, and from IV injection sites. Absorption through the bladder mucosa may range from 10% to almost 100% of the instilled dose and is enhanced by extensive tumor infiltration or acute mucosal inflammation, following endoscopic surgical procedures or radiation therapy, and in the presence of vesicoureteral reflux. Following IV administration of Thiotepea C14, serum concentrations of radioactivity reportedly begin to decline within 10 minutes, but detectable concentrations persist 72 hours.

Distribution: It is not known if thiotepea or its metabolites are distributed into milk.

Preparations: Parenteral, for injection, 15 mg.

Carmustine

Synonyms: BCNU, BICNU

Therapeutic Classification: Nitrosourea

Pharmaceutical Data: Each vial contains 100 mg of carmustine. Each

vial is packaged with sterile diluent of 3.5 ml of absolute alcohol USP.

Solution Preparation: Dissolve carmustine first with 3 ml of alcohol

diluent. Then add 17 ml water for injection. This results in a solution concentration of 5 mg/ml with pH 5.0-6.0.

Stability and Storage Requirements: Before mixing: Store unopened

vials in refrigerator. Vials may be stored at room temperature for 1 month without significant loss of potency. Drug melts and decomposes at temperatures above 27 degrees C or 80 degrees F. After mixing: After diluted for infusion, solutions are stable for 24 hours if protected from light under refrigeration and 2 hours at room temperature without light protection.

Route of Administration: I.V. infusion only.

Usual Dosage Range: 30-300mg/m²/ per course. Upper dose range for

use as single agent, dosage lower in combination with other agents. Courses usually repeated every 6-8 weeks, or dose may be given in divided portions at 3-4 week intervals. Courses should not be repeated until recovery from toxicities of previous course is adequate.

Known Side Effects and Toxicities: The most consistent toxicities

involve the bone marrow, lymphoid tissue, kidneys, lungs, liver and GI tract.

Rapid I.V. infusion is associated with intense flushing of the skin and suffusion of the conjunctiva within 2 hours. Nausea and vomiting appear within 2 hours and generally last 4 to 6 hours. Burning at the site of infusion is common. Suppression of the peripheral blood leukocytes and platelet counts is the most severe toxic manifestation and the major dose-limiting factor. Toxicity occurs 3-4 weeks after drug administration and lasts for 2-3 weeks. Elevated SGOT, alkaline phosphatase and bilirubin can occur 28 to 38 days after treatment but is reversible. Renal toxicity as measured by unexplained elevations of BUN was present in 10% of patients but was not related to time, dose, or schedule of the drug. Pulmonary fibrosis has also been reported with long-term therapy. The associated mortality rate is high. The reaction presents either as an insidious cough and dyspnea or sudden onset of respiratory failure. Also risk of developing second malignancies (leukemia) with use of nitrosoureas.

Special Precautions: Avoid contact with skin as it might cause known staining.

Status: Commercially available.

Mechanism of Action: The mechanism of action of nitrosoureas is

assumed to be due to DNA cross linking. Carmustine is an S phase non-specific drug and inhibits DNA, and to a lesser extent, RNA synthesis. Alkylation reactions account for the major effect but it is also thought that carbamylation reactions may contribute significantly to their cytotoxicity. Rapid improvement in drug-resistant terminal Hodgkin's disease indicates its lack of cross-resistance to standard alkylating agents and vinca alkaloids, further suggesting a mode of action different than alkylation alone. It is thought that the intact molecule may not be responsible for activity, but rather may be due to one or more degradation products. Furthermore, the active agent for tumor cell killing may be different from the agent responsible for delayed bone marrow toxicity. In addition, it is known that carmustine interferes selectively with the utilization of histidine.

References:

Carmustine Drug Monograph. American Hospital Formulary Service.

4.0 PATIENT ELIGIBILITY

Female patients, age 18-65 years with diagnosis of Stage IV breast carcinoma, who have received no more than one chemotherapy regimen for metastatic disease, with chemotherapy responsive or stable disease at the time of study entry. Zubrod performance status 0 or 1. Patients must be HIV negative and have creatinine less than or equal to 1.5 mg/dl; SGOT, SGPT, & bilirubin less than 2x normal, normal cardiac ejection fraction and DLCO greater than 50% of predicted. Prior to marrow collection for ex vivo expansion, patients must have WBC greater than 3,000/mm³ and platelet count greater than 100,000/mm³. Women of childbearing potential must have a negative pregnancy test within 3 weeks of study entry.

Exclusion Criteria include: History of hypersensitivity to horse serum or fetal calf serum; central nervous system (CNS) disease within 6 months of study entry; Concurrent involvement in any other clinical trial that affects engraftment (e.g. other hematopoietic growth factors); treatment with any growth factors within one week; Previous pelvic radiotherapy rendering the marrow hypocellular; Previous treatment with Mitomycin-C or Carmustine (BCNU); any co-morbid condition which, in the view of the Principal Investigator, renders the patient at high risk from treatment complications; any evidence of bone marrow involvement with tumor as demonstrated by standard histopathological examination of bilateral iliac marrow biopsies within 4 weeks of study entry.

5.0 TREATMENT PLAN

5.1 Registration

All patients must be registered with the Data Management office at 713-792-2926 for entry on study.

5.2 Bone Marrow Harvest

Patients will undergo back-up bone marrow harvest at any time prior to initiation of the ablative chemotherapy, with cryopreservation, using standard techniques. Patients must have greater than 2×10^8 /nucleated cells per kg harvested, including greater than 0.5×10^6 /CD34+ cells/kg.

The bone marrow harvest will be performed by standard technique in an operating suite under general or epidural anesthesia. In a standard harvest, approximately 500-1500 ml of marrow is withdrawn. Patients will have the back-up bone marrow collected simultaneously with the cells for ex vivo production. If a sufficient number of cells are collected, the bone marrow collected will be processed and a small fraction utilized for the ex vivo culture described below, and the remainder of the cells will be cryopreserved per standard technique and held as a back-up for use if the prescribed number of cells is not produced or if graft failure occurs.

5.3 Ex Vivo Cell Production

As mentioned in other parts of the Protocol, at the time of bone marrow harvest, all harvested marrow will be delivered to the bone marrow laboratory for processing. A portion of the harvested marrow will be used for cell production in the CPS and the balance of the harvested marrow will be cryopreserved. Twelve days prior to the scheduled bone marrow transplant, 2.5×10^8 /mononuclear cells from freshly collected marrow will be placed into the CPS in the presence of PIXY321 (5 ng/ml), hydrocortisone (final concentration 5×10^{-6} M), glutamine (4mM), gentamicin sulfate (5 Fg/ml), vancomycin (20 Fg/ml), Epo (0.1 U/ml/day) and flt3L (5 ng/ml). The tissue culture medium will be supplemented with 10% fetal calf serum and 10% horse serum. A sample of the harvested marrow will be sent for bacterial/fungal culture.

The cell production will be performed in the Aastrom CPS, which is operated in standard, validated laboratory equipment (incubators, refrigerators, gas pumps) which provide for constant temperature (37 degree C), pH (7.2-7.4), and delivery of sterile air (5% CO₂) to the hematopoietic cells.

Two days prior to the completion of cell production, the cell culture effluent will be sampled to allow for bacterial and fungal testing including gram stain, endotoxin testing and mycoplasma. At the completion of the cell expansion process (12 days), the non-adherent fraction will be removed from the cell culture devices by draining the growth medium from the cell culture devices into the harvest bag. The devices will then be rinsed by using a syringe to inject 50 ml of an HBSS solution into an access port. This is followed by agitation of the cell culture device and collection of the rinse into the harvest bag. The adherent layer will be detached from the cell culture device surface by injection of 50 ml of Trypsin-EDTA solution via an access port. This is again followed by agitation of the cell culture device and collection of the rinse into the harvest bag. The chamber will be then given a final rinse with 50 ml of HBSS, again by injection via an access port. This is followed by agitation of the cell culture device and collection of the rinse into the harvest bag.

The expanded cells will be washed according to the procedure outlined in the Operator's Manual.

All subjects will receive freshly harvested expanded cells. The expanded cells must be greater than 80% viable, as determined by Trypan blue dye, and the minimum total cell number, as determined by an automated cell counter, will be 1.6×10^9 cells.

As part of the standard laboratory in this study, the total cell count, CFU-GM and LTC-IC will be determined for the starting and final cell number. The pre and post expansion sample will be sent for cytology and immunocytochemistry for breast cancer cells.

Pre-transplant Evaluation of the cultured Cells: 48 hours prior to the collection of the expanded cells, the effluent from the CPS will be tested for bacterial and fungal contamination, as described above. If the bone marrow cultures are either visibly contaminated or are positively cultured for bacterial or fungal contamination, or if the cultures die, the expanded cells will not be returned to the subject, who will then simply receive her cryopreserved bone marrow.

Flow Cytometry: Aliquots of the ex vivo produced cells (approximately 10×10^6) will be removed at 12 days, placed in a tube containing sterile buffered medium, and shipped by overnight mail carrier to Aastrom Biosciences, Inc., Domino's Farms, 24 Frank Lloyd Wright Drive, Lobby L, Ann Arbor, MI 48105. These cells will be analyzed for the presence of several cell surface markers (CD34, CD11b, CD15, CD33, CD3, CD4, CD8, CD19, CD71, and glycophorin A and other appropriate markers) in the laboratory at Aastrom as potential correlates for the cell production process. The Aastrom Laboratory operates under GLP guidelines.

Release Criteria: Cells produced in the Aastrom CPS will be considered eligible for release and reinfusion if greater than 1.6×10^9 / nucleated cells/kg are recovered after the expansion period and cell washing, and if greater than 80% of the nucleated cells are viable as judged by exclusion of Trypan blue dye. Microbial contamination studies collected from the expansion on Day 10 must be negative.

If the expansion is not deemed sufficient, a patient will receive her backup marrow instead, without infusion of the expanded cells.

5.4 High Dose CBT and Infusion of Ex Vivo Produced Cells

5.4.1 The CBT Regimen

Cyclophosphamide 2.0 gm/m²/ IV Days -7, -6, -5 (total dose 6 gm/m²/) with Mesna 500 mg/m²/ IV 1/2 hour before the first dose of Cyclophosphamide then 2 gm/m²/ as a continuous infusion over 24 hours for 3 days. Thiotepa 240 mg/m²/ (total 720 mg/m²/) will be diluted in normal saline and given over 4 hours daily Days -7, -6, -5. BCNU 150 mg/m²/ will be dissolved in 100 ml of D5W and given IV piggyback on Days -7, -6, -5 over 40 minutes (total dose 450 mg/m²/). The ex vivo-produced cells are infused intravenously on Day 0 (the 7th day after the start of chemotherapy). Patients will be premedicated with Tylenol 650 mg PO, Benadryl 50 mg IVPB and Hydrocortisone 50 mg IVPB prior to each infusion.

5.4.2 Post-Transplant Growth Factor Support

G-CSF (5 mcg/kg/d) will be administered SQ until granulocytes greater than 2.0×10^9 /I or greater than 1.0×10^9 /I for 3 days. If granulocytes fall to less than 1.0×10^9 /I, hematopoietic growth factor treatment can be resumed as indicated to maintain an absolute granulocyte count greater than 1.0×10^9 /L. GM-CSF 250 mg/m²/d may be used in patients intolerant to G-CSF.

5.4.3 Neutrophil Engraftment and Stopping Rules

Neutrophil engraftment is defined as recovery of granulocytes to 0.5×10^9 /I. Back-up autologous bone marrow will be infused intravenously per the following stopping rules:

5.4.3.1 Background

back-up cells will always be administered to subjects on Day + 16 if ANC is less than 0.5×10^9 /I;

- . if back-up cells are administered to a subject on Day +16, it is reasonable to assume that an ANC level of $0.5 \times 10^9//I$ can only be reached between Day +16 and Day +20 if the cells produced in the CPS alone contribute to a subject's recovery, because the administration of back-up cells would not be expected to impact engraftment so rapidly, between Days +16 and +20;
- . it is relevant to point out that ANC recovery in the Day +16 to +20 timeframe is often experienced in standard bone marrow transplantation.

5.4.3.2 Stopping Rules

With the above as background, stopping rules will be as follows:

- . the trial will be stopped and reevaluated if two subjects fail to reach ANC $0.5 \times 10^9//I$ by Day +20, even with the administration of back-up cells on Day +16;
- . the trial will also be stopped and reevaluated if four of the first five subjects, or if any five of the ten total subjects, required the administration of back-up cells because they failed to reach ANC $0.5 \times 10^9//I$ on or before Day +16.

6.0 PRETREATMENT EVALUATION

- 6.1 Complete history and physical examination, including Zubrod performance status (Appendix C)
- 6.2 CBC, diff, and platelet count
- 6.3 SMA 12 and electrolytes
- 6.4 PT, PTT
- 6.5 Cardiac ejection fraction
- 6.6 Pulmonary function - DLCO
- 6.7 HIV, hepatitis, HTLV-1 (1764 panel)
- 6.8 Pregnancy test (in fertile women)
- 6.9 Tumor staging as indicated including bone scan with Xray of hot spots, CXR, CT scan abdomen, tumor markers, such as CEA will be assessed.
- 6.10 Bilateral bone marrow aspirate and biopsy

7.0 STUDY PROCEDURES AND EVALUATIONS

- 7.1 Interim history, physical examination and toxicity assessment daily while in hospital and at least weekly until WBC greater than 3000 and platelets greater than 100,000. Toxicity assessment will be made pre-infusion and 2 and 24 hours post-infusion of both the expanded and unexpanded bone marrow cells.
- 7.2 CBC, diff, platelet counts daily while hospitalized and at least twice per week as an outpatient until WBC greater than 3000/mcl and platelets greater than 100,000/mcl.
- 7.3 SMA twice per week while hospitalized. Electrolytes as indicated.

7.4 Tumor restaging as indicated including bone scan with Xray of hot spots, CXR, CT scan of abdomen, and CEA, at day 60. Subsequent follow up is as indicated for patients with this malignancy

7.5 Criteria for discharge: A study subject will be eligible for discharge from the hospital when she meets the following criteria:
afebrile for 2 or more consecutive days, ANC greater than 500 for 3 consecutive days and Zubrod status of 0, 1 or 2.

All study subjects will receive follow-up care and treatment (as appropriate) by their physician. The subjects' medical records will be available to medical study monitors should additional information be required.

8.0 DATA COLLECTION

8.1 General Information

Data will be recorded using the MD Anderson PDMS system at the time of each evaluation. Data must be recorded for all subjects from whom an Informed Consent is obtained.

8.2 Contents

Data to be collected at each of the study time period is as follows:

Pre-treatment Evaluation -----

- Eligibility criteria
- Demographic data
- Medical history
- Physical examination
- Laboratory profile
- Bone marrow biopsy
- toxicity status

Baseline (Day 0) -----

- Laboratory profile
- Bone marrow/cultured cell profile
- Transfusion record
- Toxicity assessment
- Vital signs
- Concomitant medication(s)
- Infection reporting and adverse effects greater than grade 3 - report immediately to sponsor as event occurs.

Daily Evaluations (Post-transplant)

- Laboratory profile
- Transfusion record
- Toxicity assessment (note preinfusion, 2 hour and 24 post infusion toxicity assessment above)
- Vital signs
- Concomitant medications
- Infection reporting and grade greater than or equal to 2 adverse effects - report immediately to sponsor as event occurs.

Hospital Discharge (study completion)

- Laboratory profile
- Vital signs
- Toxicity assessment
- Concomitant medications
- Infection reporting and Adverse Effects grade greater than or equal to 3 - Report immediately to sponsor as event occurs.

Early termination or Day 60

- Laboratory profile
- Assessment of late toxicity
- Transfusion record
- Vital signs
- Concomitant medications
- Study completion questionnaire

8.3 Quality System

Quality system procedures are designed to ensure that complete, timely, and accurate data are submitted, that protocol requirements are followed, and that complications and/or adverse reactions are immediately identified.

The study monitors will promptly review all incoming data to identify inconsistent or missing data and adverse effects. Data problems will be addressed in telephone calls and correspondence to the investigational site and during site visits. Clinical monitoring procedures are described in Section 12 of this protocol. The Medical Monitor will receive immediate notification of adverse reactions Grade greater than or equal to 3. Both the site and Aastrom will maintain secure hard copy Case Record Forms and data files.

9.0 ADVERSE EFFECTS

All adverse effects, whether or not considered anticipated, must be recorded in PDMS. Unanticipated effects, as defined below, must be reported promptly to

the sponsor for further evaluation and adequate required reporting to IRBs and investigators.

9.1 Anticipated Adverse Effects

The preliminary clinical experience has not identified any serious adverse effects on health or safety caused by or associated with the CPS and no adverse effects related to the ex vivo use of FLT3 ligand are anticipated. Patients undergoing high dose chemotherapy are anticipated to experience anorexia, nausea, vomiting, mucositis, pancytopenia and associated infections while neutropenia. Some patients may develop organ toxicities from high dose therapy. The anticipated events are therefore those associated with bone marrow transplantation and/or chemotherapy.

9.2 Unanticipated Adverse Effects

An unanticipated adverse effect is:

- Any serious effect on health or safety or any life-threatening problem, or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan, or any other unanticipated serious problem that relates to the rights, safety or welfare of subjects.
[21 CFR 312.3(s)]
- In particular, any unexpected grade III or IV toxicities or any other serious event that might be attributable to the infusion of the expanded hematopoietic cells.

Reporting requirements:

- Unanticipated adverse effects should be reported to the Aastrom Study Director, Thomas E. Muller, Ph.D., Vice President Regulatory Affairs, immediately by the Investigator and subsequently to BRI.
- Aastrom requires an immediate telephone report followed by a written report within 5 days.
- An investigator shall submit to Aastrom and the reviewing IRB a report of any unanticipated adverse device effect occurring as soon as possible, but no later than 10 working days after the investigator learns of the effect [21 CFR 312.150(a)(1)]. Aastrom shall immediately conduct an evaluation and report the results of the evaluation to FDA and to reviewing IRB's and participating investigator(s) within 10 working days after the sponsor first receives the notice of the effect [21 CFR 312.150(b)(1)]. If Aastrom determines that an unanticipated adverse effect presents an unreasonable risk to subjects, all

investigations or parts of investigations presenting that risk shall be terminated as soon as possible [21 CFR 812.46(b)].

9.3 DEPARTURE FROM PROTOCOL

When a situation occurs which requires a departure from the protocol, the Principal Investigator or other physician in attendance will contact the Medical Monitor by telephone:

Thomas E. Muller, Ph.D.
Vice President Regulatory Affairs
Aastrom Biosciences, Inc.
24 Frank Lloyd Wright, Lobby L
Ann Arbor, MI 48105
Telephone: 313-930-5555
Fax: 313-665-0485

Contact with the Medical Monitor will be made as soon as possible in order to discuss the situation and agree on an appropriate course of action. The patient's medical records and source documents will describe the departure from the protocol and the circumstance requiring it.

10. STATISTICAL CONSIDERATIONS AND DATA ANALYSIS

10.1 Evaluation of the Data

All subjects will be evaluated. Descriptive statistics will be presented for demographic variables and baseline characteristics such as age, sex, medical history, physical examination results, cost information (especially as this relates to morbidity).

The primary endpoint is the safety of the cells produced in the CPS. To assess the hematopoietic recovery post-infusion with ex vivo-produced cells, the day of engraftment is defined by the first day on which granulocytes are greater than 0.5 times $10^9/I$ are observed. Other secondary endpoints include nadir WBC and platelet count, febrile days, treatment related complications, antitumor response, and survival.

Secondary Endpoints:

- a. The day of platelet transfusion independence with platelet count greater than $20,000/mm^3$, $50,000/mm^3$ and $100,000/mm^3$ as defined by first of two consecutive time points on which platelet counts meet these endpoints not related to transfusion
- b. Packed red blood cell transfusion and platelet transfusion requirements.
- c. Number of documented infections.
- d. Number of bleeding episodes.
- e. Number of days of hospitalization.

- f. Tumor response and response duration
- g. Patient survival at 90 days post transplant.

10.2 Safety variables

Safety variables summarized will include incidence of adverse effects (including duration, severity, and outcome). Other safety variables reported will include the incidence and types of laboratory abnormalities. When the frequencies are sufficiently large, a Fisher's exact test or Chi-square test may be used to compare enrolled subjects and historical controls including approximately 65 patients receiving autologous bone marrow transplants without expansion using the same preparative regimen (DM92-060).

10.3 Biological Effect Variables

The following biological effects will be summarized:

- Incidence of febrile neutropenia
- Time to platelet transfusion independence
- Antibiotic usage:
 - Number of days on antibiotics
 - Number of total antibiotic days (Number antibiotics times number days)
 - Number of days on antifungals
 - Number of days on antivirals
- Number of documented infections
- Time to neutrophil engraftment
- Length of initial hospital stay

11.0 CLINICAL SUPPLIES

A complete CPS description is provided in the Operator's Manual.

11.1 Materials and Supplies

11.1.1 CPS

Astrom will supply the CPS, which includes the cell culture device. This device consists of three rigid plastic parts (top, cell bed, and base), and a gas-permeable, water-impermeable membrane. Additional components include the means to facilitate air removal, seals to maintain leak-tight integrity, and mechanical fasteners.

11.1.2 Growth Medium

The culture medium is prepared at the clinical site by supplementing a custom medium, produced to Astrom specifications in a FDA-registered facility in compliance with cGMPs (21 CFR 820), with glutamine and growth factors in

accordance with a standard operating procedure. Medium components are shipped to or procured by the clinical trial site according to instructions, specifications and acceptance criteria defined by Aastrom.

11.1.3 Supporting Tubing and Materials

Aastrom will supply the supporting tubing, harvest container, and waste container. These components will be supplied in sterile packages (for single use only).

11.2 Packaging and Labeling

The package labeling includes the statement "Caution, Investigational Device-Limited by United States Law to Investigational Use," Lot Number, "Sterile unless unit package is opened or damaged," and "Manufactured for Aastrom Biosciences, Inc."

11.3 Assembly

Components of the CPS will be received at the clinical test sites in sterile packages. The elements of the system will be connected under a laminar flow hood using aseptic technique provided in the Instructions for Use. The instructions for use will be provided by Aastrom.

11.4 Storage Requirements

The devices may be stored indefinitely under typical laboratory conditions (50 degrees F to 90 degrees F) and may be transported at temperatures up to 125 degrees F.

11.5 Retrieval and/or Disposal of Investigational Materials

At the completion of the cell production process and harvest, the devices will be considered biohazardous waste and disposed of in accordance with standard procedures at the test site. Record will be made of the date of disposal and initials of the individual responsible for their disposition.

12.0 STUDY MONITORING

12.1 Medical Monitor

The Medical Monitor will review the investigational plan, review adverse reactions and/or unanticipated device effects as reported by the Investigator and interpret clinical results. The Medical Monitor for this study is:

Thomas E. Muller, Ph.D.
Vice President Regulatory Affairs
Aastrom Biosciences, Inc.

Domino's Farms
24 Frank Lloyd Wright Dr., Lobby L
Ann Arbor, MI 48105
Telephone: 313-930-5555
Fax: 313-665-0485

12.2 Clinical Monitor

Aastrom has designated BRI International, Inc., as Clinical Monitor for this study. The Clinical Monitor is qualified by training and experience to oversee the conduct of the study. The Clinical Monitor's responsibilities include maintaining regular contact with the investigational site, through telephone contact, correspondence and on-site visits, to ensure that the investigational plan and FDA regulations are followed, that complete, timely and accurate data are submitted, that problems with inconsistent and incomplete data are addressed, and that the site facilities continue to be adequate. Any questions regarding these matters should be addressed to:

Diane Goleb, Senior Project Director
BRI International, Inc.
15825 Shady Grove Road
Rockville, MD 20850
Telephone: 301-548-0500
Fax: 301-548-0519

12.3 Monitoring Procedures

12.3.1 Preinvestigational Site Visit

The Preinvestigational Site Visit, conducted by the Clinical Monitor, will involve review of relevant FDA regulations and inspection procedures, the investigational plan, requirements for IRB review and approval, completion and submission of forms, record keeping requirements, and administrative reports.

The adequacy of the facilities, the availability of the investigators, the potential number of study participants, and the provisions for staff support will also be assessed during the Preinvestigational Site Visit.

12.3.2 Routine Monitoring Visits

Regular clinical monitoring visits to the investigational site will be conducted by Aastrom and BRI.

To ensure that the Principal Investigator and his staff understand and accept their defined responsibilities, the Clinical Monitor will maintain regular correspondence and perform periodic site visits during the course of the study to verify the continued acceptability of the facilities, compliance with the

investigational plan and relevant FDA regulations, and the maintenance of complete records. Clinical monitoring will include review and resolution of missing or inconsistent results and source document checks (i.e., comparison of submitted study results to original reports) to assure the accuracy of the reported data.

The Clinical Monitor will evaluate and summarize the results of each site visit in written reports, identifying any repeated data problems with any investigator and specifying recommendations for resolution of noted deficiencies.

12.3.3 Termination/Close-out Procedures

The Clinical Monitor, BRI, will notify the investigator in writing of study completion/termination. The letter will include the reason for termination, document unresolved study discrepancies, and remind the investigator of her obligation to retain records according to FDA regulations.

BRI will be responsible for meeting the FDA regulations with regards to record keeping and records retention.

BRI will conduct a standard closure monitoring site visit. The objectives of the closing visit are:

- verify compliance with protocol and FDA regulations;
- ensure accuracy and completeness of subject and administrative files;
- resolve any outstanding questions/problems;
- verify accountability for the test devices;
- ensure the proper disposition of test devices and completed case report forms;
- confirm the investigator's understanding of his/her regulatory obligations, including record retention requirements.

13.0 INVESTIGATOR OBLIGATIONS

13.1 Principal Investigator Responsibilities

13.1.1 Compliance

The Principal Investigator is responsible for ensuring that the study is conducted according to the signed Investigator Agreement, the investigational plan, and applicable FDA regulations for protecting the rights, safety and welfare of subjects under the Investigator's care. The Principal Investigator must follow the Investigator Agreement, the investigational plan, and all conditions of FDA and IRB approval.

13.1.2 Awaiting Approval

Written confirmation of IRB approval must be provided to Aastrom prior to the start of the study. The Principal Investigator may determine whether potential subjects would be interested in participating in a study but may not request signature of the Informed Consent or allow any subject to participate until FDA and the reviewing IRB have approved the study.

13.1.3 Supervising Device Use

The Principal Investigator must supervise all use of the CPS involving human subjects and may not supply the device to any person not specifically authorized to receive it according to the investigational plan and applicable regulations.

13.1.4 Informed Consent

The Principal Investigator shall make known to each subject the nature, expected duration, and purpose of the study; the administration and hazards of treatment; and available alternative therapy. Signed, written Informed Consent must be obtained prior to treatment. The original will be kept by the Principal Investigator and will be subject to review by Aastrom. Subjects will be informed that their medical records will be subject to review by Aastrom and the FDA. Subjects shall be informed that they are free to refuse participation in this clinical investigation; and if they participate, that they may withdraw from the study at any time without prejudicing future care.

13.1.5 Device Disposal

Upon completion or termination of the study or the Principal Investigator's participation in this study, or at Aastrom's request, the Principal Investigator must return to Aastrom the device(s) or otherwise dispose of the device(s) as Aastrom directs.

13.1.6 Reporting Requirements

Any life-threatening and/or unexpected serious (grade 3 or 4) toxicities will be reported immediately to the Study Chairman who, in turn, will notify the IRB (Surveillance Committee) and the study sponsor.

13.1.7 Inspections and Records

In accordance with the Investigator Agreement, the Principal Investigator shall permit authorized FDA employees to enter and inspect any site where the device or records pertaining to the device are held, and to inspect and copy all records relating to an investigation, included subject records.

13.1.8 Investigator Records

The Principal Investigator will maintain complete, accurate and current study records, including the following materials:

- Correspondence with FDA, Aastrom, BRI, and the IRB;
- Record of receipt of the device;
- Instructions for device use;
- Subject Records, including Informed Consent, copies of Case Report Forms and supporting documents (laboratory reports, medical records, etc.);
- Log Book;
- Current study protocol and a log of any significant protocol deviations (e.g., lack of informed consent or treatment of ineligible subjects);
- Adverse event reports;
- Certification that the investigational plan has been approved by all of the necessary approving authorities;
- The approved blank informed consent form and blank subject report forms.
- Signed Investigator's Agreement with CV's of the Principal Investigator and all participating sub-investigators attached.

These records shall be maintained for a period of 2 years after the latter of the following two dates: the date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or notice of completion of a product development protocol.

13.1.9 Investigator Reports

The Principal Investigator will be responsible for the following reports:

13.1.9.1 Unanticipated Adverse Effects

The Investigator will report any serious adverse effect, death or life-threatening problems that may reasonably be regarded as caused by the CPS to Aastrom and the reviewing IRB as soon as possible but no later than 10 working days after the event. All anticipated serious adverse effects should be documented with an explanation of any medical treatment administered.

An unanticipated serious adverse effect is defined as any serious adverse effect on health or safety, or any life-threatening problem or death caused by, or associated with this device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in this investigational plan.

13.1.9.2 Withdrawal of IRB Approval

The Principal Investigator will immediately notify to Aastrom (within 5 working days) if, for any reason, the IRB withdraws approval to conduct the investigation.

The report will include a complete description of the reason(s) for which approval was withdrawn.

13.1.9.3 Departure from Protocol

The Principal Investigator shall notify Aastrom and the IRB of any deviation from the investigational plan made to protect the life or physical well-being of a subject in an emergency. A full report should be made as soon as possible and in no case later than 5 working days after the emergency. NOTE: Except in such an emergency, prior approval by Aastrom is required for changes in, or deviations from, the investigational plan. If such changes or deviations may affect the scientific soundness of the plan or the rights, safety or welfare of subjects, FDA and IRB approval are also required.

13.1.9.4 Progress Reports

The Principal Investigator is required to submit progress and administrative reports to Aastrom, and to the reviewing IRB. Reports will include the number of study subjects, a summary of all adverse reactions, and a general description of the study's progress.

13.1.9.5 Final Report

The Principal Investigator will submit a final report to Aastrom within four weeks following termination of the study or that site's participation in the study, and within three months to the IRB.

13.1.9.6 Other Reports

Upon request, the Principal Investigator will provide accurate, complete, and current information to Aastrom Biosciences, Inc., the FDA, and to the reviewing IRB.

13.1.9.7 Investigator Materials Accountability

All devices received and used by the Principal Investigator will be inventoried and accounted for throughout the study. The devices will be stored in a secured area. Upon study completion, all unused devices will be returned to Aastrom. A final inventory will then be performed.

13.1.9.8 Laboratory Normal Values

The investigational site must maintain a current copy of normal values used by that site's clinical laboratory. The Principal Investigator must assess the clinical significance of all abnormal laboratory values. All clinically significant abnormalities must be characterized by the Principal Investigator as treatment-

related, not treatment-related, or of uncertain etiology; all abnormalities judged treatment-related or of uncertain etiology must be repeated. Any abnormal values that persist should be followed at the Principal Investigator's discretion. In some cases, significant changes within the normal range will require similar judgment.

13.1.9.9 Disclosure of Data

All information concerning this clinical study are considered confidential. The Principal Investigator agrees to use this information only to accomplish this study and will not use it for other purposes without Aastrom's written consent.

It is understood by the Principal Investigator that the information developed in the clinical study may be disclosed as required to the United States Food and Drug Administration.

In order to allow for the use of the information derived from the clinical studies, it is understood that there is an obligation to provide Aastrom with complete test results and all data developed in the study.

Aastrom has no objection to the publication of the results of this study by the investigator. However, a pre-publication manuscript must be provided to Aastrom at least 30 days before the manuscript is submitted to a publisher.

Aastrom agrees that before it publishes any results of the study, a pre-publication manuscript will be provided to the investigator for review at least 30 days prior to the submission to a publisher.

13.1.10 Records Retention and Access

FDA regulations require that, following completion of a clinical trial, a copy of all subject and administrative records pertaining to that study be maintained by the Investigator for 2 years after FDA approval of the investigational device, or, if no application for approval is filed or intended to be filed, for 2 years after all investigations have been completed, terminated, or discontinued, whichever time period is longer.

Completed data records must be made available for review by Aastrom, the Clinical Monitor, and FDA. To ensure the accuracy of data submitted, it is mandatory that representatives of Aastrom and of the FDA have access to source documents (i.e., subject medical records, charts, laboratory reports, etc.). Subject confidentiality will be protected at all times.

Aastrom reserves the right to terminate the study for refusal of the Principal Investigator to supply source documentation of work performed in this study.

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APPENDIX A

TOXICITY CRITERIA

(Bearman et al., J Clin Oncol, 6:1562, 1988)

	Grade 1	Grade 2	Grade 3
Cardiac	Mild EKG abnormality, not requiring medical intervention; or noted heart enlargement on CXR with no clinical symptoms	Moderate EKG abnormalities requiring and responding to medical intervention; or requiring continuous monitoring without treatment; or congestive heart failure responsive to digitalis or diuretics	Severe EKG abnormalities with no or only partial response to medical intervention; or heart failure with no or only minor response to medical intervention; or decrease in voltage by more than 50%
Bladder	Macroscopic hematuria after 2 d from last chemotherapy dose with no subjective symptoms of cystitis and not caused by infection	Macroscopic hematuria after 7 d from last chemotherapy dose not caused by infection; or hematuria after 2 d with subjective symptoms of cystitis not caused by infection	Hemorrhagic cystitis with frank blood, necessitating invasive local intervention with instillation of sclerosing agents, nephrostomy or other surgical procedure
Renal	Increase in creatinine up to twice the baseline value recorded before start of conditioning	Increase in creatinine above twice baseline but not requiring dialysis	Requires dialysis
Lung	Dyspnea without CXR changes not caused by infection or congestive heart failure; or CXR showing isolated infiltrate or mild interstitial changes without symptoms not caused by infection or congestive heart failure	CXR with extensive localized infiltrate moderate interstitial changes combined with dyspnea and not caused by infection or CHF; or decrease in P02 greater than 10% from baseline but not requiring mechanical ventilation or greater than 50% O2 by facemask and not caused by infection or CHF	Interstitial changes requiring mechanical ventilatory support or greater than 50% oxygen by facemask and not caused by infection or CHF
Hepatic	Mild dysfunction with bilirubin 2.1-6 mg/dl; or weight gain greater than 2.5-5% from baseline of noncardiac origin; or SGOT/SGPT increase more than 2-fold but less than 5-fold from the lowest preconditioning	Moderate dysfunction with bilirubin 6.1-20 mg/dl; or weight gain greater than 5% from baseline of noncardiac origin; or SGOT/SGPT increase greater than 5-fold from the lowest preconditioning; or clinical ascites or image documented ascites	Severe dysfunction with bilirubin greater than 20 mg/dl; or hepatic encephalopathy; or ascites compromising respiratory function

APPENDIX B

Patient Evaluation

Tests	Pre	During Study	Post
History & Physical	X		
CBC, diff & platelets	X	daily	weekly
SMA 12	X	twice per week	weekly
PT,PTT	X	as indicated	
Cardiac ejection fraction & EKG	X		
Pulmonary function-DLCO	X		
Pregnancy test	X		
HIV, hepatitis, HTLV-1	X		
Bone marrow aspirate and biopsy	X		
Tumor Staging-Bone scan +Xray of hot spots, CT Abdomen, CXR, CEA, CA-125 as indicated	X		3,6,12,18,24 and as indicated

THE UNIVERSITY OF TEXAS
M.D. ANDERSON CANCER CENTER
INFORMED CONSENT

PROTOCOL TITLE: CLINICAL FEASIBILITY STUDY OF EXPANDED
PROGENITOR CELLS FOR HEMATOPOIETIC ENGRAFTMENT
IN PATIENTS WITH BREAST CANCER

1.

PARTICIPANT'S NAME

I.D. NUMBER

You have the right to know about the procedures that are to be used in your participation in clinical research so as to afford you an opportunity to make the decision whether or not to undergo the procedure after knowing the risks and hazards involved. This disclosure is not meant to frighten or alarm you; it is simply an effort to make you better informed so you may give or withhold your consent to participate in clinical research. This informed consent does not supersede other informed consents you may have signed.

DESCRIPTION OF RESEARCH

2.

PURPOSE OF STUDY: Chemotherapy at standard or usual doses does not always kill all the cancer cells. In such cases, higher doses of chemotherapy may be helpful. However, these higher doses may destroy normal bone marrow as well as cancer cells, so previously collected blood forming bone marrow cells are given by vein to replace the damaged bone marrow.

The goal of this clinical research study is to determine whether we can speed up recovery after high-dose chemotherapy and bone marrow transplant in patients with breast cancer growing the cells in the laboratory before infusion.

3.

DESCRIPTION OF RESEARCH:

This study will include patients with stage 4 breast cancer. 12 days before treatment begins, about 100 cc of bone marrow will be removed from patient's hip with a syringe and needle while under general anesthesia. A sample of the marrow will be placed in an investigational device that will increase (expand) the number of blood-forming cells (stem cells). Patients will also have a full bone marrow harvest under anesthesia, (approximately 1 quart), collected at the same time or another occasion. This will be saved as a back up to be given back by vein in case of poor recovery of blood counts after infusion of the expanded cells.

The patient will stay in the hospital during the high-dose chemotherapy and transplant procedure. The chemotherapy drugs in this treatment plan are cyclophosphamide, carmustine (BCNU), and thiotepa. These drugs in lower doses are FDA-approved and commercially available. These drugs, at the same or higher doses, have been used in other bone marrow transplant studies at M.D. Anderson and are considered active against breast cancer and reasonably safe. Before treatment begins, a catheter (a special tube) will be inserted into a vein in the patient's chest. The chemotherapy drugs, fluids,

antibiotics, bone marrow, and other blood products will be given through the catheter.

Each drug will be given to the patient for 3 days. One week after the start of chemotherapy, the patient will receive the expanded blood-forming cells. Patients will undergo frequent blood tests over the next several weeks to monitor their recovery and to check for side effects of the treatment. The patient will probably be in the hospital for about 3 weeks. About 10 patients will take part in this study.

4. RISKS, SIDE EFFECTS, AND DISCOMFORTS TO PARTICIPANTS:

Risks of Bone Marrow Collection

Bone marrow is collected from several places in the hip with a syringe and needle while the patient is under general anesthesia. The patient may have pain at the sites that the marrow was taken from. Rarely, patients have a reaction to the anesthesia (sometimes fatal), bleeding, infection, or injury to the sciatic nerve, which runs along the leg.

Risks of High Dose Chemotherapy

Anti-cancer drugs injure normal tissues as well as cancer cells. Side effects of these drugs may include: hair loss, nausea, vomiting, diarrhea, mouth ulcers (sores), skin rashes, bleeding and infection, weakness, slight risk of damage of the heart, lung, liver, kidney, or nervous system.

Most of these side effects can occur even at standard doses of these drugs. However, using high doses makes it more likely that patients will have bleeding, infection, and other side effects.

Risks of Bone Marrow Transplant

In a preliminary study involving 10 patients none had any side effects from the expanded cell infusion. Potential risks of infusing expanded blood-forming cells include: shortness of breath, strain on the heart, and allergic reaction to the chemicals used while processing or storing the expanded blood-forming cells.

After the high-dose chemotherapy, the patient's blood cell counts fall to very low values. When blood cell counts are low, the patient is at high risk for bleeding and infection. At this point, the patient usually requires antibiotics and transfusions of red blood cells and platelets. (Red blood cells carry oxygen through the body, and platelets help control bleeding). Approximately 5% of patients who receive an autologous transplant for breast cancer die of complications from the transplant, usually a side effect of the high dose chemotherapy or an infection that develops while blood counts are low.

This clinical research study may involve unforeseeable risks to the participant.

- 4a. This clinical research may involve unforeseeable risks to unborn children; therefore, the participants should practice adequate methods of birth control throughout the period of their involvement in the clinical research study if they are sexually active. To help prevent injury to children, female participants should refrain from breast feeding during participation in the clinical research study.

5. **POTENTIAL BENEFITS:** The expanded blood-forming cells to the bone marrow that is transplanted may help the bone marrow recover and start producing new blood cells faster. This would reduce the risk of bleeding and infection. By starting with a smaller amount of bone marrow and the effects of the cell culture, it is expected that the chance of malignant cells being infused is reduced.

Using high doses of the drugs may cause the cancer to shrink more than it would if lower doses of the same drugs were used.

6. **ALTERNATE PROCEDURES OR TREATMENTS:**
Common drugs used to treat breast cancer include mitomycin, methotrexate, doxorubicin, 5-fluorouracil, vinblastine, cyclophosphamide, taxol. Instead of taking part in the clinical research study described above, patients could receive one or a combination of these drugs at standard doses. Also, patients might be able to take part in clinical research studies of other drugs. Patients could also have a blood stem cell or bone marrow transplant without receiving the expanded blood-forming cells.

UNDERSTANDING OF PARTICIPANTS

7. I have been given an opportunity to ask any questions concerning the treatment involved and the investigator has been willing to reply to my inquiries. This treatment will be administered under the above numbered and described clinical research protocol at this institution. I hereby authorize Dr. _____, the attending physician/investigator, and designated associates to administer the treatment.
8. I have been told and understand that my participation in this clinical research study is voluntary. I may decide not to participate, or withdraw my consent and to discontinue my participation in this study at any time. Such action will be without prejudice and there shall be no penalty or loss of benefits to which I may otherwise be entitled, and I will continue to receive treatment by my physician at this institution.

Should I decide not to participate or withdraw from this clinical research if, I have been advised that I should discuss the consequences or effects of my decision with the physician.

In addition, I understand that the investigator may discontinue the clinical research study if, in the sole opinion and discretion of the investigator, the study or treatment offers me little or no future benefit, or the supply of medication ceases to be available or other causes prevent continuation of the clinical research study. The investigator will notify me should such circumstances arise and my physician will advise me about available treatments which may be of benefit at that time.

I will be informed of any new findings developed during the course of this clinical research study which may relate to my willingness to continue participation in this study.

9. I have been assured that confidentiality will be preserved except that qualified monitors from Aastrom Biosciences and the Food and Drug Administration (FDA) may review my medical record if appropriate and necessary. Qualified monitors shall include assignees authorized by the Surveillance Committee of this institution provided that confidentiality is assured and preserved. My name will not be revealed in any reports or publications resulting from this study, without my expresses consent. In special circumstances, the FDA might be required to reveal the names of participants.
10. I have been informed that should I suffer any injury as a result of participation in this research activity, reasonable medical facilities are available for treatment at this institution. I understand, however, that I cannot expect to receive any credit or reimbursement for expenses from this institution or any financial compensation from this institution for such injury.
11. I have been informed that I should inquire of the attending physician whether or not there are any services, investigational agents or devices, and/or medications being offered by the sponsor of this clinical research project at reduced cost or without cost. Should the investigational agent become commercially available during the course of the study. I understand that I may be required to cover the cost of subsequent doses.

Costs related to my medical care including expensive drugs, tests or procedures that may be specifically required by this clinical research study shall be my responsibility unless the sponsor or other agencies contribute toward said costs. I have been given the opportunity to discuss the expenses or costs associated with my participation in this research activity.

12. It is possible that this research project will result in the development of beneficial treatments, new drugs, or possible patentable procedures, in which event I cannot expect to receive any compensation or benefits from the subsequent use of information acquired and developed through participation in this research project.
13. I understand that refraining from breast feeding and practicing effective contraception are medically necessary and a prerequisite for my participation in this clinical research study. Should contraception be interrupted or if there is any suspicion of pregnancy, my participation in this clinical research study will be terminated at the sole discretion of the investigator.
14. I may discuss any questions or problems during or after this study with Dr. Richard Champlin at 713-792-3611. In addition, I may discuss any problems I may have or any questions regarding my rights during or after this study with the Chairman of the Surveillance Committee at 713-792-3220 and may in the event any problem arises during this clinical research contact the parties named above.

CONSENT

Based upon the above, I consent to participate in the research and have received a copy of the consent form.

DATE

SIGNATURE OF PARTICIPANT

WITNESS OTHER THAN PHYSICIAN
OR INVESTIGATOR

SIGNATURE OF PERSON RESPONSIBLE
AND RELATIONSHIP

I have discussed this clinical research study with the participant and/or his or her authorized representative, using a language which is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks, and I believe the participant understood this explanation.

PHYSICIAN/INVESTIGATOR

APPENDIX D

THE UNIVERSITY OF TEXAS
M.D. ANDERSON CANCER CENTER
INFORMED CONSENT

PROTOCOL TITLE: FEASIBILITY STUDY OF EXPANDED PROGENITOR CELLS FOR
HEMATOPOIETIC ENGRAFTMENT IN PATIENTS WITH
BREAST CANCER

1. _____
PARTICIPANT'S NAME I.D. NUMBER

You have the right to know about the procedures that are to be used in your participation in clinical research so as to afford you an opportunity to make the decision whether or not to undergo the procedure after knowing the risks and hazards involved. This disclosure is not meant to frighten or alarm you; it is simply an effort to make you better informed so you may give or withhold your consent to participate in clinical research. This informed consent does not supersede other informed consents you may have signed.

DESCRIPTION OF RESEARCH
- - - - -

2. PURPOSE OF STUDY: Chemotherapy at standard or usual doses does not always kill all the cancer cells. In such cases, higher doses of chemotherapy may be helpful. However, these higher doses may destroy normal bone marrow as well as cancer cells, so a bone marrow transplant is done to replace the damaged bone marrow.

The goal of this clinical research study is to determine whether we can speed up recovery after high-dose chemotherapy and bone marrow transplant in patients with breast cancer growing the cells in the laboratory before infusion. (See Section 4.1, Risks of Experimental Protocol.)

3. DESCRIPTION OF RESEARCH:

This study will include patients with breast cancer that has spread to the lymph nodes or to other organs. Twelve days before treatment begins, a full bone marrow harvest, approximately one quart, will be obtained from the patients under general anesthesia. An aliquot of the marrow, less than 10%, will be used to inoculate the investigational device, the Cell Production System (CPS), and the bulk of the harvest, other 90%, will be cryopreserved and saved as back-up in case of poor recovery of blood counts after the infusion of the cells produced in the CPS, or for later therapeutic use, if necessary.

The patients will stay in the hospital during the high-dose chemotherapy and transplant procedure. The chemotherapy drugs in this treatment plan are cyclophosphamide, carmustine (BCNU), and Thiotepa. These drugs in lower doses are FDA-approved and commercially available. These drugs, at the same or higher doses, have been used in other bone marrow transplant studies at M.D. Anderson and are considered active against breast cancer and reasonably safe. Before treatment begins, a catheter (a special tube) will be inserted into a vein the patient's chest. The chemotherapy drugs, fluids, antibiotics, bone marrow, and other blood products will be given through the catheter.

Each drug will be given to the patient for 3 days. One week after the start of chemotherapy, the patient will receive the expanded blood-forming cells. Patients will undergo frequent blood tests over the next several weeks to monitor their recovery and to check for side effects of the treatment. The patient will probably be in the hospital for about 3 weeks. About 14 patients will take part in this study.

4. RISKS, SIDE EFFECTS, AND DISCOMFORTS TO PARTICIPANTS:

4.1 Risks of Experimental Protocol

I have been advised that the Cell Production System, used in this experimental protocol, has been evaluated previously in a clinical feasibility (safety) study without any adverse events (see Section 4.4). Nevertheless, I understand that this experimental protocol may represent a relatively high risk clinical procedure that may cause delayed neutropenia (low white cell counts) and thrombocytopenia (low platelet counts), and delayed engraftment of my transplant. Prolongation of low white counts or platelet counts may increase the risk of infection and bleeding, may prolong hospitalization and can potentially increase the risk of death. However, the risk of these complications is unknown, and experience with transplants that have prolonged low white counts and platelet counts do not appear to have an increased risk of fatal complications. Prolonged time to engraftment and loss of engraftment can be occasionally seen even when standard sources of stem cells are used, such as unexpanded bone marrow or peripheral blood stem cells.

I also understand that every effort will be used to ensure my safety and recovery, including the availability and potential administration of back-up bone marrow obtained as part of my bone marrow harvest. The additional back-up marrow will be given if there is a delay in blood count recovery, or if blood counts decrease after initial engraftment. I understand that I have an option to select to have my physician employ alternate procedures of treatment for my disease, as outlined in Section 6 of this document.

4.2 Risks of Bone Marrow Collection

Bone marrow is collected (harvested) from several places in the hip with a syringe and needle while the patient is under general anesthesia. The patient may have pain at the sites that the marrow was taken from. Rarely, patients have a reaction to the anesthesia (sometimes fatal), bleeding, infection, or injury to the sciatic nerve, which runs along the leg.

4.3 Risks of High Dose Chemotherapy

Anti-cancer drugs injure normal tissues as well as cancer cells. Side effects of these drugs may include: hair loss, nausea, vomiting, diarrhea, mouth ulcers (sores), skin rashes, bleeding and infection, weakness, slight risk of damage of the heart, lung, liver, kidney, or nervous system.

Most of these side effects can occur even at standard doses of these drugs. However, using high doses makes it more likely that patients will have bleeding, infection, and other side effects.

4.4 Risks of Bone Marrow Transplant

In a preliminary study involving 10 patients none had any side effects from the expanded cell infusion. Potential risks of infusing expanded blood-forming cells include: shortness of breath, strain on the heart, and allergic reaction to the chemicals used while processing or storing the expanded blood-forming cells.

After the high-dose chemotherapy, the patient's blood cell counts fall to very low values. When blood cell counts are low, the patient is at high risk for bleeding and infection. At this point, the patient usually requires antibiotics and transfusions of red blood cells and platelets. (Red blood cells carry oxygen through the body, and platelets help control bleeding.) Approximately 5% of patients who receive an autologous transplant for breast cancer die of complications from the transplant, usually a side effect of the high dose chemotherapy or an infection that develops while blood counts are low.

This clinical research study may involve unforeseeable risks to the participant.

This clinical research may involve unforeseeable risks to unborn children; therefore, the participants should practice adequate methods of birth control throughout the period of their involvement in the clinical research study if they are sexually active. To help prevent injury to children, female participants should refrain from breast feeding during participation in the clinical research study.

5. POTENTIAL BENEFITS:

The expanded blood-forming cells from the bone marrow that is transplanted may help the bone marrow recover and start producing new blood cells faster. This would reduce the risk of bleeding and infection. By starting with a smaller amount of bone marrow it is expected that the chances of malignant cells being in the marrow collection is less.

Using higher doses of the drugs may cause the cancer to shrink more than it would if lower doses of the same drugs were used.

The back-up bone marrow, obtained as part of my bone marrow harvest, may be available for my further treatment later, should this become necessary.

6. ALTERNATE PROCEDURES OR TREATMENTS:

Common drugs used to treat breast cancer include mitomycin, methotrexate, doxorubicin, 5-fluorouracil, vinblastine, cyclophosphamide, taxol. Instead of taking part in the clinical research study described above, patients could receive one or several of these drugs at standard doses. Also, patients might be able to take part in clinical research studies of other drugs. Patients could also have a blood stem cell or bone marrow transplant without receiving the expanded blood-forming cells.

UNDERSTANDING OF PARTICIPANTS

- - - - -

7. I have been given an opportunity to ask any questions concerning the treatment involved and the investigator has been willing to reply to my inquiries. This treatment will be administered under the above numbered and described clinical research protocol at this institution. I hereby authorize Dr. _____, the attending physician/investigator, and designated associates to administer the treatment.
8. I have been told and understand that my participation in this clinical research study is voluntary. I may decide not to participate, or withdraw my consent and to discontinue my participation in this study at any time. Such action will be without prejudice and there shall be no penalty or loss of benefits to which I may otherwise be entitled, and I will continue to receive treatment by my physician at this institution.

Should I decide not to participate or withdraw from this clinical research if, I have been advised that I should discuss the consequences or effects of my decision with the physician.

In addition, I understand that the investigator may discontinue the clinical research study if, in the sole opinion and discretion of the investigator, the study or treatment offers me little or no future benefit, or the supply of medication ceases to be available or other causes prevent continuation of the clinical research study. The investigator will notify me should such circumstances arise and my physician will advise me about available treatments which may be of benefit at that time.

I will be informed of any new findings developed during the course of this clinical research study which may relate to my willingness to continue participation in this study.

9. I have been assured that confidentiality will be preserved except that qualified monitors from or representing Aastrom Biosciences and the Food and Drug Administration may review my medical and hospital records if appropriate and necessary. Qualified monitors shall include assignees authorized by the Surveillance Committee of this institution provided that confidentiality is assured and preserved. My name will not be revealed in any reports or publications resulting from this study; without my express consent.
10. I have been informed that should I suffer any injury as a result of participation in this research activity, reasonable medical facilities are available for treatment at this institution. I understand, however, that I cannot expect to receive any credit or reimbursement for expenses from this institution or any financial compensation from this institution for such injury.
11. I have been informed that I should inquire of the attending physician whether or not there are any services, investigational agents or devices, and/or medications being offered by the sponsor of this clinical research project at reduced cost or without cost. Should the investigational agent become commercially available during the course of the study, I understand that I may be required to cover the cost of subsequent doses.

Costs related to my medical care including expensive drugs, tests or procedures that may be specifically required by this clinical research study shall be my responsibility unless the sponsor or other agencies contribute toward said costs. I have been given the opportunity to discuss the expenses or costs associated with my participation in this research activity.
12. It is possible that this research project will result in the development of beneficial treatments, new drugs, or possible patentable procedures, in which event I cannot expect to receive any compensation or benefits from the subsequent use of information acquired and developed through participation in this research project.
13. I understand that refraining from breast feeding and practicing effective contraception are medically necessary and a prerequisite for my participation in this clinical research study. Should contraception be interrupted or if there is any suspicion of pregnancy, my participation in this clinical research study will be terminated at the sole discretion of the investigator.
14. I may discuss any questions or problems during or after this study with Dr. Richard Champlin at 713/792-3611. In addition, I may discuss any problems I may have or any questions regarding my rights during or after this study with the Chairman of the Surveillance Committee at 713/792-3220 and may in the event of any problem arises during this clinical research contact the parties named above.

CONSENT
- - - - -

Based upon the above, I consent to participate in the research and have received a copy of the consent form.

- - - - -	- - - - -
DATE	SIGNATURE OF PARTICIPANT

- - - - -	- - - - -
WITNESS OTHER THAN PHYSICIAN OR INVESTIGATOR	SIGNATURE OF PERSON RESPONSIBLE AND RELATIONSHIP

I have discussed this clinical research study with the participant and/or his or her authorized representative, using a language which is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks, and I believe the participant understood this explanation.

- - - - -
PHYSICIAN/INVESTIGATOR

APPENDIX E
CASE REPORT FORMS

ELIGIBILITY FORM 1 + AASTROM BIOSCIENCES, INC. CPS Replacement Feasibility Trial + AAS02
Subject Initials FOR BRI USE ONLY
[]FI []MI []LI
Social Security Number/Hospital I.D. BRIDOCID:
[][][][][][][][][][]
P.I. Name Visit Date AAS-2-ELIG-12/1/95
[][][][][][][][]M [][]D [][]Y

INCLUSION CRITERIA

Yes No N/A
("X" one)
1. Subject is female and is greater than or equal to 18 years old and less than or equal to 65 years old.....[]1 []2
2. Subject is not pregnant, not lactating, and has a negative serum pregnancy test (within last 2 weeks).....[]1 []2 []3
3. Subject is diagnosed with stage II, III, or IV breast carcinoma and has received no more than two chemotherapy regimens, is currently chemoresponsive or has stable disease.....[]1 []2
4. Subject has a Zubrod performance status of 0 or 1.....[]1 []2
5. Subject's baseline laboratory tests are within protocol specified limits (HIV negative and estimated creatine clearance greater than 50 mL/min; SGOT, SGPT, and bilirubin less than 2x normal: normal cardiac ejection fraction and DLCO greater than 50% predicted; WBC greater than 3,000/mm/3/ and platelet count greater than 100,000/mm/3/).....[]1 []2
6. Subject is a candidate for autologous bone marrow transplantation.....[]1 []2
7. Subject is willing and able to comply with protocol and follow-up requirements.....[]1 []2
8. Subject or authorized representative has signed informed consent.....[]1 []2

Questions 1 - 8 must be marked "Yes" for study participation.

EXCLUSION CRITERIA

Yes No
("X" one)
9. Subject has known bone marrow involvement with tumor, as demonstrated by standard histopathological examination of bilateral iliac marrow biopsies (within last 2 weeks).....[]1 []2
10. Subject has history of central nervous system (CNS) disease.....[]1 []2
11. Subject has known hypersensitivities to bovine and/or horse serum.....[]1 []2
12. Subject is currently involved in another clinical trial that affects engraftment.....[]1 []2
13. Subject has been treated with growth factors within the last week (7 days).....[]1 []2
14. Subject has had previous pelvic radiotherapy.....[]1 []2
15. Subject has been previously treated with BCNU, mitomycin-C.....[]1 []2
16. Subject has a co-morbid condition which, in the view of the Investigator, renders the subject at high risk from treatment complications.....[]1 []2

Questions 9 - 16 must be marked "No" for study participation.

+ + / /
Investigator Signature Date Signed

Copyright BRI.

PRETREATMENT MEDICAL HISTORY

AASTROM BIOSCIENCES, INC.
CPS Replacement Feasibility Trial

AAS02

FORM 2 +

+

Subject Initials:
[] FI [] MI [] LI
Social Security Number/Hospital I.D.
[] [] [] [] [] [] [] []
P.I. Name
[] [] [] [] [] [] [] []

FF FOR BRI USE ONLY
BRIDOCID:
AAS-2-PTH-11/14/95

ALL ITEMS MUST BE COMPLETED. MISSING OR INCORRECTLY COMPLETED ITEMS WILL REQUIRE ADDITIONAL FOLLOW-UP.

VISIT DATE

1. Visit Date: [] [] [] [] [] []
Month Day Year

MEDICAL HISTORY

IF SUBJECT HAS CURRENT DIAGNOSIS OF CONDITION, PLEASE INDICATE BY MARKING
ABNORMAL AND DESCRIBING THE CONDITION IN THE SPACE PROVIDED.

		("X" one)		Specify abnormalities other than those associated with the leukemia/lymphoma
		Normal	Abnormal	
2.	Skin.....	[]1	[]2	2. _____
3.	Eyes, Ears, Nose, Throat.....	[]1	[]2	3. _____
4.	Ophthalmic.....	[]1	[]2	4. _____
5.	Mouth and Gum.....	[]1	[]2	5. _____
6.	Respiratory.....	[]1	[]2	6. _____
7.	Cardiovascular.....	[]1	[]2	7. _____
8.	Musculoskeletal	[]1	[]2	8. _____
9.	Gastrointestinal.....	[]1	[]2	9. _____
10.	Hepatic.....	[]1	[]2	10. _____
11.	Urogenital.....	[]1	[]2	11. _____
12.	Renal.....	[]1	[]2	12. _____
13.	Endocrine and Metabolic.....	[]1	[]2	13. _____
14.	Neurological.....	[]1	[]2	14. _____
15.	Psychological.....	[]1	[]2	15. _____
16.	Hematopoietic/Lymphatic.....	[]1	[]2	16. _____
17.	Extremities.....	[]1	[]2	17. _____
18.	Allergies.....	[]1	[]2	18. _____
19.	Other.....	[]1	[]2	19. _____

Recorder Signature

Date Signed

Subject Initials FOR BRI USE ONLY
[]FI []MI []LI
Social Security Number/Hospital I.D. BRIDOCID:
[] [] [] [] [] [] [] [] []
P.I. Name Date AAS-2-LAB-12/07/95
[] [] [] [] [] [] [] [] [] [] []M [] []D [] []Y

LABORATORY TEST RESULTS

1. CBC:
- a. Hemoglobin (gm/dl).....[] [] [.] [] []
 - b. Hematocrit (%).....[] [] [.] [] []
 - c. Platelet Count (x10³/ per cumm).....[] [] [] []
 - d. WBC (x10³/ per cumm).....[] [] [.] [] []
WBC differential:
 - 1) Neutrophils (%).....[] []
 - 2) Lymphocytes (%).....[] []
 - 3) Monocytes (%).....[] []
 - 4) Eosinophils (%).....[] []
 - 5) Basophils (%).....[] []
 - 6) Bands (%).....[] []
 - 7) ANC.....[] [] [] []
2. Coagulation:
- a. PT (sec).....[] [] [.] [] []
 - b. PTT (sec).....[] [] [] [.] [] []
- Chemistry:
- a. Sodium (mEq/L).....[] [] [] []
 - b. Potassium (mEq/L).....[] [.] [] []
 - c. Chloride (mEq/L).....[] [] [] []
 - d. CO₂ (mEq/L).....[] [] [.] [] []
 - e. BUN (mg/dl).....[] [] [] []
 - f. Creatinine (mg/dl).....[] [] [.] [] []
 - g. Glucose (mg/dl).....[] [] [] []
 - h. Total Protein (g/dl).....[] [] [.] [] []
 - i. Albumin (g/dl).....[] [.] [] [] []
 - j. Calcium (mg/dl).....[] [] [.] [] []
 - k. Uric Acid (mg/dl).....[] [] [.] [] []
 - l. Total Bilirubin (mg/dl).....[] [.] [] [] []
 - m. ALT (SGPT) (IU/L).....[] [.] [] [] []
 - n. LDH (IU/L).....[] [] [] [] []
 - o. Alk. Phosphatase (IU/L).....[] [] [] [] []
 - p. Magnesium (mEq/L).....[] [] [.] [] []
4. Other (at pretreatment only) (check one) POS NEG
- a. HIV.....[] []
 - b. Hepatitis
 - Hepatitis B surface antigen.....[] []
 - Hepatitis B core antibody.....[] []
 - Hepatitis C virus.....[] []
 - c. HTLV-1 (1764 panel).....[] []
 - d. Pregnancy test (if applicable).....[] []
 - e. CMV antibody.....[] []

. If any of the abnormal values are clinically significant, also report on Adverse Event Form

BM HARVEST PROFILE
FORM 5

AASTROM BIOSCIENCES, INC.
CPS Replacement Feasibility Trial

+
AAS02

Subject Initials

FOR BRI USE ONLY

☐ FI ☐ MI ☐ LI

Social Security Number/Hospital I.D.

BRIDOCID:

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

P.I. Name

AAS-2-BMH-12/05/95

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

PRE-TREATMENT BONE MARROW EVALUATION

1. Bone Marrow Evaluation

a. Type of bone marrow specimen: Aspirate ☐1 Biopsy ☐2 Both ☐3

b. Percent cellularity: ☐☐% (Estimate to nearest 10%)

c. Biopsy results: Marrow involvement ☐1
No marrow involvement ☐2

BONE MARROW HARVEST

2. Date of harvest: ☐☐M ☐☐D ☐☐Y

3. Total cells obtained: x10⁹/ per kg Volume obtained: cc Cell concentration: 10⁹/ per ml

Cells cryopreserved (for back-up): x10⁹/ per kg

CELL EXPANSION PROFILE

4. Days of cell expansion: ☐☐

5. Results of preharvest culture: Positive ☐1 Negative ☐2

6. Cell viability: ☐☐%

7. Cell markers: (Forward sample to Aastrom Biosciences, Inc. for analysis)

8. Were the expanded cells infused to subject? Yes ☐1 No ☐2

If yes:

Date: ☐☐M ☐☐D ☐☐Y Time: (24 hours clock): ☐☐ : ☐☐

9. Total number of expanded cells transfused x 10⁹/

BACK-UP MARROW INFUSION

10. Was the back-up marrow infused to subject? Yes ☐1 No ☐2

If yes:

Date: ☐☐M ☐☐D ☐☐Y Time: (24 hours clock): ☐☐ : ☐☐

11. Total number of Back-up marrow cells infused: x 10⁹/

+

+

/

/

Investigator Signature

Date Signed

Copyright BRI. Forward WHITE and YELLOW copies to BRI. Retain PINK copy for your files.

TOXICITY FORM 6

Page 1 of 1

AASTROM BIOSCIENCES, INC.
CPS Replacement Feasibility Trial

AAS02
+

Subject Initials
[]FI []MI []LI

FOR BRI USE ONLY

Social Security Number/Hospital I.D.
[] [] [] [] [] [] [] [] [] []

BRIDOCID:
AAS-2-F6-4/3/96

P.I. Name
[] [] [] [] [] [] [] []

INFUSION TOXICITY GRADING

1. Assessment

Pretreatment..... [] []M [] []D [] []Y 24 Hour..... [] []M [] []D [] []Y
Day 0 Pre-Infusion:..... [] []M [] []D [] []Y Day [] [] (Insert Day) [] []M [] []D [] []Y
0-2 Hours Post-infusion
of Expanded Cells:..... [] []M [] []D [] []Y OTHER:..... [] []M [] []D [] []Y

TOXICITY ASSESSMENT

EFFECT	Maximum Toxicity Grade at Assessment	Date Maximum Grade Occurred	Treatment Relatedness (See codes A-E)	Treatment Received?		Toxicity?	
				Yes	No	New	Ongoing
2. Cardiac.....	[]	[] []M [] []D [] []Y	[]1	[]1	[]2	[]1	[]2
3. Bladder.....	[]	[] []M [] []D [] []Y	[]1	[]1	[]2	[]1	[]2
4. Renal.....	[]	[] []M [] []D [] []Y	[]1	[]1	[]2	[]1	[]2
5. Pulmonary.....	[]	[] []M [] []D [] []Y	[]1	[]1	[]2	[]1	[]2
6. Hepatic.....	[]	[] []M [] []D [] []Y	[]1	[]1	[]2	[]1	[]2
7. CNS.....	[]	[] []M [] []D [] []Y	[]1	[]1	[]2	[]1	[]2
8. Stomatitis.....	[]	[] []M [] []D [] []Y	[]1	[]1	[]2	[]1	[]2
9. GI.....	[]	[] []M [] []D [] []Y	[]1	[]1	[]2	[]1	[]2

(Questions 2-9 use Bearman, et al toxicity grading)

10. Circulatory							
a. Hypertension.....	[]	[] []M [] []D [] []Y	[]1	[]1	[]2	[]1	[]2
b. Hypotension.....	[]	[] []M [] []D [] []Y	[]1	[]1	[]2	[]1	[]2
11. Dermatologic							
a. Local.....	[]	[] []M [] []D [] []Y	[]1	[]1	[]2	[]1	[]2
b. Skin rash.....	[]	[] []M [] []D [] []Y	[]1	[]1	[]2	[]1	[]2
c. Blistering.....	[]	[] []M [] []D [] []Y	[]1	[]1	[]2	[]1	[]2
d. Erythema.....	[]	[] []M [] []D [] []Y	[]1	[]1	[]2	[]1	[]2
12. Allergy	[]	[] []M [] []D [] []Y	[]1	[]1	[]2	[]1	[]2
13. Miscellaneous							
a. Weight gain.....	[]	[] []M [] []D [] []Y	[]1	[]1	[]2	[]1	[]2
b. Weight loss.....	[]	[] []M [] []D [] []Y	[]1	[]1	[]2	[]1	[]2

(Questions 10-13 use SWOG toxicity grading)

For toxicity grade criteria, please see protocol
Treatment relatedness: A-definitely related B-probably related C-possibly related D-unrelated E-unknown

+

Investigator Signature

+

/

/

Date Signed

VITAL SIGNS
FORM 8

AASTROM BIOSCIENCES, INC.
CPS Replacement Feasibility Trial

+
AAS02

Subject Initials
[]FI []MI []LI

FOR BRI USE ONLY

Social Security Number/Hospital I.D.
[] [] [] [] [] [] [] [] []

BRIDOCID:
AAS-2-VIT-11/15/95

P.I. Name
[] [] [] [] [] [] [] []

VITAL SIGNS							
Date	Maximum Temperature (degrees Celsius)	Fever Code* (see below)	Respirations (breaths/min)	Pulse (beats/min)	Blood Pressure (mm Hg)		
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	systolic	diastolic	
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	[] [] []	/ [] [] []	
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	systolic	diastolic	
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	[] [] []	/ [] [] []	
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	systolic	diastolic	
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	[] [] []	/ [] [] []	
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	systolic	diastolic	
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	[] [] []	/ [] [] []	
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	systolic	diastolic	
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	[] [] []	/ [] [] []	
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	systolic	diastolic	
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	[] [] []	/ [] [] []	
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	systolic	diastolic	
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	[] [] []	/ [] [] []	

* Code fever in text field on clinical evaluation form.

FEVER CODES:

1=No fever
2=blood products

3=treatment/medication
4=documented infection (positive culture)

5=presumed infection
9=unexplained

+ + / /

Recorder Signature Date Signed

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BM HARVEST PROFILE
FORM 5

AASTROM BIOSCIENCES, INC.
CPS Replacement Feasibility Trail

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AAS02

Subject Initials

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Social Security Number/Hospital I.D.

BRIDOCID:

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

P.I. Name

AAS-2-BMH-12/05/95

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

PRE-TREATMENT BONE MARROW EVALUATION

1. Bone Marrow Evaluation

a. Type of bone marrow specimen: Aspirate ☐1 Biopsy ☐2 Both ☐3

b. Percent cellularity: ☐☐% (Estimate to nearest 10%)

c. Biopsy results: Marrow involvement ☐1
No marrow involvement ☐2

BONE MARROW HARVEST

2. Date of harvest: ☐☐M ☐☐D ☐☐Y

3. Total cells obtained: x10⁹/ per kg Volume obtained: cc Cell concentration: 10⁹/ per ml

Cells cryopreserved (for back-up): x10⁹/ per kg

CELL EXPANSION PROFILE

4. Days of cell expansion: ☐☐

5. Results of preharvest culture: Positive ☐1 Negative ☐2

6. Cell viability: ☐☐%

7. Cell markers: (Forward sample to Aastrom Biosciences, Inc. for analysis)

8. Were the expanded cells infused to subject? Yes ☐1 No ☐2

If yes:

Date: ☐☐M ☐☐D ☐☐Y Time: (24 hours clock): ☐☐ : ☐☐

9. Total number of expanded cells transfused x 10⁹/

BACK-UP MARROW INFUSION

10. Was the back-up marrow infused to subject? Yes ☐1 No ☐2

If yes:

Date: ☐☐M ☐☐D ☐☐Y Time: (24 hours clock): ☐☐ : ☐☐

11. Total number of Back-up marrow cells infused: x 10⁹/

+

+

/

/

Investigator Signature

Date Signed

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BRIDOCID:

AAS-2-TRAN-11/15/95

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AAS-2-TRAN-11/15/95

TRANSFUSION OF BLOOD PRODUCTS

have been given

[illegible]

Note: 4 units per transfusion event

+ / /

Date Signed

VITAL SIGNS
FORM 8

AASTROM BIOSCIENCES, INC.
CPS Replacement Feasibility Trial

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AAS02

Subject Initials
[]FI []MI []LI
Social Security Number/Hospital I.D.
[] [] [] [] [] [] [] [] []
P.I. Name
[] [] [] [] [] [] [] []

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BRIDOCID:
AAS-2-VIT-11/15/95

VITAL SIGNS

Date	Maximum Temperature (degrees Celsius)	Fever Code* (see below)	Respirations (breaths/min)	Pulse (beats/min)	Blood Pressure (mm Hg)
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	systolic diastolic [] [] [] / [] [] []
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	systolic diastolic [] [] [] / [] [] []
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	systolic diastolic [] [] [] / [] [] []
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	systolic diastolic [] [] [] / [] [] []
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	systolic diastolic [] [] [] / [] [] []
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	systolic diastolic [] [] [] / [] [] []
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	systolic diastolic [] [] [] / [] [] []
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	systolic diastolic [] [] [] / [] [] []
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	systolic diastolic [] [] [] / [] [] []
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	systolic diastolic [] [] [] / [] [] []
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	systolic diastolic [] [] [] / [] [] []
[] []M [] []D [] []Y	[] [] . []	[]	[] []	[] [] []	systolic diastolic [] [] [] / [] [] []

* Code fever in text field on clinical evaluation form.

EVER CODES:

1=No fever
2=blood products

3=treatment/medication
4=documented infection (positive culture)

5=presumed infection
9=unexplained

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CONCOMITANT MEDICATIONS
FORM 5

AASTROM BIOSCIENCES, INC.
CPS Replacement Feasibility Trial

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AAS02

Subject Initials
[] [] [] []

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Social Security Number/Hospital I.D.
[] [] [] [] [] [] [] [] []

BRIDOCID:
AAS-2-MED-11/15/95

P.I. Name
[] [] [] [] [] [] [] []

CONCOMITANT MEDICATIONS

List all concomitant medications (including antibiotics, antifungals, and antivirals) taken by the subject during the study, i.e., pretreatment through hospital discharge.

Medication	Start date	Stop date	Indication
1. _____	[] [] M [] [] D [] [] Y	[] [] M [] [] D [] [] Y	_____
2. _____	[] [] M [] [] D [] [] Y	[] [] M [] [] D [] [] Y	_____
3. _____	[] [] M [] [] D [] [] Y	[] [] M [] [] D [] [] Y	_____
4. _____	[] [] M [] [] D [] [] Y	[] [] M [] [] D [] [] Y	_____
5. _____	[] [] M [] [] D [] [] Y	[] [] M [] [] D [] [] Y	_____
6. _____	[] [] M [] [] D [] [] Y	[] [] M [] [] D [] [] Y	_____
7. _____	[] [] M [] [] D [] [] Y	[] [] M [] [] D [] [] Y	_____
8. _____	[] [] M [] [] D [] [] Y	[] [] M [] [] D [] [] Y	_____
9. _____	[] [] M [] [] D [] [] Y	[] [] M [] [] D [] [] Y	_____
10. _____	[] [] M [] [] D [] [] Y	[] [] M [] [] D [] [] Y	_____

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Recorder Signature

+
Date Signed

INFECTION EVALUATION

AASTROM BIOSCIENCES, INC.

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FORM 10

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CPS Replacement Feasibility Trial

AAS02

Subject Initials

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Social Security Number/Hospital I.D.

[] [] [] [] [] [] [] [] []

BRIDOCID:

P.I. Name

[] [] [] [] [] [] [] []

AAS-2-INF-11/15/95

INFECTION EVALUATION

1. Date of onset.....[] []M [] []D [] []Y

2. Site of infection: ("X" one)

blood.....[]1

urinary tract.....[]2

pulmonary.....[]3

GI tract.....[]4

other (specify)_____ []5

3. Has infrection been resolved? Yes []1 No []2

If yes, date ended.....[] []M [] []D [] []Y

4. Infection Type: ("X" one)

viral (specify agent)_____ []1

bacterial (specify agent)_____ []2

fungal (specify agent)_____ []3

protozoan (specify agent)_____ []4

5. Means of diagnosis: ("X" one)

presumed.....[]1

documented.....[]2

if documented, specify means: ("X" all that apply)

clinical.....[]1

radiographic.....[]1

blood culture.....[]1

bronchoscopy specimen.....[]1

swab culture.....[]1

other biopsy specimen.....[]1

urinalysis.....[]1

other (specify)_____ []1

6. Was treatment given? Yes []1 No []2

If yes, specify treatment _____

+

+

/

/

Investigator Signature

Date Signed

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ADVERSE EFFECT		AASTROM BIOSCIENCES, INC.		+	
FORM 11		CPS Replacement Feasibility Trial		AAS02	
Subject Initials				FOR BRI USE ONLY	
[]FI []MI []LI					
Social Security Number/Hospital I.D.				BRIDOCID:	
[] [] [] [] [] [] [] []				AAS-2-11-11/15/95	
P.I. Name					
[] [] [] [] [] [] [] []					
ADVERSE EFFECT					
COMPLETE THIS FORM FOR EACH UNANTICIPATED ADVERSE DEVICE EFFECT EXPERIENCED.					
An UNANTICIPATED adverse effect is any serious effect or health or safety or any life-threatening problem caused by, or associated with, a device, if that effect problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan. For this study, this includes: hypotension, anaphylaxis, serositis, dyspnea and/or hypoxemia, renal or hepatic dysfunction, or sudden death					
Serious and unanticipated device effects should be reported by the investigator to Aastrom immediately. The investigator must report the event to Aastrom and the IRB in writing within 10 working days of learning of the event.					
1. Description of effect:					
2. a. Onset date: [] [] M [] [] D [] [] Y					
5. Action taken: ("X" all that apply)					
b. Has the event ended? Yes [] 1 Continuing [] 2					
None..... [] 1					
Medication (specify) [] 1					
Other (specify) [] 1					
If YES date ended: [] [] M [] [] D [] [] Y					
3. Severity of adverse effect:					
("X" one)					
Mild..... [] 1					
Moderate..... [] 2					
Severe..... [] 3					
4. Relationship of adverse effect to treatment:					
("X" one)					
Definitely..... [] 1					
Probably..... [] 2					
Possibly..... [] 3					
Unlikely..... [] 4					
Not known..... [] 5					
6. Results:					
("X" one)					
Resolved with treatment..... [] 1					
Resolved without treatment..... [] 2					
Not resolved, continuing..... [] 3					
Death..... [] 4					
Outcome unknown..... [] 5					
7. Assessment:					
("X" one)					
Non-Serious..... [] 1					
Serious, expected..... [] 2					
Serious, unanticipated..... [] 3					
+ / /					
Investigator Signature					
Date Signed					
Copyright BRI.					

EXHIBIT C

SCHEDULE OF LABORATORY AND CLINICAL EQUIPMENT

Item	Supplier	Cat. No.	UNIT QTY:	UNIT/PKG:	PKG:	COST/PKG:	Total Cost:
Equipment:							
CCD Handling Fixture	Aastrom		1	1	2	\$750.00	\$1,500.00
CCD Support Clamp	Aastrom		1	1	6	\$50.00	\$300.00
CO2 Incubator	Forma Scientific	3956	1	1	1	\$7,000.00	\$7,000.00
Incubator Organizer	Aastrom		2	1	2	\$850.00	\$1,700.00
4 degree C Refrigerator	Fisher Scientific	126GW-2	1	1	1	\$3,500.00	\$3,500.00
Media Supply Pump	Watson Marlow	202U/AA	3	1	3	\$1,400.00	\$4,200.00
Media Supply Pump Head	Watson Marlow	202U/AA	3	1	3	\$1,200.00	\$3,600.00
Electrical Power Strip	Aastrom		1	1	1	\$14.95	\$14.95
18 degree C to 50 degree C thermometer	SP		2	1	2	\$36.00	\$72.00
neg 5 degree C to 20 degree C thermometer	SP		2	1	2	\$21.91	\$43.82
P-1000 Pipetman	Gilson		1	1	1	\$219.50	\$219.50
P-200 Pipetman	Gilson		1	1	1	\$219.50	\$219.50
P-20 Pipetman	Gilson		1	1	1	\$219.50	\$219.50
Gas Regulator Assembly	Aastrom		6	1	6	\$360.00	\$2,160.00
Repeater Plpet	Eppendorf		1	1	1	\$350.00	\$350.00
Tubing Stretcher	Aastrom		1	1	1	\$18.00	\$18.00
Pliers	Aastrom		1	1	1	\$8.00	\$8.00
Gas Flow Indicator	Aastrom		1	1	1	\$130.00	\$130.00
Gas Humidifier Cap Adapter	Aastrom		9	1	9	\$6.00	\$54.00
Nikon Dark Field Microscope			1	1	1	\$2,600.00	\$2,600.00
modification of incubator organizer for horizontal waste shelves					1	\$1,000.00	\$1,000.00
horizontal waste shelves			8	1	8	\$100.00	\$800.00
CPS Processor	Aastrom		1	1	1	\$26,940.00	\$26,940.00
CPS Incubator	Aastrom		5	1	5	\$15,518.00	\$77,590.00
Interim Monitor	Aastrom		1	1	1	\$3,000.00	\$3,000.00
18 degree C to 50 degree C thermometer	SP		2	1	2	\$36.00	\$72.00
neg 5 degree C to 20 degree C thermometer	SP		2	1	2	\$21.91	\$43.82
Gas Cylinder Support Stand	Scott Medical		1	1	1	\$25.00	\$25.00
Gas Regulator Assembly	Aastrom		3	1	3	\$360.00	\$1,080.00
Tubing Heat Sealer	Sebra		1	1	1	\$3,298.00	\$3,298.00
Incubator Rack	Metro		2	1	2	\$346.00	\$692.00
Manual + Automated CPS Equipment Cost/Study:							\$142,450.09

EXHIBIT D

SCHEDULE OF CLINICAL TRIAL BUDGET AND MILESTONE PAYMENTS

COMPENSATION AMOUNT AND SCHEDULE

1. Compensation Amount.

Aastrom agrees to provide, according to the terms and conditions set forth herein, and contingent upon conducting the Study as specified by the Protocol, a total compensation of Fifty-Five Thousand and No/100 U.S. Dollars (\$55,000.00 U.S.), or Five Thousand Five Hundred and No/100 U.S. Dollars (\$5,500.00 U.S.) per subject according to the compensation schedule set forth below in Section 2 of this Exhibit D. The \$5,500 per subject compensation includes an indirect cost of 25%, and represents any and all compensations associated with the Study. The total compensation amount is based upon the actual number of subject to be completed and may be adjusted based upon the actual number of subjects actually completed. If a subject is dropped from the Study for any reason, payment for that subject will be prorated.

2. Compensation Schedule.

The payee identified in Section 3 of this Exhibit D below will be remunerated according to the following schedule:

	Percentage -----	Amount ----- (U.S. DOLLARS)
Initial Payment	25%	\$13,750.00 -----
50% Subjects Completed	25%	\$13,750.00 -----
All Subjects Completed	25%	\$13,750.00 -----
100% Subjects Case Report Forms Completed and Submitted	15%	\$ 8,250.00 -----
Final Report	10%	\$ 5,500.00 -----

3. Name and Address of Payee

Payment made to: The University of Texas
M.D. Anderson Cancer Center
Atten: Manager, Sponsored Programs
P.O. Box 297402
Houston, TX 77297

4. TERMINATED STUDY - PAYMENT OBLIGATIONS

If either the Institution or Aastrom terminates the Study prior to its originally planned termination date, Aastrom shall compensate the Institution based upon the portion of the Study completed at the date of termination. This partial payment will be prorated according to the number of satisfactorily completed subject visits.

EXHIBIT E

INVESTIGATOR AGREEMENTS

(See Section 13 of Protocol)

ATTACHMENT 1
RESEARCH AGREEMENT
UM/Ann Arbor Stromal

LICENSE AGREEMENT

By this Agreement, Ann Arbor Stromal, Inc. (hereinafter "Ann Arbor Stromal") and the Regents of The University of Michigan, a constitutional corporation of the State of Michigan (hereinafter "University") agree as follows:

1. INCORPORATION BY REFERENCE

Incorporated by reference with full force and effect to the provisions, definitions, terms and conditions of this License Agreement (hereinafter "License") are the provisions, definitions, terms and conditions of the Research Agreement to which this License is attached, including the Option Agreement and its Appendices.

2. DEFINITIONS

- 2.1 "Effective Date" of this License shall be the date of completed execution by both Parties in accordance with the provisions of Article 9 entitled "License", in the abovementioned Research Agreement to which this License is attached.
- 2.2 "Parties", in singular or plural usage as required by the context, means Ann Arbor Stromal and/or University.

- 2.3 "Territory" means all countries of the world.
- 2.4 "Licensed Technology" means all patentable inventions and Know-how for the production of red blood cells, white blood cells, platelets and bone marrow cells, which are either described in University Project proposal, or conceived or reduced to practice as part of Project, or conceived or reduced to practice, whether or not pursuant to or as part of the Project, by Drs. Stephen G. Emerson, Michael F. Clarke or Bernhard O. Palsson, or those working under their direction, during the term of their participation in the Project and Ann Arbor Stromal's funding of the Project.
- 2.5 "Licensed Patent(s)" means any and all pending patent applications(s) included within Licensed Technology, whether now existing or hereafter filed, both domestic and foreign, and any patents issuing therefrom.
- 2.6 "Valid Claim(s)" means any claim(s) pending in a patent application or in an unexpired patent included within the Licensed Patents which has not been held unenforceable, unpatentable, or invalid by a decision of a court or other governmental agency of competent jurisdiction, unappealable or unappealed within the time allowed for appeal, and which has not been admitted to be invalid or unenforceable through reissue or disclaimer. If in any country there should be two or more such decisions conflicting with respect to the validity of the same claim, the decision of the higher or highest tribunal shall thereafter control;

however, should the tribunals be of equal rank, then the decision or decisions upholding the claim shall prevail when the conflicting decisions are equal in number, and the majority of decisions shall prevail when the conflicting decisions are unequal in number.

- 2.7 "Know-How" means (a) all information, data and knowledge contained in patent applications or patents which are at anytime included in the definition of Licensed Patents, and (b) any other methods, procedures, processes, compositions of matter, biological materials, trade secrets, experience, work products technical information, inventions, discoveries, improvements, reports, data, results from experiments, developmental efforts and demonstrations and subject matter related to the Project, whether or not contained in Licensed Patents.
- 2.8 "Product(s)" means any red blood cells, white blood cells, platelets and bone marrow cells as well as any components, by-products, progeny or derivatives thereof and any factor, composition, substance, equipment, mechanism, device or other property and combinations thereof, the manufacture, use or sale of which would, but for this License, comprise an infringement of one or more Valid Claims.
- 2.9 "Combination Sales" shall mean sales of Product by Ann Arbor Stromal, its Affiliates or subsidiaries as a combined package comprised in part of Product and in part of one or more other products or parts which constitute either an

active ingredient or a significant delivery system or mechanism and which could readily be sold by Ann Arbor Stromal, its Affiliates or subsidiaries and used for their intended purpose by their purchasers without the incorporation or use of Product.

- 2.10 "Net Sales" means the sum, over the term of this License, of all amounts of monies received and all other consideration received (when in a form other than cash or its equivalent, the fair market value thereof when received) by Ann Arbor Stromal, its Affiliates or subsidiaries from purchasers or users from or by reason of the sale, distribution or use of Product, less any amounts collected for taxes, including sales and use taxes, customer charges, allowances (including any allowance for bad debts), import and export duties and other governmental charges, prompt payment or other customary trade discounts allowed or taken, credits or refunds for goods returned and transportation and delivery charges (including insurance premiums).

If Product is sold in Combination Sales, then Net Sales shall be computed in the following manner: First, gross revenues from the Combination Sales shall be reduced by any applicable deductions itemized in the first paragraph of this definition in order to arrive at "Combination Net Sales"; second, Net Sales shall be calculated by employing the following formulas:

$C - p = \text{Net Sales.}$

In the above formula, "p" is the fair market value of all other products or parts which constitute an active ingredient or significant delivery system or mechanism within the Combination Sale and C is equal to Combination Net Sales.

All fair market value calculations made by Ann Arbor Stromal hereunder shall be in good faith determined by Ann Arbor Stromal in the event no market price is available. In the event the University disagrees with any aspect of Ann Arbor Stromal's implementation of this definition, University may request that such dispute be submitted to arbitration as described in Article 17 and Ann Arbor Stromal hereby agrees to promptly grant and fully cooperate with such request.

- 2.11 "Affiliate" shall mean any corporation, partnership, proprietorship or other entity controlled by, controlling, or under common control with Ann Arbor Stromal, and shall include any corporation, partnership, proprietorship or other entity directly or indirectly owning, owned by or under common ownership with the party in question to the

extent of twenty-five percent (25%) or more of the equity or voting shares, including shares owned beneficially by such party.

2.12 "Calendar Quarters" means the three (3) months ending on the last day of March, June, September and December of each year.

3. GRANTS

3.1 Subject to the conditions and provisions of this License, University hereby grants to Ann Arbor Stromal an exclusive world-wide license, without the right to grant sublicenses, except as described in paragraph 3.2 below, under Licensed Patents and to use Know-How to make, use, and sell Product(s), except that University hereby retains the right to use Licensed Patents and Know-How solely for research purposes, and except that to the extent funding from federal agencies results in Licensed Technology or Licensed Patents in addition to Project funding, the federal government may have its standard license rights with respect to such Licensed Technology or Licensed Patents.

3.2 If at any time Ann Arbor Stromal wishes to grant sublicense rights under its exclusive license rights granted herein, University and Ann Arbor Stromal shall negotiate in good faith in order to allow Ann Arbor Stromal to enter into such sublicensing arrangements with a royalty return on Product(s) to University comparable to royalties earned by

University under this License. Subject only to this understanding and the need to have any sublicensing arrangements reflect a fair market value return to Ann Arbor Stromal as in an arms length transaction, it is the understanding of the parties that Ann Arbor Stromal should be able to make its own decisions as to the appropriate mechanisms, including sublicensing, for exploiting the Licensed Technology.

- 3.3 The University and Ann Arbor Stromal hereby assert that, to the best of their knowledge as of the date of execution of the Option Agreement, there do not exist any University patents or pending patents, other than the Licensed Patents of this License Agreement, which would be infringed by the practice of the Licensed Patents of this License or which would otherwise prevent the practice of any of the Valid Claims. If, however, such University patents or patent applications are subsequently found to have existed prior to the date of the Option Agreement, University shall use reasonable efforts to grant to Ann Arbor Stromal a nonexclusive license to such patents and/or patent applications, to the extent necessary for the practice of the Licensed Technology of this License.

4. ROYALTIES

- 4.1 The license rights granted to Ann Arbor Stromal herein are subject to Ann Arbor Stromal's payment of royalties to University according to the provisions of this Section 4.

- 4.2 For Product(s) defined in 2.8 herein, Ann Arbor Stromal will pay University a royalty equal to two percent (2%) of Net Sales of such Product(s) by Ann Arbor Stromal and Affiliates for the life of the last to expire of Licensed Patents.
- 4.3 Where Net Sales form the basis upon which payment to University is derived, the obligation to pay University under this Section 4 is imposed only once with respect to the same unit of Product regardless of the number of Valid Claims, Licensed Patents or items of Know-How covering the same; however, for purposes of determination of payments due hereunder, whenever the term Product may apply to a property during various stages of manufacture, use or sale, Net Sales, as otherwise defined shall be derived from the sale, distribution or use of such Product by Ann Arbor Stromal and Affiliates at the stage of its highest invoiced value to unrelated third parties.
- 4.4 If at any time or from time to time an unrelated third party in any country shall, under right of a compulsory license granted or ordered to be granted by a competent governmental authority, manufacture, use or sell any Product with respect to which royalties shall be payable pursuant to Paragraph 4.2 of this Section, then Ann Arbor Stromal, upon notice to University and during the period such compulsory license shall be effective, shall have the right to reduce such royalty on each unit of Product sold

in such country to an amount no greater than the amount payable by said third party in consideration of its compulsory license.

5. REPORTS

- 5.1 Within sixty (60) days after the close of each Calendar Quarter during the term of this License (including the last day of any such Calendar Quarter following any termination of this License), Ann Arbor Stromal shall report to University all royalties accruing to University under Section 4 during such Calendar Quarter. Such quarterly reports shall indicate for each Calendar Quarter the gross sales and Net Sales of Product; such reports shall also indicate Net Sales with respect to which payments are due and the amount of such payments, as well as the various calculations used to arrive at said amounts, including the quantity, description (nomenclature and type designation), country of sale and country of manufacture of Product(s). In case no payment is due for any such period, Ann Arbor Stromal shall so report.
- 5.2 Ann Arbor Stromal covenants that it will promptly establish and consistently employ a system of specific nomenclatures and type designations for Product(s) so that the various types can be identified and segregated, and Ann Arbor Stromal and Affiliates will consistently employ such system when rendering invoices thereon and henceforth agrees to inform University, or its auditors, when requested as to

the details concerning such nomenclature system as well as to all additions thereto and changes therein.

- 5.3 Ann Arbor Stromal shall keep and it shall cause its Affiliates to keep, true and accurate records and books of account containing data reasonably required for the computation and verification of payments to be made as provided by this License, which records and books shall be open for inspection upon reasonable notice during business hours by inspectors selected by and at the expense of University for the purpose of verifying the amount of payments due and payable. Said right of inspection will exist for six (6) years from the date of origination of any such record and this requirement and right of inspection shall survive any termination of this License for a period of three (3) years after such termination. However, in the event that such inspection reveals an underpayment of royalties to University in excess of five percent (5%), then said inspection shall be at Ann Arbor Stromal's expense and such underpayment shall become immediately due and payable to University.
- 5.4 The reports provided hereunder shall be certified by an authorized representative of Ann Arbor Stromal to be correct to the best of Ann Arbor Stromal's knowledge and information.

6. TIMES AND CURRENCIES OF PAYMENTS

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- 6.1 Payments accrued at the close of each Calendar Quarter shall be due and payable in Ann Arbor, Michigan on the date each quarterly report, provided for under Section 5 above, is due and shall be paid in United States dollars. Ann Arbor Stromal agrees to make all payments due hereunder to University by check addressed to the University's Intellectual Properties Office or by wire transfer to the bank account designated by University with telephonic confirmation of receipt thereof.
- 6.2 On all amounts outstanding and payable to University, interest shall accrue from the date such amounts are due and payable at a rate of two (2) points above the prime lending rate as established by the Chase Manhattan Bank, N.A. in New York City, New York, or at such lower rate as may be required by law.
- 6.3 Any United States currency payments hereunder shall be determined by converting foreign currencies into their equivalent in United States dollars at the exchange rate of such currency as reported (or if erroneously reported, as subsequently corrected) in the Wall Street Journal on the last business day of the Calendar Quarter during which such payments accrue (or if not reported on that date, as quoted by the Chase Manhattan Bank, N.A. in New York City, New York).

7. COMMERCIALIZATION

- 7.1 Ann Arbor Stromal agrees to use commercially reasonable efforts in proceeding with the development, manufacture, marketing and sale of Products to commercially exploit the Licensed Technology and in creating a supply and demand for same; provided, however, Ann Arbor Stromal shall be entitled to exercise prudent business judgment in meeting its obligations hereunder.
- 7.2 Where Ann Arbor Stromal engages in continuing development with respect to Product(s), Ann Arbor Stromal shall keep University informed of such developments in writing. Ann Arbor Stromal shall promptly inform University of any patent applications, or similar applications, relating to Product(s) or improvements thereon, filed by or on behalf of Ann Arbor Stromal or Affiliates anywhere in the world.

8. INFRINGEMENT

- 8.1 In the event a third party is infringing a Valid Claim by making, using or selling Product(s) as defined herein, Ann Arbor Stromal shall have the right to bring suit in its own name. University agrees to use reasonable efforts to cooperate in the prosecution of such suit. Ann Arbor Stromal shall bear the expense of any such litigation and, except as described in Paragraph 8.5 below, shall have full authority to negotiate a settlement on such terms as Ann Arbor Stromal shall determine. Ann Arbor Stromal shall

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8.3 In the event that during the term hereof there be made against Ann Arbor Stromal, any charge for infringement of any third-party patent by reason of Ann Arbor Stromal's or Affiliate's manufacture or sale of a Product or any customer's use of the Product which charge is grounded essentially on an asserted domination by that third-party patent of the manufacture, sale or use of such Product, Ann Arbor Stromal shall give written notice thereof to University. Ann Arbor Stromal agrees to effectuate, if possible, an acceptable change in the Product to avoid such alleged infringement. If no such satisfactory change can be effectuated, University and Ann Arbor Stromal agree to collaborate and enter into discussions with said third party for the purposes of negotiating a settlement. If no settlement can be agreed upon by Ann Arbor Stromal, University and the third party, Ann Arbor Stromal shall have the right, but not the obligation, to defend any suit for infringement brought against it by the third party, and if required by law or if requested by University, to join University as a party defendant. If Ann Arbor Stromal shall elect not to defend such infringement suit, Ann Arbor Stromal shall promptly notify University to that effect and University shall thereafter have the obligation to defend the suit provided Ann Arbor Stromal reimburses the University within thirty (30) days of invoicing for all cost and expenses (including reasonable attorney fees), and if required by law or if requested by Ann Arbor Stromal, to join Ann Arbor Stromal as a party defendant.

8.4 Ann Arbor Stromal will bear the cost of defending claims of infringement or pursuing infringers, except as allowed in Paragraph 8.2 above. However, Ann Arbor Stromal can be reimbursed for up to one-half of the unrecovered amount of such actual and reasonable expenses in the following manner: Ann Arbor Stromal can deduct from royalties otherwise due and payable to University under the License, up to fifty percent (50%) until such time as Ann Arbor Stromal has recovered one-half of its actual, reasonable, and otherwise unrecovered expenses. University's "obligation" of bearing one-half of Ann Arbor Stromal's expenses shall not exceed the ability of the above-described mechanism (i.e., a 50% reduction in royalty payments due and payable) to reimburse such expenses and University royalty payments otherwise due shall never be reduced by more than 50%. Ann Arbor Stromal will make an accounting to University of all such expenses as part of its reporting obligations under Section 5.

8.5 Neither University nor Ann Arbor Stromal shall compromise or settle any claim or action in any manner that would affect the rights of the other Party without the consent of said other Party.

9. TERMINATION

9.1 With respect to any termination of this License, and except as provided herein to the contrary, all rights and

obligations of the Parties hereunder shall cease with respect thereto, except as follows:

- 9.1.1 Obligations to pay royalties and other sums accruing hereunder up to the day of such termination;
- 9.1.2 Obligations to pay royalties on Net Sales, subsequent to said date of termination of Product(s) in Stock at the date of termination with respect to which stock Ann Arbor Stromal shall have a reasonable time to sell or liquidate in a reasonable manner as deemed necessary by Ann Arbor Stromal under the circumstances;
- 9.1.3 Obligations for record keeping and accounting reports for so long as Product(s) are sold pursuant to Paragraph 9.1.2 above. At such time as there are no sales or other dispositions of Product(s) upon termination of this License, Ann Arbor Stromal shall render a final report and royalty payment;
- 9.1.4 University's rights to audit books and records as described in Section 5 herein;
- 9.1.5 Obligations of indemnity under Section 18;
- 9.1.6 Any cause of action or claim of Ann Arbor Stromal or University accrued or to accrue because of any breach or default by the other Party hereunder;

9.2 This License will become effective on its Effective Date and, unless terminated under another, specific provision of

this License, will remain in effect until and terminate upon the expiration of the later of Ann Arbor Stromal's obligation to pay royalties under Paragraph 4.3 herein or the last to expire of Licensed Patents. After such full-term termination of this License, Ann Arbor Stromal shall have the right to make, use and sell Product(s) without further payment to University hereunder.

- 9.3 If Ann Arbor Stromal shall at any time default in the payment of any royalty or the making of any report hereunder, or shall commit any material breach of any material covenant or promise herein contained, -----
or shall make any false report and shall fail to remedy any such default, material breach or report within sixty (60) days after written notice thereof by University, University may, at its option, terminate this License by notice in writing to such effect. In the event of such termination, interest shall continue to accrue as described in Paragraph 6.2 on any amounts outstanding and payable to University and any such termination shall be without prejudice to University's other legal rights for breach of this License.
- 9.4 In the event that Ann Arbor Stromal desires to terminate this License, Ann Arbor Stromal shall serve upon University a notice of termination, including a statement of reasons for such termination, at least six (6) months before a termination date established by Ann Arbor Stromal. Such notice shall be deemed by the parties to be final, and immediately upon service of such notice of termination,

University shall have the right to begin negotiations and enter into agreements with others for the manufacture, sale and use of the Product(s), and may, at its option, disclose to said others any and all information related to Product(s) other than Confidential Information generated or developed solely by Ann Arbor Stromal. During the period of time from the notice of termination until termination pursuant to this provision, Ann Arbor Stromal shall continue to commercialize Product(s) and to make them reasonably available to the public at fair market value.

10. ASSIGNMENT

This License shall not be transferable or assignable by either Party without the prior written consent of the other Party, which consent shall not be unreasonably withheld; and any attempt to transfer or assign this License without such consent shall be void from the beginning. No transfer or assignment may be made by Ann Arbor Stromal unless and until the intended transferee or assignee agrees in writing to accept all of the terms and conditions of this License. For purposes of implementing this clause the University's consent may only be withheld:

- i) if the University reasonably believes that implementing the terms of the proposed transfer or assignment could economically discriminate against the University or its employees holding equity in Ann Arbor Stromal as compared to any of the other shareholders or investors in Ann Arbor Stromal or their principals; or

- ii) if the University reasonably believes that the proposed transfer or assignment is to a third party which is not in a financial and technical position at least equivalent to that of Ann Arbor Stromal for purposes of exploiting and commercializing the Licensed Technology.

11. REGISTRATION OR RECORDATION

- 11.1 If the terms of this License, or any assignment or license under this License are or become such as to require or make it appropriate that the Agreement or license or any part thereof be registered with or reported to a national or supranational agency of any area in which Ann Arbor Stromal, or Affiliates would do business, Ann Arbor Stromal will, at its expense, undertake such registration or report. Prompt notice and appropriate verification of the act of registration or report of any agency ruling resulting from it will be supplied by Ann Arbor Stromal to University.
- 11.2 Any formal recordation of this Agreement or any license herein granted which is required by the law of any country of the Territory as a prerequisite to enforceability of the Agreement or license in the courts of any such country or for other reasons shall also be carried out by Ann Arbor Stromal at its expense, and appropriately verified proof of recordation shall be promptly furnished to University.

12. EXPORT LAWS AND REGULATIONS OF THE UNITED STATES

12.1 The Export Regulations of the United States Department of Commerce prohibit the exportation from the United States of certain types of technical data and commodities (listed in the Export Administration Regulations), unless the exporter (e.g., Ann Arbor Stromal or Affiliates) has received the required General License or Validated License, whichever is applicable. In addition, the exporter may be required to obtain certain written assurances regarding re-export from the foreign importer for certain types of technical data and commodities. Prior to its engaging in any export activity, Ann Arbor Stromal has advised University that it will receive a copy of the then current Export Administration Regulations of the United States Department of Commerce and will arrange for a subscription under which it will receive Supplementary Bulletins from the United States Department of Commerce upon their issuance. Ann Arbor Stromal hereby agrees to comply with, and to require Affiliates to comply with, the Export Administration Regulations of the United States Department of Commerce; and Ann Arbor Stromal hereby gives University the assurances called for in the Export Administration Regulations, including the assurances called for in Part 379.4 and any successor provisions of such regulations.

12.2 This License shall be subject to all United States Government laws and regulations now or hereafter applicable to the subject matter of this License.

13. NOTICES

Any notice, request, report, or payment required or permitted to be given or made under this License by any Party shall be given by sending such notice by prepaid certified mail, return receipt requested, or by facsimile transmission to the address set forth below or such other address as such party shall have specified by written notice given in conformity herewith. Any notice not so given shall not be valid unless and until actually received, and any notice given in accordance with the provisions of this paragraph shall be effective when mailed:

TO University: The University of Michigan
Intellectual Properties Office
475 East Jefferson, Room 2354
Ann Arbor, Michigan 48109-1248
Attention: File No. 433

TO Ann Arbor Stromal: Robert Kunze
General Partner
H&Q Life Science Technology Fund I
One Bush Street
San Francisco, California 94104

With copy provided to: Kenneth L. Guernsey
Attorney at Law
Cooley, Godward, Castro, Huddleson & Tatum
One Maritime Plaza, 20th Floor
San Francisco, CA 94111-3580

14. INVALIDITY

In the event that any term, provision, or covenant of this License shall be determined by a court of competent jurisdiction to be invalid, illegal, or unenforceable, that term will be curtailed, limited, or deleted, but only to the extent necessary

to remove such invalidity, illegality, or unenforceability, and the remaining terms, provisions, and covenants shall not in any way be affected or impaired thereby. In the event that the time period of any covenant shall be held unenforceable as a matter of law, said covenant will be interpreted to be effective for an enforceable time period.

15. ENTIRE AGREEMENT AND AMENDMENT

This License contains the entire understanding of the Parties with respect to the matter contained herein, and supersedes all prior agreements, oral or written, and all other communication between them relating to the subject matter hereof. The Parties hereto may, from time to time during the continuance of this License, modify, vary or alter any of the provisions of this License, but only by an instrument duly executed by authorized officials of both Parties hereto.

16. GOVERNING LAW

This License and the relationships between the Parties shall be governed in all respects by the law of the State of Michigan, the United States of America, except that questions affecting the construction and effect of any patent shall be determined by the law of the country in which the patent has been granted.

17. ARBITRATION AND DISPUTE RESOLUTION

Any dispute relating to the interpretation or performance of this Agreement or the grounds for the termination hereof shall be resolved at the request of either party through final and binding arbitration by a single arbitrator in accordance with the Commercial Arbitration rules of the American Arbitration Association ("AAA"). Such arbitrator shall be selected by the mutual agreement of the parties or, failing such agreement, shall be selected according to the relevant AAA rules. The parties shall bear the costs of such arbitrator and arbitration equally. The prevailing party in any such arbitration shall be entitled to its reasonable attorney's fees and costs solely at the discretion of the arbitrator in addition to any other amount of recovery ordered by such arbitrator. The arbitrator or court, as the case may be, shall determine which party is the "prevailing party" for purposes of this section. If judicial enforcement or review of such arbitrator's award is sought by either party, judgment may be entered upon such award in any court of competent jurisdiction. Ann Arbor Stromal hereby consents to venue and personal jurisdiction in Ann Arbor, Michigan for any such arbitration proceeding and for any court proceeding. The duty of the parties to arbitrate any dispute relating to the interpretation or performance of this Agreement or the grounds for the termination thereof shall survive any termination of this Agreement.

18. INDEMNITY: INSURANCE

18.1 Ann Arbor Stromal shall defend, indemnify and hold harmless and shall require Affiliates to defend, indemnify and hold harmless University, its fellows, officers, employees and agents, for and against any and all claims, demands, damages, losses, and expenses of any nature (including attorneys' fees and other litigation expenses), resulting from, but not limited to, death, personal injury, illness, property damage or products liability arising from or in connection with, any of the following:

18.1.1 Any manufacture, use, sale or other disposition by Ann Arbor Stromal, Affiliates, or other transferees of Products;

18.1.2 The direct or indirect use of Products by any person;

18.1.3 The use by Ann Arbor Stromal or Affiliates of any invention, discovery, data, information, product or process related to Licensed Patents or Know-How.

18.2 University shall be entitled to participate at its option and expense through counsel of its own selection, and may join in any legal actions related to any such claims, demands, damages, losses and expenses under Paragraph 18.1.

19. NO WARRANTY: LIMITATIONS OF LIABILITY

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- 19.1 UNIVERSITY MAKES NO REPRESENTATIONS, EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, INCLUDING BUT NOT LIMITED TO THE IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, AND ASSUMES NO RESPONSIBILITIES WHATEVER WITH RESPECT TO DESIGN, DEVELOPMENT, MANUFACTURE, USE, SALE OR OTHER DISPOSITION BY ANN ARBOR STROMAL OR AFFILIATES OF PRODUCTS. Regardless of any testing which may have been done at University, University makes no representations regarding how Product can or should be used in any specific process.
- 19.2 THE ENTIRE RISK AS TO PERFORMANCE OF PRODUCTS IS ASSUMED BY ANN ARBOR STROMAL AND AFFILIATES. Every user of Product must do its own verification testing and define for itself any processes for its use of Product. In no event shall University be responsible or liable for any direct, indirect, special, incidental, or consequential damages or lost profits to Ann Arbor Stromal, Affiliates, users or any other individual or entity regardless of legal theory. The above limitations on liability apply even though University may have been advised of the possibility of such damage.
- 19.3 University represents that to the best of its knowledge and belief it has the lawful right to grant the license set forth herein without breaching the terms or conditions of any agreements with any third parties.

20. PUBLICITY

Ann Arbor Stromal agrees to refrain from using and to require Affiliates to refrain from using quotes or opinions attributed or attributable to University or any employee of University in publicity, advertising, or news releases without the prior written approval of an authorized representative of University. Reports in scientific literature and presentations of joint research and development work are not considered publicity.

21. PRODUCT MARKING

Ann Arbor Stromal and Affiliates agree to mark Products with the appropriate patent notice as approved by University.

22. NON-WAIVER

No waiver, no matter how long continuing or how many times extended, by either Party of a breach of any term or condition of this License shall be considered as a permanent waiver or as an amendment to this instrument.

23. ARTICLE HEADINGS

The Article headings herein are for purposes of convenient reference only and shall not be used to construe or modify the terms written in the text of this agreement.

24. FORCE MAJEURE

Neither Party hereto shall be deemed to be in default of any provision of this License, or for any failure in performance, resulting from acts or events beyond the reasonable control of such Party. For purposes of this License, such acts shall include, but not be limited to, acts of God, acts of civil or military authority, civil disturbance, war, strikes, fires, power failures, other catastrophes, or other "force majeure" events beyond the Parties' reasonable control.

25. NO AGENCY RELATIONSHIP

Except as clearly and specifically provided under the terms and provisions of this License, neither Party shall be deemed to be an agent of the other in connection with the exercise of any rights hereunder, and neither shall have any right or authority to assume or create any obligation or responsibility on behalf of the other.

26. CONFIDENTIALITY PROVISIONS

26.1 University and Ann Arbor Stromal each agree not to disclose or use, except as required by law or contemplated by this License and the Research Agreement to which this License is attached, the following ("Confidential Information"): (i) any of the terms of this License and the Exhibits hereto (except for disclosure of basic terms which may be required under University policy), or (ii) except as otherwise

provided for in the Research Agreement's Article 7 (Publications), any Project related Know-How, data, process, technique, drawing, formula, future development, or engineering or manufacturing development of either party and any marketing, business plan, servicing, financial or personnel matter relating to the other party, its present or future products, sales, suppliers, customers, employees, investors or business except as Ann Arbor Stromal finds reasonably necessary to conduct its business or raise capital or (iii) any information received from the other party which is in written form and marked "Confidential", "Proprietary", "Secret" or the like.

26.2 The parties hereto agree that the provisions of this Article 26 shall survive, whether or not the other provisions hereof remain in full force and effect, for a period of three (3) years after any termination of this License.

26.3 Confidential Information shall not include and neither party shall be obligated to hold in confidence or restrict the use of any information (i) which is or becomes public knowledge without breach of this License, (ii) which is or becomes available without a confidentiality restriction and without breach of this License from a source other than a party hereto, (iii) which is produced in response to a court order or government action, (iv) which is disclosed with the other party's prior written approval, (v) which is independently developed by the party receiving the Confidential Information from the other party, or (vi) which is known by other means to the party receiving the

Confidential Information at the time of disclosure of same, and in the case of (v) and (vi), can be established by documentary evidence.

IN WITNESS WHEREOF, each of the Parties hereto has caused this entire agreement to be executed in duplicate originals by its duly authorized officer or representative.

FOR ANN ARBOR STROMAL, INC.

By /s/ R. DOUGLAS ARMSTRONG

(authorized representative)

Typed Name R. Douglas Armstrong

Title President and CEO

Date 3/13/92

FOR THE REGENTS OF
THE UNIVERSITY OF MICHIGAN

By /s/ ROBERT F. GAVIN

(authorized representative)

Typed Name Robert F. Gavin

Title Director, Intellectual Properties

Date 3/13/92

FIRST AMENDMENT TO LICENSE AGREEMENT

This First Amendment to License Agreement is made as of March 13, 1992,

by and between Aastrom Biosciences, Inc. (formerly Ann Arbor Stromal, Inc.),
a Michigan corporation, (hereinafter "Aastrom") and the Regents of the
University of Michigan, a constitutional corporation of the State of Michigan
(hereinafter "University").

RECITATIONS

The following is a recital of facts underlying this Agreement:

- A. On March 13, 1992 the parties hereto have executed a certain License

Agreement ("License Agreement") as contemplated by a certain Research
Agreement between the parties hereto which was executed by them during
August of 1989 (the "Research Agreement"). Defined terms not otherwise
defined in this First Amendment shall have the meanings set forth in the
License Agreement.
- B. The parties now wish to amend the License Agreement in certain respects.

NOW, THEREFORE, in consideration of their mutual promises, the parties hereto
agree as follows:

1. The License Agreement is hereby amended as follows.
 - (a) Licensed Technology includes:

- i) all patent applications, including related foreign patent applications, and patents issuing therefrom identified in Exhibit A attached hereto;
 - ii) all Know-How included in patents and patent applications of Exhibit A and grant proposals, papers, abstracts and other documents described in Exhibit B attached hereto; and
 - iii) all additional patentable inventions and Know-How for the production of red blood cells, white blood cells, platelets and bone marrow cells, which is either described in University Project proposal, or conceived or reduced to practice as part of Project, or conceived or reduced to practice, whether or not pursuant to or as part of the Project, by Drs. Stephen G. Emerson, Michael F. Clarke or Bernhard O. Palsson, or those working under their direction, during the term of their participation in the Project and Aastrom's funding of the Project.
- (b) Section 3.2 of the License Agreement hereby is amended to read in its entirety as follows:
- 3.2 Aastrom shall have the right to grant one or more sublicenses for third parties to use the rights granted to Aastrom under its exclusive

license rights granted in this License Agreement; and, subject to approval by Aastrom, sub-sublicense agreements may also be granted by a third party sublicensee. All sublicenses and sub-sublicenses, if any, shall provide that the sublicensee and sub-sublicensee shall comply fully with all provisions of this License Agreement, including without limitation, paying the same royalty to the University as is specified in this License Agreement. Notwithstanding any such sublicensing, Aastrom shall still remain fully responsible and liable for compliance with all terms of this License Agreement, including compliance by any and all sublicensees and sub-sublicensees. No consent from University is required for any sublicense or sub-sublicense, as described above; however, Aastrom shall provide timely notice of each sublicense hereunder along with copies of all sublicense agreements. Should Aastrom propose to enter into a sublicense which reduces any royalties payable to University, or which otherwise modifies any of the rights of University under this License Agreement, then no such sublicense can be entered into without the prior written consent of University and any

such sublicense entered into without prior written consent of University shall be void from the beginning. For example, if the proposed sublicensee is to issue stock to Aastrom in lieu of royalties, or if a proposed sublicensee is to make a lump sum front-end payment as a set-off against or in lieu of future royalties, then there shall be negotiations between Aastrom and University for an equitable allocation of said consideration in lieu of royalties, with the mutual consent of Aastrom and University required for any such non-conforming sublicense agreement.

2. Article 13 of the License Agreement, entitled "Notices", is amended as follows:

- i) Provision for notice to Robert Kunze and Kenneth Guernsey is hereby deleted; and
- ii) Notice to Aastrom shall be provided to:

Aastrom Biosciences, Inc.
President/CEO
P.O. Box 130469
Ann Arbor, Michigan 48113-0469

3. As amended hereby, the License Agreement shall continue in full force and effect.

IN WITNESS WHEREOF, the parties hereto have caused their duly authorized representatives to execute and deliver this First Amendment as of the date set forth above.

FOR AASTROM BIOSCIENCES, INC.	FOR THE REGENTS OF THE UNIVERSITY OF MICHIGAN
By /s/ R. DOUGLAS ARMSTRONG ----- (authorized representative)	By /s/ ROBERT F. GAVIN ----- (authorized representative)
Typed Name R. Douglas Armstrong -----	Typed Name Robert F. Gavin -----
Title President and CEO -----	Title Director, Intellectual Properties -----

License Agreement Amendment dated March 13, 1992
between UM and Aastrom Biosciences

DOCUMENTATION FOR LICENSE AMENDMENT AGREEMENT

1. The following U.S. patent applications and all related foreign applications:

- A. U.S. APPLICATION, SER. #07/366,639, OSMMN REF. #2363-022-55
Methods, Compositions and Devices for Growing Cells.
Filed: 6/15/89
- B. U.S. APPLICATION, SER. #07/628,343, OSMMN REF. #2363-023-55 CIP
Methods and Compositions for the Ex Vivo Replication of Stem Cells
and for the Optimization of Hematopoietic Progenitor Cell Cultures.
Filed: 12/17/90
- E. U.S. APPLICATION, SER. #07/737,024, OSMMN REF. #2363-034-55
Methods and Compositions for the Ex Vivo Replication of Stem Cells,
for the Optimization of Hematopoietic Progenitor Cell Cultures,
and for Increasing the Metabolism, GM-CSF Secretion and/or IL-6
Secretion of Human Stromal Cells.
Filed: 7/29/91
- F. U.S. APPLICATION, SER. #07/740,590, OSMN REF. #2363-035-55
Methods for Human Gene Therapy, Including Methods and Compositions
for the Ex Vivo Replication and Stable Genetic Transformation of Human
Stem Cells, for the Optimization of Human Hematopoietic Progenitor Cell
Cultures and Stable Genetic and/or IL-6 Secretion of Human Stromal
Cells.
Filed: 8/5/91
- H. U.S. APPLICATION, SER. #07,815,513, OSMMN REF. #2363-036-55
Methods for Regulating the Specific Lineages of Cells Produced in
a Human Hematopoietic Cell Culture, Methods for Assaying the Effect
of Substances on Lineage-Specific Cell Production, and Cell Compositions
Produced by these Cultures.
Filed: 1/2/92
- I. U.S. APPLICATION, SER. #07/822,136, OSMMN REF. #2363-055-55
Targeted Virus.
Filed: 1/17/92
- J. PENDING U.S. APPLICATION, OSMMN REF. #2363-043-55
Methods, Compositions and Devices for Maintaining and Growing Human
Stem and/or Hematopoietic Cells.
Filed: 3/4/92

	DESCRIPTION -----	AUTHOR -----	DATE ----
2.	Business Plan and Strategy	AASTROM Biosciences, Inc.	Dec., 1991
3.	Research Plan	AASTROM Biosciences, Inc.	Sept., 1991
4.	Goals, Science/Business, Personnel & Structure	Ann Arbor Stromal, Inc.	Undated
5.	Research Agreement	Appendix C to Option Agreement	3/24/89
6.	SBIR Proposal: Hematopoietic Cell Expansion System	R. Douglas Armstrong	12/12/91
7.	NRA-91-OSSA-18 Proposal: Shear Sensitivities of Human Bone Marrow Cultures	Bernard O. Palsson	11/25/91
8.	ACS Proposal: Hematopoietic Bioreactor System to Improve Bone Marrow Transplantation for Treatment of Cancer	Bernard O. Palsson	10/30/91
9.	Aastrom System One (Version 1.00 - Draft)	Bernard O. Palsson	10/19/91
10.	NRA-91-OSSA-13 Proposal: Reconstructing Human Bone Marrow Ex Vivo	Bernard O. Palsson	8/15/91
11.	NSF Proposal: Optimal Growth Factor Combinations for Human Bone Marrow Cultures and Large- Scale Cell Production	Bernard O. Palsson	7/3/90
12.	Naval Medical Command Proposal: Ex vivo Bone Marrow: Construction of a Perfusion Device	Bernard O. Palsson	2/20/89
13.	SBIR Proposal: Bioreactor for Retrovirus Infection of hemato- poietic Cells	R. Douglas Armstrong	12/12/91
14.	Experiment (Clarke)	Michael F. Clarke	1/9/92
15.	NIH Proposal: In Vitro Expanded Hematopoietic Progenitors for ABMT	Stephen G. Emerson	1/16/92
16.	NIH Proposal: Stromal Cell CSF Regulation and Hematopoiesis	Stephen G. Emerson	9/20/91
17.	Aplastic Anemia Foundation of America (Postdoctoral application): Leslie G. Blesecker	Stephen G. Emerson	7/1/92 (beg. date)

	DESCRIPTION -----	AUTHOR -----	DATE ----
18.	The Leukemia Society of America (Scholarship application): Stem Cell Cytoadhesion Molecules in Chronic Myelogenous Leukemia	Stephen G. Emerson	8/29/89
19.	The Leukemia Society of America (Scholarship application - continuation) Stem Cell Cytoadhesion Molecules in Chronic Myelogenous Leukemia	Stephen G. Emerson	4/26/91
20.	NIH Proposal: Optimization and Manipulation of Human Marrow Cultures	Stephen G. Emerson	7/20/90
21.	NSF Proposal: (Research Experience for Undergraduates) Effect of Serum Concentration and Perfusion Rate on Stromal Cell Metabolism	Stephen G. Emerson	1/30/89
22.	NSF Proposal: Construction and Maintenance of Functioning Bone Marrow Tissue Ex Vivo	Stephen G. Emerson	5/15/89
23.	NSF Proposal: Construction of a High Efficiency Ex Vivo Bone Marrow	Stephen G. Emerson	5/10/88
24.	NRA-88-OSSA-5 Proposal: Development of a Device for the Large-Scale Cultivation of Human Bone Marrow: Space Flight Applications	Stephen G. Emerson	8/15/88
25.	Presidential Initiations Proposal: Development of an Artificial Bone Marrow	Stephen G. Emerson	Undated
26.	Paper: In Vitro Myelopoiesis Stimulated by Rapid Medium Exchange and Supplementation with hematopoietic Growth Factors	Schwartz RM, Emerson SG, Clarke MF, Palsson BO	Blood, 78:12, pp 3155-3161, (12/15/91)
27.	Paper: Can Dexter Cultures Support Stem Cell Proliferation?	Varma A, El-Awar FY, Palsson BO, Emerson SG, Clarke MF	Experimental Hematology, 20:87-91 (1992)
28.	Paper: Rapid medium perfusion rate significantly increases the productivity and longevity of human bone marrow cultures	Schwartz RM, Palsson BO, Emerson SG	PNAS, 88:6760-6764 (8/91)
29.	Paper: The Construction of High Efficiency Human Bone Marrow Tissue Ex Vivo	Emerson SG, Palsson BO, Clarke MF	J Cell. Biochem 45:268-272 (1991)

DESCRIPTION -----	AUTHOR -----	DATE -----
30. Paper: Culture Perfusion Schedules Influence the Metabolic Activity and Granulocyte-Macrophage Colony-Stimulating Factor Production Rates of Human Bone Marrow Stromal Cells	Caldwell J, Palsson BO, Locey B, Emerson SG	J Cell Phys 147:344-353 (1991)
31. Paper: Influence of Medium Exchange Schedules of Metabolic, Growth, and GM-CSF Secretion Rates of Genetically Engineered NIH-3T3 Cells	Caldwell J, Locey B, Clarke MF, Emerson SG Palsson BO	Biotechnol. Progress Vol. 7, No.1 Jan/Feb, 1991
32. Paper: The Influence of Extra-Cellular Matrix and Stroma Remodeling on the Productivity of Long-Term Human Bone Marrow Cultures	Schwartz RM, Caldwell J, Clarke MF, Emerson SG, Palsson BO	Submitted to Cytotechnology Sept., 1991
33. Advanced Technology Program Proposal: ATP 91-01: Human Stem Cell and Hematopoietic Expansion Systems	R. Douglas Armstrong	9/24/91
34. Thesis: Optimization of Human Long-Term Bone Marrow Cultures	Richard M. Schwartz	1991
35. Chapter: The Role of Physiologic Perfusion in the Metabolism and Genetic Regulation of Cytokine Production in Mesenchymal Stromal Cells	Caldwell J, Palsson BO, Clarke MF, Emerson SG	Undated
36. UM Disclosure #715 "Mouse Tyrosine Kinase partial cDNA sequences A1, A8, P4, P7, P21"	Emerson SG	Biotechnol

SECOND AMENDMENT TO
LICENSE AGREEMENT

This Second Amendment to License Agreement is entered into as of October 8, 1993, by and between Aastrom Biosciences, Inc. (formerly Ann Arbor Stromal, Inc., a Michigan corporation, hereinafter called "Aastrom"), and the Regents of the University of Michigan, a constitutional corporation of the State of Michigan (hereinafter called "University").

RECITATIONS

The following is a recital of facts underlying this Agreement.

- A. In August, 1989, the parties hereto entered into a certain Research Agreement (the "Research Agreement") pursuant to which Aastrom provided funding to the University for the University to conduct a certain research project. Pursuant to an Extension Agreement dated March 2, 1992, the parties extended the term of the Research Agreement until June 30, 1993, and extended the scope of the research projects and funding under the Research Agreement. As used hereinafter, the term "Research Agreement" shall include said Extension Agreement. Pursuant to the Research Agreement, Aastrom is entitled to an exclusive license to utilize any and all inventions, technology, and know-how (i) resulting from the research projects funded by Aastrom at the University, or (ii) related to the research projects (subject to certain qualifications).
- B. On March 13, 1992, the parties entered into a certain License Agreement (the "License Agreement"), as contemplated by the Research Agreement; and on March 13, 1992, the parties also entered into that certain First Amendment to License Agreement (the "First Amendment to License Agreement") for the purpose of modifying and clarifying certain terms in the original License Agreement. As used hereinafter, the term "License Agreement" shall include said First Amendment.
- C. Subsequent to entering into the First Amendment to License Agreement, some additional patent rights, technology, know-how and other intellectual property rights have been identified which are to be licensed to Aastrom pursuant to the License Agreement. This Second Amendment is being entered into for the purpose of identifying said additional rights.

NOW THEREFORE, in consideration of their mutual promises, the parties hereto agree as follows:

- 1. LICENSED TECHNOLOGY. In addition to all other Licensed Technology (as defined in the License Agreement) which is already identified as being covered by the License Agreement, the Licensed Technology shall also include the additional patent-

related matters identified in Exhibit A attached hereto, as well as the additional technology and know-how identified in the documents described in Exhibits B (1) and B(2) attached hereto, which technology and know-how have resulted from research pursuant to the Research Agreement.

2. EFFECT. Excepting only as otherwise expressly set forth above, all other terms and provisions of the License Agreement shall remain in full force and effect.

IN WITNESS WHEREOF, the parties hereto have caused their duly authorized representatives to execute and deliver this Second Amendment as of the date set forth above.

FOR:

AASTROM BIOSCIENCES, INC.

BY: /s/ R. DOUGLAS ARMSTRONG

R. DOUGLAS ARMSTRONG, PH.D.
PRESIDENT AND CEO

FOR:

THE REGENTS OF
THE UNIVERSITY OF MICHIGAN

BY: /s/ ROBERT L. ROBB

ITS: Director Technology/Management
Office

EXHIBIT A

PATENT MATTERS

All of the following patent applications and patent matters, including all related foreign patent rights and all patents issued and patent rights related thereto:

- A. U.S. APPLICATION #07/990,299, CAMPBELL & FLORES REF.#P-UM 9380
Novel Embryonic Tyrosine Kinase Sequences and Uses Thereof
Biesecker, Leslie G.; Emerson, Stephen Gx.
filed: 12/8/92
- B. PENDING U.S. APPLICATION, CAMPBELL & FLORES REF. #P-UM 9430
P53-Mediated Apoptosis for the Therapeutic Treatment of Diseases
Clarke, Michael F.
- C. PENDING U.S. APPLICATION, CAMPBELL & FLORES REF. #P-AA 9609
Directed Motion of Gene-Transfer Vectors for Increased Infectivities
Palsson, Bernhard O.

EXHIBIT B (1)

Know-how and Technology Items

All of the following and attached grant proposals, papers, abstracts and other documents, together with all inventions, know-how and/or technology described therein or resulting therefrom:

DESCRIPTION	AUTHOR	DATE
1. PAPER: BONE MARROW STROMAL FIBROBLASTS SECRETE INTERLEUKIN-6 AND GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR IN THE ABSENCE OF INFLAMMATORY STIMULATION: DEMONSTRATION BY SERUM-FREE BIOASSAY, ENZYME-LINKED IMMUNOSORBENT ASSAY, AND REVERSE TRANSCRIPTASE POLYMERASE CHAIN REACTION	GUBA, SC; SARTOR, CL; GOTTSCHALK, LR; YE-HE, J; MULLIGAN, T; EMERSON, SG	BLOOD 80(5):1190-1198 SEPT., 1992)
2. ABSTRACT: MOLECULAR REGULATION OF THE HUMAN IL-3 GENE IN T-CELLS: EXPRESSION REQUIRES AN INTACT AP-1 AND ELF-1 NUCLEAR PROTEIN BINDING SITE	GOTTSCHALK, LR; GIANNOLA, DM; EMERSON, SG	ASH, 1992
3. ABSTRACT: EX VIVO EXPANSION OF HEMATOPOIETIC PROGENITOR CELLS AND LTCIC BY CONTINUOUS PERFUSION CULTURE	PALSSON, BO; SCHWARTZ, RM; PALSSON, M; ARMSTRONG, RD; CLARKE, MF; EMERSON, SG	ASH, 1992
4. ABSTRACT: IL-1 ALPHA AND TNF-ALPHA ACT SYNERGISTICALLY TO STIMULATE PRODUCTION OF MYELOID COLONY-STIMULATING FACTORS BY CULTURED HUMAN BONE MARROW STROMAL CELLS AND CLONED STROMAL CELL STRAINS	CALDWELL, J; EMERSON, SG	ASH, 1992
5. ABSTRACT: THE CLONING OF 5 NOVEL TYROSINE KINASE PARTIAL CDNAS ENCODING CANDIDATE STEM CELL CYTOKINE RECEPTORS	BIESECKER, LG; GOTTSCHALK, LR; EMERSON, SG	ASH, 1992
6. PAPER: IDENTIFICATION OF FOUR MURINE CDNAS ENCODING PUTATIVE PROTEIN KINASES FROM PRIMITIVE EMBRYONIC STEM CELLS DIFFERENTIATED IN VITRO	BIESECKER, L.G., ET AL	PNAS 90, 7044-7048 (1993)

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|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|
| 7. PAPER: INTERLEUKIN 6 IS A COMPONENT OF HUMAN UMBILICAL CORD SERUM AND STIMULATES HEMATOPOIESIS IN EMBRYONIC STEM CELLS IN VITRO | BIESECKER, LG;
EMERSON, SG | EXPERIMENTAL
HEMATOLOGY,
21:774-778
1993 |
| 8. PAPER: MOLECULAR REGULATION OF THE HUMAN IL-3 GENE: INDUCIBLE T-CELL RESTRICTED EXPRESSION REQUIRES INTACT AP-1 AND ELF-1 NUCLEAR PROTEIN BINDING SITES | GOTTSCHALK, LR;
GIANNOLA, DM;
EMERSON, SG | JOURNAL OF
EXPERIMENTAL
MEDICINE
IN PRESS
NOV., 1993 |
| 9. PAPER: IL-1 ALPHA AND TNF-ALPHA ACT SYNERGISTICALLY TO STIMULATE PRODUCTION OF MYELOID COLONY-STIMULATING FACTORS BY CULTURED HUMAN BONE MARROW STROMAL CELLS AND CLONED STROMAL CELL STRAINS | CALDWELL, J;
EMERSON, SG | JOURNAL OF
CELLULAR
PHYSIOLOGY
ACCEPTED
1994 |
| 10. ABSTRACT: PHASE I EVALUATION OF EX VIVO EXPANDED HEMATOPOIETIC CELLS PRODUCED BY PERFUSION CULTURES IN AUTOLOGOUS BONE MARROW TRANSPLANTATION (BMT). | SILVER, SM;
ADAMS, PT;
HUTCHINSON, RJ;
DOUVILLE, JW;
PAUL, LA; CLARKE,
MF; PALSSON, BO;
EMERSON, SG | ASH, 1993 |
| 11. ABSTRACT: EXPANSION IN BIOREACTORS OF HUMAN PROGENITOR POPULATIONS FROM CORD BLOOD AND MOBILIZED PERIPHERAL BLOOD | VAN ZANT, G;
LARSON, DB;
DRUBACHEVSKY, I;
PALSSON, M;
EMERSON, SG | ASH, 1993 |
| 12. ABSTRACT: CLINICAL SCALE PRODUCTION OF STEM AND HEMATOPOIETIC CELLS EX VIVO | ARMSTRONG, RD;
KOLLER, MR; PAUL,
L; DOUVILLE, J;
MALUTA, J; FISH,
R; PALSSON, BO;
VAN ZANT, G;
EMERSON,SG | ASH, 1993 |
| 13. ABSTRACT: EXPANSION OF HUMAN HEMATOPOIETIC STEM/PROGENITOR CELLS RESISTANT TO TREATMENT WITH 4-HYDROPEROXYCYCLOPHOSPHAMIDE | RUMMEL, SA;
EMERSON, SG; VAN
ZANT, G | ASH, 1993 |
| 14. ABSTRACT: BIOREACTOR EXPANSION OF WHOLE, DENSITY-SEPARATED, AND CD34-ENRICHED HUMAN BONE MARROW | KOLLER, MR;
NEWSOM, B; VAN
ZANT, G; EMERSON,
SG, PALSSON, BO | ASH, 1993 |
| 15. SEMINAR: PROGRESS REPORT | PETER G. EIPERS | 10/19/92 |
| 16. PAPER: MEL CELLS, THE ONCOGENE C-MYB | CLARKE, MF | SUBMITTED TO
NATURE 1/93 |

17.	PAPER: CELL CYCLE ANALYSIS OF P53-INDUCED CELL DEATH IN MURINE ERYTHROLEUKEMIA CELLS	RYAN, JJ; RIZWAN, D; GOTTLIEB, CA; CLARKE, MF	MOLECULAR AND CELLULAR BIOLOGY 13(1) (JAN, 1993)
18.	SEMINAR: MY PRIMARY OBJECT..	ALICE CURRY	1/25/93
19.	SEMINAR: PROGRESS REPORT, FEB. 1993	PETER G. EIPERS	3/8/93
20.	SEMINAR: CONSTRUCTION OF A RETROVIRUS PACKAGING CELL LINE	FAISAL EL-AWAR	4/19/93
21.	SEMINAR: FIRST CD 18 INFECTION.....	PETER G. EIPERS	6/14/93
22.	SEMINAR: GENERATION OF AN HIV-BASED PACKAGING LINE	ALICE M. CURRY	7/26/93
23.	PROGRESS REPORTS	ALICE M. CURRY	JAN., APR., MAY, JULY, 1993
24.	PAPER: EFFECT OF STROMAL AGE ON HEMATOPOIESIS IN HUMAN LONG-TERM BONE MARROW CULTURES	EL-AWAR, FY; EMERSON, SG; CLARKE, MF	SUBMITTED TO EXP. HEMATOLOGY
25.	ABSTRACT: RETROVIRUS-MEDIATED GENE TRANSFER IN HUMAN BONE MARROW MONONUCLEAR CELLS GROWN IN CONTINUOUS PERFUSION CULTURES	EIPERS, PG; KRAUSS, JC; TODD, RF; EMERSON, SG; PALSSON, BO; CLARKE, MF	ASH, 1993
26.	NIH GRANT APPLICATION: ANALYSIS OF THE KINETICS OF HEMATOPOIETIC CELL DIVISION BY RETROVIRUS TAGGING	MICHAEL F. CLARKE	9/30/93
27.	ABSTRACT: FLOW CYTOMETRIC ANALYSIS OF BIOREACTOR EXPANDED HUMAN BONE MARROW; ERYTHROID DEVELOPMENT AND CORRELATION WITH BURST-FORMING UNIT-ERYTHROID (BFU-E).	ROGERS, CE; BRADLEY, MS; PALSSON, BO; KOLLER, MR	ASH, 1993
28.	ABSTRACT: EXTENDED GROWTH OF STEM AND PROGENITOR CELLS FROM ADULT HUMAN BONE MARROW IN SEQUENTIAL BIOREACTOR CULTURES	OH, DJ; KOLLER, MR; PALSSON, BO	ASH, 1993
29.	ABSTRACT: GROWTH FACTOR CONSUMPTION AND PRODUCTION IN EX VIVO PERFUSION CULTURES OF HUMAN BONE MARROW	PALSSON, BO; BRADLEY, MS; KOLLER, MR	ASH, 1993
30.	SEMINAR: INTRO TO MICROENCAPSULATION	MINETTE LEEVE	10/13/92

31.	SEMINAR: FLOW CYTOMETRY & HUMAN MARROW	CLARE ROGERS	11/30/92
32.	SEMINAR: CULTIVATION OF BONE MAROW CELLS IN HEMOGEN 107 (DIAMOND SHAPE) REACTORS	DUK JAE OH	1/18/93
33.	SEMINAR: ENCAPSULATED BONE MARROW CULTURES AS A POTENTIAL ASSAY FOR HUMAN HEMATOPOIETIC PROGENITORS	LEVEE, MG; LEE, GM; PAEK, SH; PALSSON, BO	3/29/93
34.	SEMINAR: FLOW CYTOMETRIC ANALYSIS OF HUMAN MYELOID LINEAGE DEVELOPMENT IN HEMATOPOIETIC BIOREACTOR SYSTEMS	ROGERS, CE; BRADLEY, S; KOLLER, MR; PALSSON, BO	3/29/93
35.	SEMINAR: OXYGEN TRANSPORT IN THE HEMOGEN BIOREACTORS	PENG, CA; PALSSON, BO	4/5/93
36.	SEMINAR: TISSUE ENGINEERING	BERNHARD O. PALSSON	4/12/93
37.	SEMINAR: DYNAMICS OF CELL GROWTH AND DIFFERENTIATION IN HEMOGENS	PENG, CA; ROGERS, C; OH, DJ; BRADLEY, S; PALSSON, BO	6/7/93
38.	SEMINAR: METABOLIC STUDY IN BONE MARROW CULTURE	DUK JAE OH	8/23/93
39.	MINUTES & NOTES, GENE THERAPY PROJECT MEETINGS	BERNHARD O. PALSSON ET AL	6/21/93 THRU 9/28/93
40.	SBIR GRANT APPLICATION: A CLONAL HEMATOPOIETIC PROGENITOR CELL ASSAY	MANFRED R. KOLLER	8/14/92
41.	SBIR GRANT APPLICATION: HIGH TITER RETROVIRAL SUPERNATANTS	R. DOUGLAS ARMSTRONG	8/14/92

DESCRIPTION -----	AUTHOR -----	DATE -----
PROPOSALS:		
1. American Cancer Society - Development of a Clinical Hematopoietic Bioreactor System to Improve Bone Marrow Transplantation	Bernhard O. Palsson	10/15/92
2. National Science Foundation - Hematopoietic Bioengineering and Biotechnology	Bernhard O. Palsson	1/27/93
3. NIH - Hematopoietic Tissue Engineering	Bernhard O. Palsson	1/28/93
4. NIH - Human Hematopoietic Differentiation and Lineage Development Ex Vivo	Bernhard O. Palsson	5/27/93
PAPERS:		
5. The Influence of Extra-Cellular Matrix and Stroma Remodeling on the Productivity of Long-Term Human Bone Marrow Cultures	Schwartz, R.M., Caldwell, J., Clarke, M.F., Emerson, S.G., and Palsson, B.O.	Cytotechnology 10:217-224 (1993)
6. Expansion of Human Bone Marrow Progenitor Cells in a High Cell Density Continuous Perfusion System	Palsson, B.O., et al	Bio/Technology 11,368-372 (1993)
7. Large-Scale Expansion of Human Stem and Progenitor Cells from Bone Marrow Mononuclear Cells in Continuous Perfusion Cultures	Koller, M.R., Emerson, S.G., and Palsson, B.O.	Blood 82,378-384 (1993)
8. Retroviral Gene Transfer into Human Hematopoietic Cells Using Rapidly Perfused Long-Term Bone Marrow Cultures	Clarke, M.F., et al	The Cancer Bulletin 45:2, 153-158 (1993)
9. Tissue Engineering: Reconstitution of Human Hematopoiesis Ex Vivo	Koller, M.R. and Palsson, B.O.	Biotechnology & Bioengineering 42, in press (1993)

	DESCRIPTION -----	AUTHOR -----	DATE -----
10.	Kinetics of Retroviral Production from the Amphotropic VCRIP Murine Producer Cell Line	Shen, B.O., Clarke, M.F., Palsson, B.O.	Biotechnology & Bioengineering Accepted with revisions
11.	Microencapsulated Bone Marrow Cultures as a Potential Assay for Human Hematopoietic Progenitor Cells	Levee, M.G., Lee, G-M., Paek, S-H.,	Biotechnology & Bioengineering Submitted
12.	Unilineage Model of Hematopoiesis Predicts Self-Renewal of Stem and Progenitor Cells from Observed Ex Vivo Growth Patterns	Peng, C-A., Koller, M.R., and Palsson, B.O.	Biotechnology & Bioengineering Submitted
13.	Extended Growth of Adult Mononuclear Human Bone Marrow Cells Through Repeated Harvesting and Replating	Oh, D.J., Koller, M.F. and Palsson, B.O.	To be submitted

REPORTS:

14.	Development of the HemoGen 106 Bone Marrow Expansion System	B.O. Palsson and S-H Paek	April 15, 1992
15.	Research and Development Program for the HemoGen 106 Bioreactor System (Unfinished document)	B.O. Palsson	September 22, 1992
16.	The HemoGen 107/108 Series: Progress Report	R.M. Schwartz and B.O. Palsson	October 27, 1992
17.	Progress Report on Residence Time Distribution	C-A. Peng and B.O. Palsson	December 17, 1992
18.	Partial Cell Harvesting and Replating Experiments	D.J. Oh and B.O. Palsson	December 17, 1992
19.	Oxygen Transport in the HemoGen Bioreactors	C-A. Peng and B.O. Palsson	April 5, 1993
20.	Growth Factor Delivery in the HemoGen Bioreactors:	B.O. Palsson and C-A. Peng	May 21, 1993
21.	Slides to accompany 16 above	B.O. Palsson	April 12, 1993
22.	Dynamics of Cell Growth and Differentiation in HemoGens	B.O. Palsson	June 7, 1993

BD
7/20/93

7(b)

Additionally, as specified in the Research Agreement, University hereby licenses to Aastrom, pursuant to the terms of the License Agreement, all of the inventions, technology and know-how which are either (i) described in the Research Projects referenced in the Research Agreement, or (ii) conceived or reduced to practice as part of said Research Projects, or (iii) conceived or reduced to practice, whether or not pursuant to or as part of said Research Projects, by Drs. Stephen G. Emerson, Michael F. Clarke or Bernhard O. Palsson, or those working under their direction (including without limitation, research scientists, technicians, and/or post-doctoral training fellows), during the term of their participation in the Research Projects and Company's funding of the Research Projects, provided that such inventions, technology and know-how are related to the work described in said Research Projects. Further, the parties hereby acknowledge that Drs. Emerson, Clarke and Palsson serve as consultants to Company, as well as employees of University, and that inventions, know-how and technology conceived, reduced to practice or developed by these scientists in the course of their consulting work for Company shall be included in subparagraph (iii) above, such that they shall be covered by this License Agreement as Licensed Technology.

THIRD AMENDMENT TO
LICENSE AGREEMENT

This Third Amendment to License Agreement is entered into as of June 21, 1995, by and between Aastrom Biosciences, Inc. (formerly Ann Arbor Stromal, Inc., a Michigan corporation, hereinafter called "Aastrom"), and the Regents of the University of Michigan, a constitutional corporation of the State of Michigan (hereinafter called "University").

RECITATIONS

The following is a recital of facts underlying this Agreement.

- A. In August, 1989, the parties hereto entered into a certain Research Agreement (the "Research Agreement") pursuant to which Aastrom provided funding to the University for the University to conduct a certain research project. On March 2, 1992, the parties extended the term of the Research Agreement until June 30, 1993. Pursuant to a further Extension Agreement dated October 20, 1993, and Request Letter dated June 13, 1994, the term of the Agreement was further extended to June 30, 1994, and December 31, 1994, respectively, and the scope of the research projects and funding under the Research Agreement extended accordingly. As used hereinafter, the term "Research Agreement" shall include said Extension Agreements and Letter. Pursuant to the Research Agreement, Aastrom is entitled to an exclusive license to utilize any and all inventions, technology, and know-how (i) resulting from the research projects funded by Aastrom at the University, or (ii) related to the research projects (subject to certain qualifications).
- B. On March 13, 1992, the parties entered into a certain License Agreement (the "License Agreement"), as contemplated by the Research Agreement; and on March 13, 1992, the parties also entered into that certain First Amendment to License Agreement (the "First Amendment to License Agreement") for the purpose of modifying and clarifying certain terms in the original License Agreement. On October 8, 1993, the parties entered into a Second Amendment to License Agreement. As used hereinafter, the term "License Agreement" shall include said First and Second Amendments and this Third Amendment.
- C. Subsequent to entering into the First and Second Amendments to License Agreement, some additional patent rights, technology, know-how and other intellectual property rights have been identified which are to be licensed to Aastrom pursuant to the License Agreement. This Third Amendment is being entered into for the purpose of identifying said additional rights.

NOW THEREFORE, in consideration of their mutual promises, the parties hereto agree as follows:

1. LICENSED TECHNOLOGY. In addition to all other Licensed Technology (as defined in the License Agreement) which is already identified as being covered by the License Agreement, the Licensed Technology shall also include the additional patent-related matters identified in Exhibit A attached hereto, as well as the additional technology and know-how identified in the documents described in Exhibits B (1) and B(2) attached hereto, to the extent such technology and know-how are described by Section E of the Extension Agreement.
2. EFFECT. Excepting only as otherwise expressly set forth above, all other terms and provisions of the License Agreement shall remain in full force and effect.

IN WITNESS WHEREOF, the parties hereto have caused their duly authorized representatives to execute and deliver this Third Amendment as of the date set forth above.

FOR:

AASTROM BIOSCIENCES, INC.

BY: /s/ R. DOUGLAS ARMSTRONG

R. Douglas Armstrong, Ph.D.
President and CEO

FOR:

THE REGENTS OF
THE UNIVERSITY OF MICHIGAN

BY: /s/ ROBERT L. ROBB

ITS: Director, Technology Management
Office

EXHIBIT A

Patent Matters

All of the following patent applications and patent matters, including all related foreign patent rights and all patents issued and patent rights related thereto:

- A. U.S. APPLICATION NO. 08/100,337
Filed: 7/30/93; (Continuation to U.S. App. #07/628,343)
- B. U.S. APPLICATION NO. 08/164,779
Filed: 12/10/93; (Continuation to U.S. App. #07/737,024)
Amendment filed: 8/1/94
- C. AMENDMENT TO U.S. APP. #07/740,590
Filed: 8/9/94
- D. U.S. APP. NO. 08/178,433
Filed: 1/6/94 (Continuation to U.S. App. #07/845,969)
- E. U.S. APPLICATION, SER. #08/143,751

Methods and Compositions for the ex vivo Replication of Stem Cells, for the Optimization of Hematopoietic Progenitor Cell Cultures, and for Increasing the Metabolism, GM-CSF Secretion and/or IL-6 Secretion of Human Stromal Cells

Filed: 11/1/93 as a divisional of 07/845,969 (ex vivo mitotic stem cells)

- F. U.S. APPLICATION, SER. #08/187,509

Methods and Compositions for the ex vivo Replication of Stem Cells, for the Optimization of Hematopoietic Progenitor Cell Cultures, and for Increasing the Metabolism, GM-CSF Secretion and/or IL-6 Secretion of Human Stromal Cells

Filed: 1/28/94 as a continuation of 8/100,337, 7/628,343, 7/366,639; to

declare interference with Gillis et al patents.

- G. U.S. APPLICATION, SER. #08/307,862

Stabilized Virus for Gene Therapy
Filed: 9/15/94

- H. U.S. APPLICATION, SER. #08/353,531

Methods, Compositions and Apparatus for Cell Transfection
Filed: 12/9/94

EXHIBIT B (1)

KNOW-HOW AND TECHNOLOGY ITEMS

ALL OF THE FOLLOWING AND ATTACHED GRANT PROPOSALS, PAPERS, ABSTRACTS AND OTHER DOCUMENTS, TOGETHER WITH ALL INVENTIONS, KNOW-HOW AND/OR TECHNOLOGY DESCRIBED THEREIN TO THE EXTENT DESCRIBED BY SECTION E OF THE EXTENSION AGREEMENT:

DESCRIPTION	AUTHOR	DATE
1. NIH GRANT APPLICATION: ANALYSIS OF HEMATOPOIETIC CELL DIVISION BY RETROVIRUS TAGGING*	MICHAEL F. CLARKE	1/11/94
2. PAPER: RETROVIRAL-MEDIATED GENE TRANSFER IN HUMAN BONE MARROW CELLS GROWN IN CONTINUOUS PERFUSION CULTURE VESSEL*	EIPERS, P; KRAUSS, J; PALSSON, B; EMERSON, S; TODD, R; CLARKE, M.	REC'D. 8/1/94
3. PAPER: TISSUE ENGINEERING: ENGINEERING CHALLENGES	BERNHARD PALSSON	REC'D. 11/21/93
4. PAPER: GROWTH FACTOR CONSUMPTION AND PRODUCTION IN AASTROM'S PERFUSION BIOREACTOR SYSTEMS	BERNHARD PALSSON	1/20/94
5. MANUSCRIPT: KINETICS OF RETROVIRAL INFECTION AND THE INFLUENCE OF CELL CYCLE: IMPLICATIONS FOR GENE THERAPY	ANDREADIS, STYLIANOS; PALSSON, BERNHARD O.	7/8/94
6. FOLDER: ALICE CURRY NOTES (75 PAGES)	ALICE CURRY	5/31/94
7. PROGRESS REPORTS	ALICE M. CURRY	NOV, 1993; JAN. & FEB, 1994
8. ABSTRACT: LTC-IC EXPANSION REQUIRES RAPID MEDIUM EXCHANGE COMBINED WITH THE PRESENCE OF STROMAL AND OTHER ACCESSORY CELLS	KOLLER, M.R.; PALSSON, M.A.; MANCHEL, I; NEWSOM, B.S.; PALSSON, BERNHARD O.	ASH, 1994
9. ABSTRACT: EXPANSION POTENTIAL OF CD34+ CELLS FROM PATIENTS IS LOWER AND MORE STROMAL-DEPENDENT THAN FROM NORMAL DONORS	KOLLER, M.R.; MANCHEL, I; PALSSON, M.A.; BROTT, D.A.; SILVER, S.M.; PALSSON, B.O.	ASH, 1994

*These materials especially may include some inventions, know-how and technology not described by Section E of the Extension Agreement (and thus not included in Licensed Technology); including inventions, know-how and technology developed by or under the direction of Dr. Robert Todd related to leukocyte adhesion deficiency disease.

10. SBIR GRANT APPLICATION: NOVEL APPROACHES TO ENHANCING RETROVIRAL STABILITY	BERNHARD O. PALSSON	4/14/94 (PHASE I)
11. SBIR GRANT APPLICATION: HEMATOPOIETIC CELL EXPANSION SYSTEM	BERNHARD O. PALSSON	4/14/94 (PHASE II)
12. ATP GRANT APPLICATION: GENE TRANSFER SYSTEM FOR ENABLEMENT OF HUMAN GENE THERAPY	R. DOUGLAS ARMSTRONG	6/21/94
13. SEMINAR: CD18 CELL EXPANSION*	PETER EIPERS	10/25/93
14. THESIS: MEETING PRESENTATION	ALICE CHUCK	6/29/94
15. THESIS: MEETING PRESENTATION	ALICE CHUCK	9/28/93
16. PAPER: GROWTH FACTOR CONSUMPTION AND PRODUCTION IN PERFUSION BIOREACTOR CULTURES OF HUMAN BONE MARROW CORRELATES WITH SPECIFIC CELL PRODUCTION	M.R.KOLLER, M.S. BRADLEY, B.O.PALSSON	SUBMITTED TO EXP. HEMATOLOGY, 9/28/94
17. ABSTRACT: CHARACTERIZATION OF HUMAN STEM AND PROGENITOR CELL EXPANSION IN BIOREACTORS	M.R.KOLLER, B.NEWSOM, C.E.ROGERS, G.VAN ZANT, S.G.EMERSON, B.O.PALSSON	KEYSTONE CONFERENCE, TAOS, NM, 2/94
18. PAPER: GROWTH FACTOR CONSUMPTION AND PRODUCTION IN PERFUSION BIOREACTOR CULTURES OF HUMAN BONE MARROW	M.R.KOLLER, B.O.PALSSON	6/13/94
19. INTERNAL REPORT: RETROVIRUS PRODUCTION AND CONCENTRATION PROJECT: EXPERIENCE WITH THE OPTICELL SYSTEM; FILE NO. 4.3.1-001	TIMOTHY M. EISFELD	8/29/94; REVISED 8/30/94
20. INTERNAL REPORT: SUMMARY REPORT ON VIRUS STABILIZATION PROJECT: JANUARY 1994 TO PRESENT; FILE NO. 4.3.2-001	TIMOTHY M. EISFELD	8/22/94
21. PAPER: BIOREACTOR EXPANSION OF HUMAN BONE MARROW: COMPARISON OF UNPROCESSED, DENSITY-SEPARATED, AND CD34-ENRICHED CELLS	KOLLER,M.R.	SUBMITTED TO BLOOD, 1994 (MANUSCRIPT NO. 1-94-5-192)

*These materials especially may include some inventions, know-how and technology not described by Section E of the Extension Agreement (and thus not included in Licensed Technology); including inventions, know-how and technology developed by or under the direction of Dr. Robert Todd related to leukocyte adhesion deficiency disease.

22. PAPER: IL-1A REGULATES EXPRESSION OF THE 75 KDA BUT NOT THE 55 KDA TNF RECEPTOR BY CDCL STROMAL CELLS: IMPLICATIONS FOR IL-1/TNF SYNERGY.	JERRY CALDWELL, STEPHEN G. EMERSON	BLOOD 84 (10), SUPPLEMENT 1, 11/15/94 (NO. 1109)
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*These materials especially may include some inventions, know-how and technology not described by Section E of the Extension Agreement (and thus not included in Licensed Technology); including inventions, know-how and technology developed by or under the direction of Dr. Robert Todd related to leukocyte adhesion deficiency disease.

EXHIBIT B(2)

DESCRIPTION - - - - -	AUTHOR - - - - -	DATE - - - -
PEER-REVIEWED PAPERS:		
2. Microencapsulated Human Bone Marrow Cultures: A Potential Culture System for the Clonal Outgrowth of Hematopoietic Progenitor Cells	M. Levee, G.M. Lee, S.H. Paek, B.O. Palsson	Biotechnology & Bioengineering 43, 734-739 (1994)
3. Retroviral Infection is Limited by Brownian Motion	A.S. Chuck, C.A. Peng, M.F. Clarke B.O. Palsson	Submitted to Science Dec. 1993
4. Frequent Harvesting from Perfused Bone Marrow Cultures Results in Increased Overall Cell and Progenitor Expansion	D.J. Oh, M.R. Koller, B.O. Palsson	Biotechnology & Bioengineering 44, 609-616 (1994)
5. Replating of Bioreactor-Expanded Human Bone Marrow Results in Extended Growth of Primitive and Mature Cells	D.J. Oh, B.O. Palsson, M.R. Koller	Submitted to Experimental Hematology May 1994
6. Bioreactor Expansion of Human Bone Marrow: Comparison of Unprocessed, Density-Separated and CD34-enriched Cells	M.R. Koller, I. Manchel et al	Submitted to J. Hematotherapy 9/6/94
7. Unilineage Model of Hematopoiesis Predicts Self-Renewal of Stem and Progenitor Cells from Observed ex vivo Growth Patterns	C.A. Peng, M.R. Koller, and B.O. Palsson	Submitted to Biotechnology & Bioengineering 9/93

EXHIBIT B(2)

DESCRIPTION - - - - -	AUTHOR - - - - -	DATE - - - -
CHAPTERS IN BOOKS:		
8. The Role of Physiological Perfusion in the Metabolism and Genetic Regulation of Cytokine Production in Mesenchymal Stromal Cells in The Hematopoietic Microenvironment: The Functional and Structural Basis of Blood Cell Development	J. Caldwell, B.O. Palsson, M.F. Clarke, and S.G. Emerson Eds. M. W. Long and M.S. Wicha	Johns Hopkins University Press 1993 Baltimore
ABSTRACTS:		
9. Biomedical Expansion of Human Stem and Progenitor Cells is More Efficient with Mononuclear Cells Than with CD34-Enriched Cells	M.R. Koller, B. Newsom, G. Van Zant, S.G. Emerson, B.O. Palsson	NIH Workshop on Hematopoietic Stem Cell Purification and Biology, Rockville, MD., 9/21/1993
10. Growth Factor Consumption and Production in ex vivo Perfusion Cultures of Human Bone Marrow	B.O. Palsson, M.S. Bradley, and M.R. Koller	ASH Meeting, St. Louis, MO Dec. 1993
11. Extended Growth of Stem and Progenitor Cells from Adult Human Bone Marrow in Sequential Bioreactor Cultures	B.O. Palsson, D.J. Oh, and M.R. Koller	ASH Meeting, St. Louis, MO Dec. 1993
12. Bioreactor Expansion of Whole, Density-Separated, and CD34-Enriched Human Bone Marrow	M.R. Koller, B. Newsom, G. Van Zant, S.G. Emerson, B.O. Palsson	ASH Meeting, St. Louis, MO Dec. 1993
13. Flow Cytometric Analysis of Bioreactor Expanded Human Bone Marrow: Erythroid Development and Correlation with Burst-Forming Unit-Erythroid (BFU-E)	C.E. Rogers, M.S. Bradley, B.O. Palsson, and M.R. Koller	ASH Meeting, St. Louis, MO Dec. 1993
14. Clinical Scale Production of Stem and Hematopoietic Cells Ex Vivo	R.D. Armstrong, M.R. Koller, L. Paul, J. Douville, J. Maluta, R. Fish, B.O. Palsson, G. Van Zant, S.G. Emerson	ASH Meeting, St. Louis, MO Dec. 1993

EXHIBIT B(2)

DESCRIPTION - - - - -	AUTHORS - - - - -	DATE - - - -
15. Hematopoietic Bioreactor Engineering for Transplantation Rapid Detection and Control of Progenitor Cell Production	B.O. Palsson	Engineering Foundation Conference: Cell Culture Engineering IV, San Diego, CA, March 7-12, 1994
16. Growth Factor Consumption and Production in Ex Vivo Perfusion Cultures of Human Bone Marrow	B.O. Palsson and M.R. Koller	American Chemical Soc. Spring National Meeting, San Diego, CA March 7-12, 1994

Prepared by
Barbara Dunn
8/10/94

AASTROM BIOSCIENCES, INC.

EMPLOYEE PROPRIETARY INFORMATION AND INVENTION AGREEMENT

In consideration of my employment or continued employment by AASTROM BIOSCIENCES, INC. (the "Company"), and the compensation now and hereafter paid to me, I hereby agree as follows:

1. Recognition of Company's Rights; Nondisclosure. At all times during

the term of my employment and thereafter, I will hold in strictest confidence and will not disclose, use, lecture upon or publish any of the Company's Proprietary Information (defined below), except as such disclosure, use or publication may be required in connection with my work for the Company, or unless an officer of the Company expressly authorizes such in writing. I hereby assign to the Company any rights I may have or acquire in such Proprietary Information and recognize that all Proprietary Information shall be the sole property of the Company and its assigns, and the Company and its assigns shall be the sole owner of all patent rights, copyrights, mask work rights, trade secret rights and all other rights throughout the world (collectively, "Proprietary Rights") in connection therewith.

The term "Proprietary Information" shall mean trade secrets, confidential knowledge, data or any other proprietary information of the Company. By way of illustration but not limitation, "Proprietary Information" includes (a) inventions, mask works, trade secrets, ideas, processes, formulas, source and object codes, data, programs, other works of authorship, cell lines, know-how, improvements, discoveries, developments, designs and techniques (hereafter collectively referred to as "Inventions"); and (b) plans for research, development, new products, marketing and selling; information regarding business plans, budgets, and unpublished financial statements; licenses; prices and costs; information regarding suppliers and customers; and information regarding the skills and compensation of employees of the Company.

2. Third Party Information. I understand, in addition, that the Company

has received and in the future will receive from third parties confidential or proprietary information ("Third Party Information") subject to a duty on the Company's part to maintain the confidentiality of such information and to use it only for certain limited purposes. During the term of my employment and thereafter, I will hold Third Party Information in the strictest confidence and will not disclose or use Third Party Information except as permitted by the agreement between the Company and such third party, unless expressly authorized by an officer of the Company in writing.

3. Assignment of Inventions.

a. I hereby assign to the Company all my right, title and interest in and to any and all Inventions (and all Proprietary Rights with respect thereto) whether or not patentable

or registrable under copyright or similar statutes, made or conceived or reduced to practice or learned by me, either alone or jointly with others, during the period of and within the scope of my employment with the Company. I agree that all such Inventions are the sole property of the Company.

b. I hereby also assign to or as directed by the Company all my right, title and interest in and to any and all Inventions, full title to which is required to be in the United States by a contract between the Company and the United States or any of its agencies.

c. I acknowledge that all original works of authorship which are made by me (solely or jointly with others) within the scope of my employment and which are protectable by copyright are "works made for hire," as that term is defined in the United States Copyright Act (17 U.S.C., Section 101). Inventions assigned to or as directed by the Company by this paragraph 3 are hereinafter referred to as "Company Inventions."

4. Enforcement of Proprietary Rights. I will assist the Company in every

proper way to obtain and from time to time enforce United States and foreign Proprietary Rights relating to Company Inventions in any and all countries. To that end I will execute, verify and deliver such documents and perform such other acts (including appearances as a witness) as the Company may reasonably request for use in applying for, obtaining, perfecting, evidencing, sustaining and enforcing such Proprietary Rights and the assignment thereof. In addition, I will execute, verify and delivery assignments of such Proprietary Rights to the Company or its designee. My obligation to assist the Company with respect to Proprietary Rights relating to such Company Inventions in any and all countries shall continue beyond the termination of my employment for a period of one year, but the Company shall compensate me at a reasonable rate after my termination for the time actually spent by me at the Company's request on such assistance.

In the event the Company is unable for any reason, after reasonable effort, to secure my signature on any document needed in connection with the actions specified in the preceding paragraph, I hereby irrevocably designate and appoint the Company and its duly authorized officers and agents as my agent and attorney in fact, to act for and in my behalf to execute, verify and file any such documents and to do all other lawfully permitted acts to further the purposes of the preceding paragraph thereon with the same legal force and effect as if executed by me. I hereby waive and quit claim to the Company any and all claims, of any nature whatsoever, which I now or may hereafter have for infringement of any Proprietary Rights assigned hereunder to the Company.

5. Obligation to Keep Company Informed. During the period of my

employment, I will promptly disclose to the Company fully and in writing and will hold in trust for the sole right and benefit of the Company any and all Inventions relating to the Company's business. In addition, after termination of my employment, I will disclose a summary of all patent applications filed by me within one year after termination of employment.

6. Prior Inventions. Inventions, if any, patented or unpatented, which I

made prior to the commencement of my employment with the Company are excluded from the scope of this Agreement. To preclude any possible uncertainty, I have set forth on Exhibit A attached hereto a complete and exhaustive list of all inventions that I have, alone or jointly with others, conceived, developed or reduced to practice or caused to be conceived, developed or reduced to practice prior to the commencement of my employment with the Company, that I consider to be my property or the property of third parties and that I wish to have excluded from the scope of this Agreement. If disclosure of any such invention on Exhibit A would cause me to violate any prior confidentiality agreement, I understand that I am not to list such inventions in Exhibit A, but am to inform the Company that all such inventions have not been listed for that reason.

7. Additional Activities. I agree that during the period of my

full-time employment by the Company I will not, without the Company's express written consent, engage in any employment or business activity other than for the Company, and for the period of my employment by the Company and for one (1) year after the date of termination of my employment by the Company, I will not (i) induce any employee of the Company to leave the employ of the Company or (ii) solicit the business of any client or customer on behalf of a competitor of the Company (other than on behalf of the Company).

8. No Improper Use of Materials. During my employment by the Company I

will not improperly use or disclose any confidential information or trade secrets, if any, of any former employers or any other person to whom I have an obligation of confidentiality, and I will not bring onto the premises of the Company any unpublished documents or any property belonging to any former employer or any other person to whom I have an obligation of confidentiality unless consented to in writing by that former employer or person.

9. No Conflicting Obligation. I represent that my performance of all the

terms of this Agreement and as an employee of the Company does not and will not breach any agreement to keep in confidence information acquired by me in confidence or in trust prior to my employment by the Company. I have not entered into, and I agree I will not enter into, any agreement either written or oral in conflict herewith.

10. Return of Company Documents. When I leave the employ of the Company,

I will deliver to the Company any and all drawings, notes, memoranda, specifications, devices, formulas, molecules, cells and documents, together with all copies thereof, and any other material containing or disclosing any Company Inventions, Third Party Information or Proprietary Information of the Company.

11. Legal and Equitable Remedies. Because my services are personal and

unique and because I may have access to and become acquainted with the Proprietary Information of the Company, the Company shall have the right to enforce this Agreement and any of its provisions by injunction, specific performance or other equitable relief, without bond, without prejudice to any other rights and remedies that the Company may have for a breach of this Agreement.

12. Notices. Any notices required or permitted hereunder shall be given

to the appropriate party at the address specified below or at such other address as the party shall specify in writing. Such notice shall be deemed given upon personal delivery to the appropriate address or if sent by certified or registered mail, three days after the date of mailing.

13. General Provisions.

13.1 Governing Law. This Agreement will be governed by and construed according to the laws of the State of Michigan.

13.2 Entire Agreement. This Agreement is the final, complete and exclusive

agreement of the parties with respect to the subject matter hereof and supersedes and merges all prior discussions between us. No modification of or amendment to this Agreement, nor any waiver of any rights under this Agreement, will be effective unless in writing signed by the party to be charged. Any subsequent change or changes in my duties, salary or compensation will not affect the validity or scope of this Agreement. As used in this Agreement, the period of my employment includes any time during which I may be retained by the Company as a consultant.

13.3 Severability. If one or more of the provisions in this Agreement are

deemed unenforceable by law, then the remaining provisions will continue in full force and effect.

13.4 Successors and Assigns. This Agreement will be binding upon my heirs,

executors, administrators and other legal representatives and will be for the benefit of the Company, its successors, and its assigns.

13.5 Survival. The provisions of this Agreement shall survive the

termination of my employment and the assignment of this Agreement by the Company
to any successor in interest or other assignee.

13.6 Employment. I agree and understand that nothing in this

Agreement shall confer any right with respect to continuation of employment by
the Company, nor shall it interfere in any way with my right or the Company's
right to terminate my employment at any time, with or without cause.

13.7 Waiver. No waiver by the Company of any breach of this Agreement

shall be a waiver of any preceding or succeeding breach. No waiver by the
Company of any right under this Agreement shall not be required to give notice
to enforce strict adherence to all terms of this Agreement.

This Agreement shall be effective as of the first day of my
employment with the Company, namely: June 1, 1991.
----- --

I UNDERSTAND THAT THIS AGREEMENT AFFECTS MY RIGHTS TO INVENTIONS I
MAKE DURING MY EMPLOYMENT, AND RESTRICTS MY RIGHT TO DISCLOSE OR USE THE
COMPANY'S CONFIDENTIAL INFORMATION DURING OR SUBSEQUENT TO MY EMPLOYMENT.

I HAVE READ THIS AGREEMENT CAREFULLY AND UNDERSTAND ITS TERMS. I HAVE
COMPLETELY FILLED OUT EXHIBIT A TO THIS AGREEMENT.

Dated: 3/30 , 1992
----- --

Signature

/s/ R. Douglas Armstrong

R. Douglas Armstrong, Ph.D.

845 Arlington Blvd.,

Address

Ann Arbor, MI 48104

ACCEPTED AND AGREED TO:

AASTROM BIOSCIENCES, INC.

By /s/ Robert Kunze

Robert Kunze, Chairman

Schedule I

AASTROM BIOSCIENCES, INC.
University of Michigan
3074 H. H. Dow Building
Ann Arbor, Michigan 48109-2136

Gentlemen:

1. The following is a complete list of all inventions or improvements relevant to the subject matter of my employment by, and/or services as a director or an officer to, AASTROM BIOSCIENCES, INC., (the "Company") that have been made or conceived or first reduced to practice by me alone or jointly with others prior to my engagement by the Company:

No inventions or improvements

X See below:

1. U.S. Patent App. #07/685,123 filed 4/12/91:

"Queueine tRNA Expression as a Diagnostic and Prognostic Marker

in Differentiation-Related Diseases"

2. U.S. Patent App. #07/681,889 filed 4/8/91:

"A Novel 23K Protein with Binding Specificity for Queueine"

Due to confidentiality agreements with prior employer, I cannot
----- disclose certain inventions that would otherwise be included on
the above-described list.

X Additional sheets attached

2. I propose to bring to my employment/service as a director or officer the following device(s), material(s), and document(s) of a former employer or other person to whom I have an obligation of confidentiality that are not generally available to the public, which device(s), material(s) and document(s) may be used in my employment pursuant to the express written authorization of my former employer or such other person (a copy of which is attached hereto):

_____ No devices, materials or documents

_____ See below:

_____ Additional sheets attached

Date: July 23 , 1991

Very truly yours,

/s/ R. Douglas Armstrong

R. Douglas Armstrong, Ph.D.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:)
R. DOUGLAS ARMSTRONG)
)
Filed: Herewith)
)
For: QUEUINE-tRNA EXPRESSION)
AS A DIAGNOSTIC AND)
PROGNOSTIC MARKER OF) 444 South Flower Street
DIFFERENTIATION-RELATED) Suite 2000
DISEASES) Los Angeles, California 90071

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

TRANSMITTAL OF ASSIGNMENT

Dear Sir:

Enclosed is an executed Assignment for the above-identified United States Patent Application.

A check in the amount of \$323.00 is enclosed, \$8.00 of which covers the recordation of the Assignment.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 16-2460. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

/s/ Theresa A. Brown

Theresa A. Brown
Reg. No. 32,547
Telephone: (619) 535-9001
Facsimile: (619) 535-8949

PRETTY SCHROEDER,
BRUEGGEMANN & CLARK
444 South Flower Street
Suite 2000
Los Angeles, California 90071

ASSIGNMENT

This Assignment is made by R. Douglas Armstrong of 311 Cole Ranch Road, Encinitas, California, Assignor, to THE LA JOLLA CANCER RESEARCH FOUNDATION, Assignee, having a place of business at 10901 N. Torrey Pines Road, La Jolla, California 92037.

WHEREAS, Assignor has invented a new and useful QUEUINE-tRNA EXPRESSION AS A DIAGNOSTIC AND PROGNOSTIC MARKER OF DIFFERENTIATION-RELATED DISEASES, for which an application for United States Letters Patent is filed herewith in the United States Patent and Trademark Office;

WHEREAS, Assignor believes himself to be the original inventor of the invention disclosed and claimed in said application for Letters Patent; and

WHEREAS, the parties desire to have a recordable instrument assigning the entire right, title and interest in and to said invention, said application and any Letters Patent that may be granted for said invention in the United States and throughout the world;

NOW, THEREFORE, in accordance with the obligations to assign the invention and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Assignor sells, assigns, and transfers to Assignee, the entire right, title, and interest in and to said invention, said application and any Letters Patent that may be granted for said invention in the United States and throughout the world, including the right to file foreign applications directly in the name of the Assignee and to claim for any such foreign applications any priority rights to which such applications are entitled under international conventions, treaties, or otherwise.

Assignor agrees that, upon request and without further compensation, but at no expense to Assignor, he and his legal representatives and assigns will do all lawful acts, including the execution of papers and the giving of testimony, that may be necessary or desirable for obtaining, sustaining, reissuing, or enforcing Letters Patent in the United States and throughout the world for said invention, and for perfecting, recording, or maintaining the title of Assignee, its successors and assigns, to said invention, said application, and any Letters Patent granted for said invention in the United States and throughout the world.

Assignor represents and warrants that he has not granted and will not grant to others any rights inconsistent with the rights granted herein.

Assignor authorizes and requests the Commissioner of Patents and Trademarks of the United States and of all foreign countries to issue any Letters Patent granted for said invention, whether on said application or on any subsequently filed division, continuation, continuation-in-part or reissue application, to Assignee, its successors and assigns, as the assignee of the entire interest in said invention.

IN WITNESS WHEREOF, Assignor has executed this Assignment on the date first above written.

Assignor: R. DOUGLAS ARMSTRONG

/s/ R. DOUGLAS ARMSTRONG

STATE OF CALIFORNIA)
COUNTY OF SAN DIEGO)

On this 12th day of April, in the year 1991, before me personally appeared
----- personally known to me or proved to me on the basis
of satisfactory evidence to be the person whose name is subscribed to this
instrument, and acknowledged to me that he executed it.

IN WITNESS WHEREOF, I have hereunto set my hand and affixed my official
seal the day and year in this certificate first above written.

/s/ Crystal K. Herndon

Notary Public in and/or
said County and State

OFFICIAL SEAL CRYSTAL K. HERNDON NOTARY PUBLIC CALIFORNIA SAN DIEGO COUNTY MY COMM. EXPIRES MAR. 7, 1996

EMPLOYMENT AGREEMENT

This Employment Agreement (the "Agreement") is entered into as of June 19, 1992, by and between AASTROM BIOSCIENCES, INC., a Michigan corporation ("Employer") and JAMES MALUTA ("Employee").

NOW, THEREFORE, the parties agree as follows:

1. **EMPLOYMENT** Employer hereby engages Employee, and Employee hereby accepts such engagement, upon the terms and conditions set forth herein.

2. **DUTIES** Employee is engaged as Vice President, Product Development. Employee shall perform faithfully and diligently the duties customarily performed by persons in the position for which employee is engaged, together with such other reasonable and appropriate duties as Employer shall designate from time to time. Employee shall devote Employee's full business time and efforts to the rendition of such services and to the performance of such duties. As a full-time employee of Employer, Employee shall not be entitled to provide consulting services or other business or scientific services to any other party, without the prior written consent of Employer.

3. **COMPENSATION**

3.1 **BASE SALARY** During the term of this Agreement, as compensation for the proper and satisfactory performance of all duties to be performed by Employee hereunder, Employer shall pay Employee a salary of \$90,000 per year, payable in arrears in equal bi-weekly installments, less required deductions for state and federal withholding tax, Social Security and all other employee taxes and payroll deductions. The base salary shall be subject to review and adjustment on an annual basis.

3.2 **BONUS COMPENSATION** Employee may receive bonus in the form of a stock option, stock, or cash, the amount and timing of which shall be determined in the sole discretion of the Board of Directors of Employer.

4. **TERM**

4.1 **COMMENCEMENT** The employment relationship pursuant to this Agreement shall commence no later than August 1, 1992.

4.2 **TERMINATION AT WILL** Although Employer and Employee anticipate a long and mutually rewarding employment relationship, either party may terminate this Agreement, without cause, upon fourteen (14) days' prior written notice delivered to the other. It is expressly understood and agreed that the employment relationship is "at will", and with no agreement for employment for any specified term, and with no agreement for employment for so long as Employee performs satisfactorily. Provided, however, before Employer

exercises this right of termination at will, Employer shall first either (i) discuss with Employee the needs of Employer and why Employee no longer meets those needs, or (ii) discuss with Employee any concerns or dissatisfactions which Employer has with Employee's performance, and give to Employee a reasonable opportunity to remedy those concerns or dissatisfactions, to the reasonable satisfaction of Employer.

4.3 TERMINATION FOR CAUSE Either party may terminate this employment relationship immediately upon notice to the other party in the event of any good cause, such as a default, dishonesty, neglect of duties, failure to perform by the other party, or death or disability of Employee.

4.4 PAYMENT OF COMPENSATION UPON TERMINATION Upon termination for cause, Employee shall be entitled to the compensation set forth as "base salary" herein, prorated to the effective date of such termination as full compensation for any and all claims of Employee under this Agreement.

5. FRINGE BENEFITS

5.1 CUSTOMARY FRINGE BENEFITS Employee shall be entitled to such fringe benefits as Employer customarily makes available to employees of Employer engaged in the same or similar position as Employee ("Fringe Benefits"). Such Fringe Benefits may include vacation leave, sick leave, and health insurance coverage. Employer reserves the right to change the Fringe Benefits on a prospective basis, at any time, effective upon delivery of written notice to Employee.

5.2 ACCUMULATION Employee shall not earn and accumulate unused vacation and sick leave, or other Fringe Benefits in excess of an unused amount equal to twice the amount earned for one year. Further, Employee shall not be entitled to receive payments in lieu of said Fringe Benefits, other than for unused vacation leave earned and accumulated at the time the employment relationship terminates.

6. INVENTION, TRADE SECRETS AND CONFIDENTIALITY

6.1 DEFINITIONS

6.1.1 Invention Defined. As used herein "Invention" means inventions, discoveries, concepts, and ideas, whether patentable or copyrightable or not, including but not limited to processes, methods, formulas, techniques, devices, designs, programs (including computer programs), computer graphics, apparatus, products, as well as improvements thereof or know-how related thereto, relating to any present or anticipated business or activities of Employer.

6.1.2 Trade Secret Defined. As used herein "Trade Secret" means, without limitation, any document or information relating to Employer's products, processes or services, including documents and information relating to Inventions, and to the research, development, engineering or manufacture of

Inventions, and to Employer's purchasing, customer or supplier lists, which documents or information have been disclosed to Employee or known to Employee as a consequence of or through Employee's employment by Employer (including documents, information or Inventions conceived, originated, discovered or developed by Employee), which is not generally known in the relevant trade or industry.

6.2 INVENTIONS

6.2.1 Disclosure. Employee shall disclose promptly to Employer each Invention, whether or not reduced to practice, which is conceived or learned by Employee (either alone or jointly with others) during the term of his employment with Employer. Employee shall disclose in confidence to Employer all patent applications filed by or on behalf of Employee during the term of his employment and for a period of three (3) years thereafter. Any disclosure of an Invention, or any patent application, made within one (1) year after termination of employment shall be presumed to relate to an Invention made during Employee's term of Employment with Employer, unless Employee clearly proves otherwise.

6.2.2 Employer Property; Assignment. Employee acknowledges and agrees that all Inventions which are discovered, conceived, developed, made, produced or prepared by Employee (alone or in conjunction with others) during the duration of Employee's employment with Employer shall be the sole property of Employer. Said property rights of Employer include without limitation all domestic and foreign patent rights, rights of registration or other protection under the patent and copyright laws, and all other rights pertaining to the Inventions. Employee further agrees that all services, products and Inventions that directly or indirectly result from engagement with Company shall be deemed "works for hire" as that term is defined in Title 17 of the United States Codes, and accordingly all rights associated therewith shall vest in the Company. Notwithstanding the foregoing, Employee hereby assigns to Employer all of Employee's right, title and interest in any such services, products and Inventions, in the event any such services, products and Inventions shall be determined not to constitute "works for hire."

6.2.3 Exclusion Notice. The Assignment by Employee of Inventions under this Agreement does not apply to any Inventions which are owned or controlled by Employee prior to the commencement of employment of Employee by Employer (all of which are set forth on Exhibit "A" hereto). Additionally, Employee is not required to assign an idea or invention where the invention or idea meets all of the following criteria; namely if the invention or idea: (i) was created or conceived without the use of any of Employer's equipment, supplies, facilities, or trade secret information, and (ii) was developed entirely on Employee's own time, and (iii) does not relate to the business of Employer, and (iv) does not relate to Employer's actual or demonstrably anticipated research or development, and (v) does not result from any work performed by Employee for Employer.

6.2.4 Patents and Copyrights; Attorney-in Fact. Both before and after termination of this Agreement (and with reasonable compensation paid by Employer to Employee after termination), Employee agrees to assist the Employer to apply for, obtain and enforce patents on, and to apply for, obtain and enforce copyright protection and registration of, the Inventions described in Section 6.2.2 in any and all countries. To that end, Employee shall (at Employer's request) without limitation, testify in any proceeding, and execute any documents and assignments determined to be necessary or convenient for use in applying for, obtaining, registering and enforcing patent or copyright protection involving any of the Inventions. Employee hereby irrevocably appoints Employer, and its duly authorized officers and agents, as Employee's agent and attorney-in-fact, to act for and in behalf of Employee in filing all patent applications, applications for copyright protection and registration, amendments, renewals, and all other appropriate documents in any way related to the Inventions described in Section 6.2.2.

6.3 TRADE SECRETS

6.3.1 Acknowledgment of Proprietary Interest. Employee recognizes the proprietary interest of Employer in any Trade Secrets of Employer. Employee acknowledges and agrees that any and all Trade Secrets of Employer, whether developed by Employee alone or in conjunction with others or otherwise, shall be and are the property of Employer.

6.3.2 Covenant Not to Divulge Trade Secrets. Employee acknowledges and agrees that Employer is entitled to prevent the disclosure of Trade Secrets of Employer. As a portion of the consideration for the employment of Employee and for the compensation being paid to Employee by Employer, Employee agrees at all times during the term of the employment by Employer and thereafter to hold in strictest confidence, and not to use, disclose or allow to be disclosed to any person, firm, or corporation, Trade Secrets of Employer, including Trade Secrets developed by Employee, other than disclosures to persons engaged by Employer to further the business of Employer, and other than use in the pursuit of the business of Employer.

6.3.3 Confidential Information of Others. Employee represents and warrants that if Employee has any confidential information belonging to others, Employee will not use or disclose to Employer any such information or documents. Employee represents that his employment with Employer will not require him to violate any obligation to or confidence with any other party.

6.4 NO ADVERSE USE Employee will not at any time use Employer's Trade Secrets or Inventions in any manner which may directly or indirectly have an adverse effect upon Employer's business, nor will Employee perform any acts which would tend to reduce Employer's proprietary value in Employer's Trade Secrets or Inventions.

6.5 RETURN OF MATERIALS AT TERMINATION In the event of any termination of Employee's employment, Employee will promptly deliver to Employer all materials, property, documents, data, and other information belonging to Employer or pertaining to Trade Secrets or Inventions. Employee shall not take any materials, property, documents or other information, or any reproduction or excerpt thereof, belonging to Employer or containing or pertaining to any Trade Secrets or Inventions.

6.6 REMEDIES UPON BREACH In the event of any breach by Employee of the provision in this Section 6, Employer shall be entitled, if it so elects, to institute and prosecute proceedings in any court of competent jurisdiction, either in law or in equity, to enjoin Employee from violating any of the terms of this Section 6, to enforce the specific performance by Employee of any of the terms of this Section 6, and to obtain damages for any of them, but nothing herein contained shall be construed to prevent such remedy or combination of remedies as Employer may elect to invoke. The failure of Employer to promptly institute legal action upon any breach of this Section 6 shall not constitute a waiver of that or any other breach hereof.

7. COVENANT NOT TO COMPETE Employee agrees that, during Employee's employment, Employee will not directly or indirectly compete with Employer in any way, and that Employee will not act as an officer, director, employee, consultant, shareholder, lender or agent of any other entity which is engaged in any business of the same nature as, or in competition with, the business in which Employer is now engaged, or in which Employer becomes engaged during the term of Employee's employment, or which is involved in science or technology which is similar to Employer's science or technology.

8. GENERAL PROVISIONS

8.1 ATTORNEYS' FEES In the event of any dispute or breach arising with respect to this Agreement, the party prevailing in any negotiations or proceedings for the resolution or enforcement thereof shall be entitled to recover from the losing party reasonable expenses, attorneys' fees and costs incurred therein.

8.2 AMENDMENTS No amendment or modification of the terms or conditions of this Agreement shall be valid unless in writing and signed by both parties hereto. There shall be no implied-in-fact contracts modifying the terms of this Agreement.

8.3 ENTIRE AGREEMENT This Agreement constitutes the entire agreement between the parties with respect to the employment of Employee. This Agreement supersedes all prior agreements, understandings, negotiations and representation with respect to the employment relationship.

8.4 SUCCESSORS AND ASSIGNS The Rights and obligations of Employer under this Agreement shall inure to the benefit of and shall be

binding upon the successors and assigns of Employer. Employee shall not be entitled to assign any of Employee's rights or obligations under this Agreement.

8.5 WAIVER Either party's failure to enforce any provision of this Agreement shall not in any way be construed as a waiver of any such provision, or prevent that party thereafter from enforcing each and every other provision of this Agreement.

8.6 SEVERABLE PROVISIONS The provisions of this Agreement are severable, and if any or more provisions may be determined to be judicially unenforceable, in whole or in part, the remaining provisions shall nevertheless be binding and enforceable.

9. EMPLOYEE'S REPRESENTATIONS Employee represents and warrants that Employee (i) is free to enter into this Agreement and to perform each of the terms and covenants contained herein, (ii) is not restricted or prohibited, contractually or otherwise, from entering into and performing this Agreement, and (iii) will not be in violation or breach of any other agreement by reason of Employee's execution and performance of this Agreement.

10. SUPPLEMENTAL MATTERS Pursuant to a separate letter agreement, Employee shall be entitled to reimbursement for certain relocation costs. Subject to ultimate decision by Employer's Board of Directors, Employee may receive a stock option agreement for 125,000 (one hundred twenty five thousand) shares of Employer's common stock.

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date set forth above.

EMPLOYER:

Aastrom Biosciences, Inc.

By: /s/ R. DOUGLAS ARMSTRONG

R. Douglas Armstrong, Ph.D.
President/CEO

EMPLOYEE:

/s/ James Maluta
- -----
James Maluta

Address: 29253 Thimbleberry Lane
Evergreen, CO 80439

Exhibit A

List of Prior Inventions (Section 6.2.3)

None, other than the following:

None

[illegible]

EMPLOYMENT AGREEMENT

This Employment Agreement (the "Agreement") is entered into as of December 8, 1995, by and between AASTROM BIOSCIENCES, INC., a Michigan corporation ("Employer") and TODD E. SIMPSON, C.P.A. ("Employee").

NOW, THEREFORE, the parties agree as follows:

1. **EMPLOYMENT** Employer hereby engages Employee, and Employee hereby accepts such engagement, upon terms and conditions set forth herein.

2. **DUTIES** Employee is engaged as a Vice President Finance & Administration and Chief Financial Officer. Employee shall perform faithfully and diligently the duties customarily performed by persons in the position for which employee is engaged, together with such other reasonable and appropriate duties as Employer shall designate from time to time. Employee shall devote Employee's full business time and efforts to the rendition of such services or other business or scientific services to any other party, without the prior written consent of Employer.

3. **COMPENSATION**

3.1 **BASE SALARY** During the term of this Agreement, as compensation for the proper and satisfactory performance of all duties to be performed by Employee hereunder, Employer shall pay Employee at an annual salary rate of One Hundred Twenty-Two Thousand Five Hundred Dollars (\$122,500), payable in arrears in equal bi-weekly installments, less required deductions for state and federal withholding tax, Social Security and all other employee taxes and payroll deductions. The base salary shall be subject to review and adjustment on an annual basis.

4. **TERM**

4.1 **COMMENCEMENT** The employment relationship pursuant to this Agreement shall commence on or before January 2, 1996.

4.2 **TERMINATION AT WILL** Although Employer and Employee anticipate a long and mutually rewarding employment relationship, either party may terminate this Agreement, without cause, upon fourteen (14) days' prior written notice delivered to the other. It is expressly understood and agreed that the employment relationship is "at will", and with no agreement for employment for any specified term, and with no agreement for employment for so long as Employee performs satisfactorily. Provided, however, before Employer exercises this right of termination at will, Employer shall first either (i) discuss with Employee the needs of Employer and why Employee no longer meets those needs, or (ii) discuss with Employee any concerns or dissatisfactions which

Employer has with Employee's performance, and give to Employee a reasonable opportunity to remedy those concerns or dissatisfactions, to the reasonable satisfaction of Employer.

4.3 TERMINATION FOR CAUSE Either party may terminate this employment relationship immediately upon notice to the other party in the event of any good cause, such as a default, dishonesty, neglect of duties, failure to perform by the other party, or death or disability of Employee.

4.4 PAYMENT OF COMPENSATION UPON TERMINATION Upon termination for cause, Employee shall be entitled to the compensation set forth as "base salary" herein, prorated to the effective date of such termination as full compensation for any and all claims of Employee under this Agreement.

5. FRINGE BENEFITS

5.1 CUSTOMARY FRINGE BENEFITS Employee shall be entitled to such fringe benefits as Employer customarily makes available to employees of Employer engaged in the same or similar position as Employee ("Fringe Benefits"). Such Fringe Benefits may include vacation leave, sick leave, and health insurance coverage. Employer reserves the right to change the Fringe Benefits on a prospective basis, at any time, effective upon delivery of written notice to Employee.

5.2 ACCUMULATION Employee shall not earn and accumulate unused vacation in excess of Fifteen (15) days. Employee shall not earn and accumulate sick leave or other Fringe Benefits in excess of an unused amount equal to twice the amount earned for one year. Further, Employee shall not be entitled to receive payments in lieu of said Fringe Benefits, other than for unused vacation leave earned and accumulated at the time the employment relationship terminates.

6. INVENTION, TRADE SECRETS AND CONFIDENTIALITY

6.1 DEFINITIONS

6.1.1 Invention Defined. As used herein "Invention" means inventions, discoveries, concepts, and ideas, whether patentable or copyrightable or not, including but not limited to processes, methods, formulas, techniques, materials, devices, designs, programs (including computer programs), computer graphics, apparatus, products, as well as improvements thereof or know-how related thereto, relating to any present or anticipated business or activities of Employer.

6.1.2 Trade Secret Defined. As used herein "Trade Secret" means, without limitation, any document or information relating to Employer's products, processes or services, including documents and information relating to Inventions, and to the research, development, engineering or manufacture of Inventions, and to Employer's purchasing, customer or supplier lists, which

documents or information have been disclosed to Employee or known to Employee as a consequence of or through Employee's employment by Employer (including documents, information or Inventions conceived, originated, discovered or developed by Employee), which is not generally known in the relevant trade or industry.

6.2 INVENTIONS

6.2.1 Disclosure. Employee shall disclose promptly to Employer each Invention, whether or not reduced to practice, which is conceived or learned by Employee (either alone or jointly with others) during the term of his employment with Employer. Employee shall disclose in confidence to Employer all patent applications filed by or on behalf of Employee during the term of his employment and for a period of three (3) years thereafter. Any disclosure of an Invention, or any patent application, made within one (1) year after termination of employment shall be presumed to relate to an Invention made during Employee's term of Employment with Employer, unless Employee clearly proves otherwise.

6.2.2 Employer Property; Assignment. Employee acknowledges and agrees that all Inventions which are discovered, conceived, developed, made, produced or prepared by Employee (alone or in conjunction with others) during the duration of Employee's employment with Employer shall be the sole property of Employer. Said property rights of Employer include without limitation all domestic and foreign patent rights, rights of registration or other protection under the patent and copyright laws, and all other rights pertaining to the Inventions. Employee further agrees that all services, products and Inventions that directly or indirectly result from engagement with Company shall be deemed "works for hire" as that term is defined in Title 17 of the United States Codes, and accordingly all rights associated therewith shall vest in the Company. Notwithstanding the foregoing, Employee hereby assigns to Employer all of Employee's right, title and interest in any such services, products and Inventions, in the event any such services, products and Inventions shall be determined not to constitute "works for hire."

6.2.3 Exclusion Notice. The Assignment by Employee of Inventions under this Agreement does not apply to any Inventions which are owned or controlled by Employee prior to the commencement of employment of Employee by Employer (all of which are set forth on Exhibit "A" hereto). Additionally, Employee is not required to assign an idea or invention where the invention or idea meets all of the following criteria; namely if the invention or idea: (i) was created or conceived without the use of any of Employer's equipment, supplies, facilities, or trade secret information, and (ii) was developed entirely on Employee's own time, and (iii) does not relate to the business of Employer, and (iv) does not relate to Employer's actual or demonstrably anticipated research or development, and (v) does not result from any work performed by Employee for Employer.

6.2.4 Patents and Copyrights; Attorney-in Fact. Both before and after termination of this Agreement (and with reasonable

compensation paid by Employer to Employee after termination), Employee agrees to assist the Employer to apply for, obtain and enforce patents on, and to apply for, obtain and enforce copyright protection and registration of, the Inventions described in Section 6.2.2 in any and all countries. To that end, Employee shall (at Employer's request) without limitation, testify in any proceeding, and execute any documents and assignments determined to be necessary or convenient for use in applying for, obtaining, registering and enforcing patent or copyright protection involving any of the Inventions. Employee hereby irrevocably appoints Employer, and its duly authorized officers and agents, as Employee's agent and attorney-in-fact, to act for and in behalf of Employee in filing all patent applications, applications for copyright protection and registration, amendments, renewals, and all other appropriate documents in any way related to the Inventions described in Section 6.2.2.

6.3 TRADE SECRETS

6.3.1 Acknowledgment of Proprietary Interest. Employee recognizes the proprietary interest of Employer in any Trade Secrets of Employer. Employee acknowledges and agrees that any and all Trade Secrets of Employer, whether developed by Employee alone or in conjunction with others or otherwise, shall be and are the property of Employer.

6.3.2 Covenant Not to Divulge Trade Secrets. Employee acknowledges and agrees that Employer is entitled to prevent the disclosure of Trade Secrets of Employer. As a portion of the consideration for the employment of Employee and for the compensation being paid to Employee by Employer, Employee agrees at all times during the term of the employment by Employer and thereafter to hold in strictest confidence, and not to use, disclose or allow to be disclosed to any person, firm, or corporation, Trade Secrets of Employer, including Trade Secrets developed by Employee, other than disclosures to persons engaged by Employer to further the business of Employer, and other than use in the pursuit of the business of Employer.

6.3.3 Confidential Information of Others. Employee represents and warrants that if Employee has any confidential information belonging to others, Employee will not use or disclose to Employer any such information or documents. Employee represents that his employment with Employer will not require him to violate any obligation to or confidence with any other party.

6.4 NO ADVERSE USE Employee will not at any time use Employer's Trade Secrets or Inventions in any manner which may directly or indirectly have an adverse effect upon Employer's business, nor will Employee perform any acts which would tend to reduce Employer's proprietary value in Employer's Trade Secrets or Inventions.

6.5 RETURN OF MATERIALS AT TERMINATION In the event of any termination of Employee's employment, Employee will promptly deliver to Employer all materials, property, documents, data, and other information

belonging to Employer or pertaining to Trade Secrets or Inventions. Employee shall not take any materials, property, documents or other information, or any reproduction or excerpt thereof, belonging to Employer or containing or pertaining to any Trade Secrets or Inventions.

6.6 REMEDIES UPON BREACH In the event of any breach by Employee of the provision in this Section 6, Employer shall be entitled, if it so elects, to institute and prosecute proceedings in any court of competent jurisdiction, either in law or in equity, to enjoin Employee from violating any of the terms of this Section 6, to enforce the specific performance by Employee of any of the terms of this Section 6, and to obtain damages for any of them, but nothing herein contained shall be construed to prevent such remedy or combination of remedies as Employer may elect to invoke. The failure of Employer to promptly institute legal action upon any breach of this Section 6 shall not constitute a waiver of that or any other breach hereof.

7. COVENANT NOT TO COMPETE Employee agrees that, during Employee's employment, Employee will not directly or indirectly compete with Employer in any way, and that Employee will not act as an officer, director, employee, consultant, shareholder of more than 2 1/2 percent, lender or agent of any other entity which is engaged in any business of the same nature as, or in competition with, the business in which Employer is now engaged, or in which Employer becomes engaged during the term of Employee's employment, or which is involved in science or technology which is similar to Employer's science or technology.

8. GENERAL PROVISIONS

8.1 ATTORNEYS' FEES In the event of any dispute or breach arising with respect to this Agreement, the party prevailing in any negotiations or proceedings for the resolution or enforcement thereof shall be entitled to recover from the losing party reasonable expenses, attorneys' fees and costs incurred therein.

8.2 AMENDMENTS No amendment or modification of the terms or conditions of this Agreement shall be valid unless in writing and signed by both parties hereto. There shall be no implied-in-fact contracts modifying the terms of this Agreement.

8.3 ENTIRE AGREEMENT This Agreement constitutes the entire agreement between the parties with respect to the employment of Employee. This Agreement supersedes all prior agreements, understandings, negotiations and representation with respect to the employment relationship.

8.4 SUCCESSORS AND ASSIGNS The Rights and obligations of Employer under this Agreement shall inure to the benefit of and shall be binding upon the successors and assigns of Employer. Employee shall not be entitled to assign any of Employee's rights or obligations under this Agreement.

8.5 WAIVER Either party's failure to enforce any provision of this Agreement shall not in any way be construed as a waiver of any such provision, or prevent that party thereafter from enforcing each and every other provision of this Agreement.

8.6 SEVERABLE PROVISIONS The provisions of this Agreement are severable, and if any or more provisions may be determined to be judicially unenforceable, in whole or in part, the remaining provisions shall nevertheless be binding and enforceable.

9. EMPLOYEE'S REPRESENTATIONS Employee represents and warrants that Employee (i) is free to enter into this Agreement and to perform each of the terms and covenants contained herein, (ii) is not restricted or prohibited, contractually or otherwise, from entering into and performing this Agreement, and (iii) will not be in violation or breach of any other agreement by reason of Employee's execution and performance of this Agreement.

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date set forth above.

EMPLOYER:

Aastrom Biosciences, Inc.

By: /s/ R. DOUGLAS ARMSTRONG

R. Douglas Armstrong, Ph.D.
President and Chief Executive Officer

EMPLOYEE:

/s/ TODD E. SIMPSON

- ----
Todd E. Simpson, C.P.A.

Address: 12623 Salmon River Road
San Diego, CA 92125

Exhibit A

List of Prior Inventions
(Section 6.2.3)

None, other than the following:

As noted in the preceding.

[illegible]

EMPLOYMENT AGREEMENT

This Employment Agreement (the "Agreement") is entered into as of February 10, 1994, by and between AASTROM BIOSCIENCES, INC., a Michigan corporation ("Employer") and WALTER C. OGIER ("Employee").

NOW, THEREFORE, the parties agree as follows:

1. EMPLOYMENT Employer hereby engages Employee, and Employee hereby accepts such engagement, upon the terms and conditions set forth herein.

2. DUTIES Employee is engaged as Director of Marketing. Employee shall perform faithfully and diligently the duties customarily performed by persons in the position for which employee is engaged, together with such other reasonable and appropriate duties as Employer shall designate for time to time. Employee shall devote Employee's full business time and efforts to the rendition of such services and to the performance of such duties. As a full-time employee of Employer, Employee shall not be entitled to provide consulting services or other business or scientific services to any other party, without the prior written consent of Employer.

3. COMPENSATION

3.1 BASE SALARY During the term of this Agreement, as compensation for the proper and satisfactory performance of all duties to be performed by Employee hereunder, Employer shall pay Employee at an annual salary rate of Eighty-Seven Thousand Five Hundred Dollars (\$87,500), payable in arrears in equal bi-weekly installments, less required deductions for state and federal withholding tax, Social Security and all other employee taxes and payroll deductions. The base salary shall be subject to review and adjustment on an annual basis.

4. TERM

4.1 COMMENCEMENT The employment relationship pursuant to this Agreement shall commence on or before March 21, 1994.

4.2 TERMINATION AT WILL Although Employer and Employee anticipate a long and mutually rewarding employment relationship, either party may terminate this Agreement, without cause, upon fourteen (14) days' prior written notice delivered to the other. It is expressly understood and agreed that the employment relationship is "at will", and with no agreement for employment for any specified term, and with no agreement for employment for so long as Employee performs satisfactorily. Provided, however, before Employer exercises this right of termination at will, Employer shall first either (i) discuss with Employee the needs of Employer and why Employee no longer meets those needs, or (ii) discuss with Employee any concerns or dissatisfactions which

Employer has with Employee's performance, and give to Employee a reasonable opportunity to remedy those concerns or dissatisfactions, to the reasonable satisfaction of Employer.

4.3 TERMINATION FOR CAUSE Either party may terminate this employment relationship immediately upon notice to the other party in the event of any good cause, such as a default, dishonesty, neglect of duties, failure to perform by the other party, or death or disability of Employee.

4.4 PAYMENT OF COMPENSATION UPON TERMINATION Upon termination for cause, Employee shall be entitled to the compensation set forth as "base salary" herein, prorated to the effective date of such termination as full compensation for any and all claims of Employee under this Agreement.

5. FRINGE BENEFITS

5.1 CUSTOMARY FRINGE BENEFITS Employee shall be entitled to such fringe benefits as Employer customarily makes available to employees of Employer engaged in the same or similar position as Employee ("Fringe Benefits"). Such Fringe Benefits may include vacation leave, sick leave, and health insurance coverage. Employer reserves the right to change the Fringe Benefits on a prospective basis, at any time, effective upon delivery of written notice to Employee.

5.2 ACCUMULATION Employee shall not earn and accumulate unused vacation in excess of Fifteen (15) days. Employee shall not earn and accumulate sick leave or other Fringe Benefits in excess of an unused amount equal to twice the amount earned for one year. Further, Employee shall not be entitled to receive payments in lieu of said Fringe Benefits, other than for unused vacation leave earned and accumulated at the time the employment relationship terminates.

6. INVENTION, TRADE SECRETS AND CONFIDENTIALITY

6.1 DEFINITIONS

6.1.1 Invention Defined. As used herein "Invention" means inventions, discoveries, concepts, and ideas, whether patentable or copyrightable or not, including but not limited to processes, methods, formulas, techniques, materials, devices, designs, programs (including computer programs), computer graphics, apparatus, products, as well as improvements thereof or know-how related thereto, relating to any present or anticipated business or activities of Employer.

6.1.2 Trade Secret Defined. As used herein "Trade Secret" means, without limitation, any document or information relating to Employer's products, processes or services, including documents and information relating to Inventions, and to the research, development, engineering or manufacture of Inventions, and to Employer's purchasing, customer or supplier lists, which

documents or information have been disclosed to Employee or known to Employee as a consequence of or through Employee's employment by Employer (including documents, information or Inventions conceived, originated, discovered or developed by Employee), which is not generally known in the relevant trade or industry.

6.2 INVENTIONS

6.2.1 Disclosure. Employee shall disclose promptly to Employer each Invention, whether or not reduced to practice, which is conceived or learned by Employee (either alone or jointly with others) during the term of his employment with Employer. Employee shall disclose in confidence to Employer all patent applications filed by or on behalf of Employee during the term of his employment and for a period of three (3) years thereafter. Any disclosure of an Invention, or any patent application, made within one (1) year after termination of employment shall be presumed to relate to an Invention made during Employee's term of Employment with Employer, unless Employee clearly proves otherwise.

6.2.2 Employer Property; Assignment. Employee acknowledges and agrees that all Inventions which are discovered, conceived, developed, made, produced or prepared by Employee (alone or in conjunction with others) during the duration of Employee's employment with Employer shall be the sole property of Employer. Said property rights of Employer include without limitation all domestic and foreign patent rights, rights of registration or other protection under the patent and copyright laws, and all other rights pertaining to the Inventions. Employee further agrees that all services, products and Inventions that directly or indirectly result from engagement with Company shall be deemed "works for hire" as that term is defined in Title 17 of the United States Codes, and accordingly all rights associated therewith shall vest in the Company. Notwithstanding the foregoing, Employee hereby assigns to Employer all of Employee's right, title and interest in any such services, products and Inventions, in the event any such services, products and Inventions shall be determined not to constitute "works for hire."

6.2.3 Exclusion Notice. The Assignment by Employee of Inventions under this Agreement does not apply to any Inventions which are owned or controlled by Employee prior to the commencement of employment of Employee by Employer (all of which are set forth on Exhibit "A" hereto). Additionally, Employee is not required to assign an idea or invention where the invention or idea meets all of the following criteria; namely if the invention or idea: (i) was created or conceived without the use of any of Employer's equipment, supplies, facilities, or trade secret information, and (ii) was developed entirely on Employee's own time, and (iii) does not relate to the business of Employer, and (iv) does not relate to Employer's actual or demonstrably anticipated research or development, and (v) does not result from any work performed by Employee for Employer.

6.2.4 Patents and Copyrights; Attorney-in Fact. Both before and after termination of this Agreement (and with reasonable compensation paid

by Employer to Employee after termination), Employee agrees to assist the Employer to apply for, obtain and enforce patents on, and to apply for, obtain and enforce copyright protection and registration of, the Inventions described in Section 6.2.2 in any and all countries. To that end, Employee shall (at Employer's request) without limitation, testify in any proceeding, and execute any documents and assignments determined to be necessary or convenient for use in applying for, obtaining, registering and enforcing patent or copyright protection involving any of the Inventions. Employee hereby irrevocably appoints Employer, and its duly authorized officers and agents, as Employee's agent and attorney-in-fact, to act for and in behalf of Employee in filing all patent applications, applications for copyright protection and registration, amendments, renewals, and all other appropriate documents in any way related to the Inventions described in Section 6.2.2.

6.3 TRADE SECRETS

6.3.1 Acknowledgment of Proprietary Interest. Employee recognizes the proprietary interest of Employer in any Trade Secrets of Employer. Employee acknowledges and agrees that any and all Trade Secrets of Employer, whether developed by Employee alone or in conjunction with others or otherwise, shall be and are the property of Employer.

6.3.2 Covenant Not to Divulge Trade Secrets. Employee acknowledges and agrees that Employer is entitled to prevent the disclosure of Trade Secrets of Employer. As a portion of the consideration for the employment of Employee and for the compensation being paid to Employee by Employer, Employee agrees at all times during the term of the employment by Employer and thereafter to hold in strictest confidence, and not to use, disclose or allow to be disclosed to any person, firm, or corporation, Trade Secrets of Employer, including Trade Secrets developed by Employee, other than disclosures to persons engaged by Employer to further the business of Employer, and other than use in the pursuit of the business of Employer.

6.3.3 Confidential Information of Others. Employee represents and warrants that if Employee has any confidential information belonging to others, Employee will not use or disclose to Employer any such information or documents. Employee represents that his employment with Employer will not require him to violate any obligation to or confidence with any other party.

6.4 NO ADVERSE USE Employee will not at any time use Employer's Trade Secrets or Inventions in any manner which may directly or indirectly have an adverse effect upon Employer's business, nor will Employee perform any acts which would tend to reduce Employer's proprietary value in Employer's Trade Secrets or Inventions.

6.5 RETURN OF MATERIALS AT TERMINATION In the event of any termination of Employee's employment, Employee will promptly deliver to Employer all materials, property, documents, data, and other information

belonging to Employer or pertaining to Trade Secrets or Inventions. Employee shall not take any materials, property, documents or other information, or any reproduction or excerpt thereof, belonging to Employer or containing or pertaining to any Trade Secrets or Inventions.

6.6 REMEDIES UPON BREACH In the event of any breach by Employee of the provision in this Section 6, Employer shall be entitled, if it so elects, to institute and prosecute proceedings in any court of competent jurisdiction, either in law or in equity, to enjoin Employee from violating any of the terms of this Section 6, to enforce the specific performance by Employee of any of the terms of this Section 6, and to obtain damages for any of them, but nothing herein contained shall be construed to prevent such remedy or combination of remedies as Employer may elect to invoke. The failure of Employer to promptly institute legal action upon any breach of this Section 6 shall not constitute a waiver of that or any other breach hereof.

7. COVENANT NOT TO COMPETE Employee agrees that, during Employee's employment, Employee will not directly or indirectly compete with Employer in any way, and that Employee will not act as an officer, director, employee, consultant, shareholder, lender or agent of any other entity which is engaged in any business of the same nature as, or in competition with, the business in which Employer is now engaged, or in which Employer becomes engaged during the term of Employee's employment, or which is involved in science or technology which is similar to Employer's science or technology.

8. GENERAL PROVISIONS

8.1 ATTORNEYS' FEES In the event of any dispute or breach arising with respect to this Agreement, the party prevailing in any negotiations or proceedings for the resolution or enforcement thereof shall be entitled to recover from the losing party reasonable expenses, attorneys' fees and costs incurred therein.

8.2 AMENDMENTS No amendment or modification of the terms or conditions of this Agreement shall be valid unless in writing and signed by both parties hereto. There shall be no implied-in-fact contracts modifying the terms of this Agreement.

8.3 ENTIRE AGREEMENT This Agreement constitutes the entire agreement between the parties with respect to the employment of Employee. This Agreement supersedes all prior agreements, understandings, negotiations and representation with respect to the employment relationship.

8.4 SUCCESSORS AND ASSIGNS The Rights and obligations of Employer under this Agreement shall inure to the benefit of and shall be binding upon the successors and assigns of Employer. Employee shall not be entitled to assign any of Employee's rights or obligations under this Agreement.

8.5 WAIVER Either party's failure to enforce any provision of this Agreement shall not in any way be construed as a waiver of any such provision, or prevent that party thereafter from enforcing each and every other provision of this Agreement.

8.6 SEVERABLE PROVISIONS The provisions of this Agreement are severable, and if any or more provisions may be determined to be judicially unenforceable, in whole or in part, the remaining provisions shall nevertheless be binding and enforceable.

9. EMPLOYEE'S REPRESENTATIONS Employee represents and warrants that Employee (i) is free to enter into this Agreement and to perform each of the terms and covenants contained herein, (ii) is not restricted or prohibited, contractually or otherwise, from entering into and performing this Agreement, and (iii) will not be in violation or breach of any other agreement by reason of Employee's execution and performance of this Agreement.

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date set forth above.

EMPLOYER:

AASTROM BIOSCIENCES, INC.

By: /s/ R. DOUGLAS ARMSTRONG

R. Douglas Armstrong, Ph.D.
President and CEO

EMPLOYEE:

/s/ WALTER OGIER

Walter Ogier

Address: 26101 Tono
Mission Viejo, CA 92692

Exhibit A

List of Prior Inventions
(Section 6.2.3)

None, other than the following:

None .

EMPLOYMENT AGREEMENT

This Employment Agreement (the "Agreement") is entered into as of April 19, 1994, by and between AASTROM BIOSCIENCES, INC., a Michigan corporation ("Employer") and THOMAS E. MULLER, PH.D. ("Employee").

NOW, THEREFORE, the parties agree as follows:

1. **EMPLOYMENT** Employer hereby engages Employee, and Employee hereby accepts such engagement, upon the terms and conditions set forth herein.

2. **DUTIES** Employee is engaged as Vice President Regulatory Affairs. Employee shall perform faithfully and diligently the duties customarily performed by persons in the position for which employee is engaged, together with such other reasonable and appropriate duties as Employer shall designate from time to time. Employee shall devote Employee's full business time and efforts to the rendition of such services and to the performance of such duties. As a full-time employee of Employer, Employee shall not be entitled to provide consulting services or other business or scientific services to any other party, without the prior written consent of Employer.

3. **COMPENSATION**

3.1 **BASE SALARY** During the term of this Agreement, as compensation for the proper and satisfactory performance of all duties to be performed by Employee hereunder, Employer shall pay Employee at an annual salary rate of One Hundred Ten Thousand Dollars (\$110,000), payable in arrears in equal bi-weekly installments, less required deductions for state and federal withholding tax, Social Security and all other employee taxes and payroll deductions. The base salary shall be subject to review and adjustment on an annual basis.

4. **TERM**

4.1 **COMMENCEMENT** The employment relationship pursuant to this Agreement shall commence no later than May 9, 1994.

4.2 **TERMINATION AT WILL** Although Employer and Employee anticipate a long and mutually rewarding employment relationship, either party may terminate this Agreement, without cause, upon fourteen (14) days' prior written notice delivered to the other. It is expressly understood and agreed that the employment relationship is "at will", and with no agreement for employment for any specified term, and with no agreement for employment for so long as Employee performs satisfactorily. Provided, however, before Employer exercises this right of termination at will, Employer shall first either (i) discuss with Employee the needs of Employer and why Employee no longer meets those needs, or (ii) discuss with Employee any concerns or dissatisfactions which

Employer has with Employee's performance, and give to Employee a reasonable opportunity to remedy those concerns or dissatisfactions, to the reasonable satisfaction of Employer.

4.3 TERMINATION FOR CAUSE Either party may terminate this employment relationship immediately upon notice to the other party in the event of any good cause, such as a default, dishonesty, neglect of duties, failure to perform by the other party, or death or disability of Employee.

4.4 PAYMENT OF COMPENSATION UPON TERMINATION Upon termination for cause, Employee shall be entitled to the compensation set forth as "base salary" herein, prorated to the effective date of such termination as full compensation for any and all claims of Employee under this Agreement.

5. FRINGE BENEFITS

5.1 CUSTOMARY FRINGE BENEFITS Employee shall be entitled to such fringe benefits as Employer customarily makes available to employees of Employer engaged in the same or similar position as Employee ("Fringe Benefits"). Such Fringe Benefits may include vacation leave, sick leave, and health insurance coverage. Employer reserves the right to change the Fringe Benefits on a prospective basis, at any time, effective upon delivery of written notice to Employee.

5.2 ACCUMULATION Employee shall not earn and accumulate unused vacation in excess of fifteen (15) days. Employee shall not earn and accumulate sick leave or other fringe benefits in excess of an unused amount equal to twice the amount earned for one year. Further, employee shall not be entitled to receive payments in lieu of said fringe benefits, other than for unused vacation leave earned and accumulated at the time the employment relationship terminates.

6. INVENTION, TRADE SECRETS AND CONFIDENTIALITY

6.1 DEFINITIONS

6.1.1 Invention Defined. As used herein "Invention" means inventions, discoveries, concepts, and ideas, whether patentable or copyrightable or not, including but not limited to processes, methods, formulas, techniques, materials, devices, designs, programs (including computer programs), computer graphics, apparatus, products, as well as improvements thereof or know-how related thereto, relating to any present or anticipated business or activities of Employer.

6.1.2 Trade Secret Defined. As used herein "Trade Secret" means, without limitation, any document or information relating to Employer's products, processes or services, including documents and information relating to Inventions, and to the research, development, engineering or manufacture of Inventions, and to Employer's purchasing, customer or supplier lists, which

documents or information have been disclosed to Employee or known to Employee as a consequence of or through Employee's employment by Employer (including documents, information or Inventions conceived, originated, discovered or developed by Employee), which is not generally known in the relevant trade or industry.

6.2 INVENTIONS

6.2.1 Disclosure. Employee shall disclose promptly to Employer each Invention, whether or not reduced to practice, which is conceived or learned by Employee (either alone or jointly with others) during the term of his employment with Employer. Employee shall disclose in confidence to Employer all patent applications filed by or on behalf of Employee during the term of his employment and for a period of three (3) years thereafter. Any disclosure of an Invention, or any patent application, made within one (1) year after termination of employment shall be presumed to relate to an Invention made during Employee's term of Employment with Employer, unless Employee clearly proves otherwise.

6.2.2 Employer Property; Assignment. Employee acknowledges and agrees that all Inventions which are discovered, conceived, developed, made, produced or prepared by Employee (alone or in conjunction with others) during the duration of Employee's employment with Employer shall be the sole property of Employer. Said property rights of Employer include without limitation all domestic and foreign patent rights, rights of registration or other protection under the patent and copyright laws, and all other rights pertaining to the Inventions. Employee further agrees that all services, products and Inventions that directly or indirectly result from engagement with Company shall be deemed "works for hire" as that term is defined in Title 17 of the United States Codes, and accordingly all rights associated therewith shall vest in the Company. Notwithstanding the foregoing, Employee hereby assigns to Employer all of Employee's right, title and interest in any such services, products and Inventions, in the event any such services, products and Inventions shall be determined not to constitute "works for hire."

6.2.3 Exclusion Notice. The Assignment by Employee of Inventions under this Agreement does not apply to any Inventions which are owned or controlled by Employee prior to the commencement of employment of Employee by Employer (all of which are set forth on Exhibit "A" hereto). Additionally, Employee is not required to assign an idea or invention where the invention or idea meets all of the following criteria; namely if the invention or idea: (i) was created or conceived without the use of any of Employer's equipment, supplies, facilities, or trade secret information, and (ii) was developed entirely on Employee's own time, and (iii) does not relate to the business of Employer, and (iv) does not relate to Employer's actual or demonstrably anticipated research or development, and (v) does not result from any work performed by Employee for Employer.

6.2.4 Patents and Copyrights; Attorney-in Fact. Both before and after termination of this Agreement (and with reasonable compensation paid

by Employer to Employee after termination), Employee agrees to assist the Employer to apply for, obtain and enforce patents on, and to apply for, obtain and enforce copyright protection and registration of, the Inventions described in Section 6.2.2 in any and all countries. To that end, Employee shall (at Employer's request) without limitation, testify in any proceeding, and execute any documents and assignments determined to be necessary or convenient for use in applying for, obtaining, registering and enforcing patent or copyright protection involving any of the Inventions. Employee hereby irrevocably appoints Employer, and its duly authorized officers and agents, as Employee's agent and attorney-in-fact, to act for and in behalf of Employee in filing all patent applications, applications for copyright protection and registration, amendments, renewals, and all other appropriate documents in any way related to the Inventions described in Section 6.2.2.

6.3 TRADE SECRETS

6.3.1 Acknowledgment of Proprietary Interest. Employee recognizes the proprietary interest of Employer in any Trade Secrets of Employer. Employee acknowledges and agrees that any and all Trade Secrets of Employer, whether developed by Employee alone or in conjunction with others or otherwise, shall be and are the property of Employer.

6.3.2 Covenant Not to Divulge Trade Secrets. Employee acknowledges and agrees that Employer is entitled to prevent the disclosure of Trade Secrets of Employer. As a portion of the consideration for the employment of Employee and for the compensation being paid to Employee by Employer, Employee agrees at all times during the term of the employment by Employer and thereafter to hold in strictest confidence, and not to use, disclose or allow to be disclosed to any person, firm, or corporation, Trade Secrets of Employer, including Trade Secrets developed by Employee, other than disclosures to persons engaged by Employer to further the business of Employer, and other than use in the pursuit of the business of Employer.

6.3.3 Confidential Information of Others. Employee represents and warrants that if Employee has any confidential information belonging to others, Employee will not use or disclose to Employer any such information or documents. Employee represents that his employment with Employer will not require him to violate any obligation to or confidence with any other party.

6.4 NO ADVERSE USE Employee will not at any time use Employer's Trade Secrets or Inventions in any manner which may directly or indirectly have an adverse effect upon Employer's business, nor will Employee perform any acts which would tend to reduce Employer's proprietary value in Employer's Trade Secrets or Inventions.

6.5 RETURN OF MATERIALS AT TERMINATION In the event of any termination of Employee's employment, Employee will promptly deliver to Employer all materials, property, documents, data, and other information

belonging to Employer or pertaining to Trade Secrets or Inventions. Employee shall not take any materials, property, documents or other information, or any reproduction or excerpt thereof, belonging to Employer or containing or pertaining to any Trade Secrets or Inventions.

6.6 REMEDIES UPON BREACH In the event of any breach by Employee of the provision in this Section 6, Employer shall be entitled, if it so elects, to institute and prosecute proceedings in any court of competent jurisdiction, either in law or in equity, to enjoin Employee from violating any of the terms of this Section 6, to enforce the specific performance by Employee of any of the terms of this Section 6, and to obtain damages for any of them, but nothing herein contained shall be construed to prevent such remedy or combination of remedies as Employer may elect to invoke. The failure of Employer to promptly institute legal action upon any breach of this Section 6 shall not constitute a waiver of that or any other breach hereof.

7. COVENANT NOT TO COMPETE Employee agrees that, during Employee's employment, Employee will not directly or indirectly compete with Employer in any way, and that Employee will not act as an officer, director, employee, consultant, shareholder, lender or agent of any other entity which is engaged in any business of the same nature as, or in competition with, the business in which Employer is now engaged, or in which Employer becomes engaged during the term of Employee's employment, or which is involved in science or technology which is similar to Employer's science or technology.

8. GENERAL PROVISIONS

8.1 ATTORNEYS' FEES In the event of any dispute or breach arising with respect to this Agreement, the party prevailing in any negotiations or proceedings for the resolution or enforcement thereof shall be entitled to recover from the losing party reasonable expenses, attorneys' fees and costs incurred therein.

8.2 AMENDMENTS No amendment or modification of the terms or conditions of this Agreement shall be valid unless in writing and signed by both parties hereto. There shall be no implied-in-fact contracts modifying the terms of this Agreement.

8.3 ENTIRE AGREEMENT This Agreement constitutes the entire agreement between the parties with respect to the employment of Employee. This Agreement supersedes all prior agreements, understandings, negotiations and representation with respect to the employment relationship.

8.4 SUCCESSORS AND ASSIGNS The Rights and obligations of Employer under this Agreement shall inure to the benefit of and shall be binding upon the successors and assigns of Employer. Employee shall not be entitled to assign any of Employee's rights or obligations under this Agreement.

8.5 WAIVER Either party's failure to enforce any provision of this Agreement shall not in any way be construed as a waiver of any such provision, or prevent that party thereafter from enforcing each and every other provision of this Agreement.

8.6 SEVERABLE PROVISIONS The provisions of this Agreement are severable, and if any or more provisions may be determined to be judicially unenforceable, in whole or in part, the remaining provisions shall nevertheless be binding and enforceable.

9. EMPLOYEE'S REPRESENTATIONS Employee represents and warrants that Employee (i) is free to enter into this Agreement and to perform each of the terms and covenants contained herein, (ii) is not restricted or prohibited, contractually or otherwise, from entering into and performing this Agreement, and (iii) will not be in violation or breach of any other agreement by reason of Employee's execution and performance of this Agreement.

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date set forth above.

EMPLOYER:

Aastrom Biosciences, Inc.

By: /s/ R. DOUGLAS ARMSTRONG

R. Douglas Armstrong, Ph.D.
President and CEO

EMPLOYEE:

/s/ THOMAS E. MULLER

- - - - -
Thomas E. Muller, Ph.D.

Address: 388 Lowell Road
Concord, MA 01742

Exhibit A

List of Prior Inventions
(Section 6.2.3)

None, other than the following:

See attached list of patents and publications.

[illegible]

- 1- T.E. Muller and C.B. Purves "Xanthation", Technical Report No. 192, Pulp and Paper Research Institute of Canada (July, 1960).
- 2- T.E. Muller and C.B. Purves "Xanthation and Dexanthation of Cellulose and Related Glucose Derivatives", Canadian Textile Journal 42 (March, 1963).
- 3- T.E. Muller and C. B. Purves "Xanthation", Chapter 43 in "Methods in Carbohydrate Chemistry", Vol. III, Academic Press, Inc., NY (1963).
- 4- T.E. Muller and W. J. Alexander "Fractional Turbidimetric Analysis of the Molar Substitution of Hydroxyethyl Cellulose", Journal of Applied Polymer Science 10, 1285 (1966).
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- 5- G.C. Daul and T.E. Muller "Effect of Orientation and Trace Crosslinking on the Properties of High Wet Modulus Rayon", Journal of Applied Polymer Science 12, 487 (1968).
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- 6- T.E. Muller and W.J. Alexander "Characterization of the Chain Length Distribution of Wood Celluloses by Gel Permeation Chromatography", Journal of Polymer Science Part C, 21, 283 (1968).
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- 7- D. Tunc, R.F. Bampton and T.E. Muller "Quantitative Determination of Xanthate, Byproduct and Total Sulfur in Viscose by Ultraviolet Spectrophotometry", TAPPI 52, 1882 (1969).
--
- 8- W.J. Alexander and T.E. Muller "Applications of Gel Chromatography in the Pulping Process", Journal of Polymer Science Part C, 36, 87 (1971).
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- 9- W.J. Alexander and T.E. Muller "Evaluation of Pulps, Rayon Fibers and Cellulose Acetate by GPC and Other Fractionation Methods", Separation Sciences 6, (1), 47 (FEB., 1971).
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- 10- R.L. Mitchell, T.E. Muller, H.D. Stevens and R.S. Tabke "Process and Forming Hydroxyl Cellulose Fibers Having Water Absorption and High Water Retention Properties", U.S. Patent 3,670,069 (June 13, 1972); British Patent 1,324,373 (July 25, 1973).
- 11- H.L. Hergert, T.E. Muller and S.E. Church "Chemical Cellulose for High Performance Rayon", TAPPI 1973 Dissolving Pulps Conference Preprints (Oct., 1973).
- 12- H.D. Stevens and T.E. Muller "Process for Producing High Performance Crimped Rayon Staple Fiber", U.S. Patent 3,720,743 (March 13, 1973); German Patent 1,342,805 (Jan. 3, 1974); Canadian Patent 960,422 (Jan. 7, 1975).

- 13- R.L. Mitchell, T.E. Muller, H.D. Stevens and R.S. Tabke "Wet Spinning of Cellulosic Products", U.S. Patent 3,865,918 (Feb. 11, 1975).
- 14- T.E. Muller, D.G. Unrau and L.L. Nejelski "The New Rayons", 33rd Annual Technical Conference Society Plastics Engineers, Atlanta, GA (May 5-8, 1975).
- 15- T.E. Muller, F.P. Barch and G.C. Daul "High Performance Crimped Rayon Fiber", Textile Research Journal 46, 184 (1976).
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- 16- J.B. Dykes and T.E. Muller "World Textile Fiber Demand Projected to 2000 A.D.; Technology for the Production of a Chemically Crimped HWM Rayon Fiber", SASMIRA Conference, New Delhi, India (Jan. 19-21, 1976); "Proceedings of the International Conference on Man-Made Fibres for Developing Countries" (1976).
- 17- T.E. Muller and J.B. Dykes "Process Technology and Applications for a Chemically Crimped HWM Rayon Fiber", Eighth Shirley International Seminar, Manchester, England (April 27-29, 1976).
- 18- T.E. Muller "Man-Made Cellulosic Fibers - A View in 1976", Comite International de la Rayonne et des Fibres Synthetiques, Paris, France (Oct. 14, 1976).
- 19- T.E. Muller "Review of Modern Viscose Processing and Recovery Techniques" Seminars Presented at the U.S. Embassy, Moscow (Jan. 10-12, 1978).
- 20- H.L. Hergert and T.E. Muller "Modified Cellulosics - An Overview of the Future", Modified Cellulosics, Academic Press, Inc., NY (1978).
- 21- T.E. Muller "Research, Development and Production of Silvichemicals", Natl. Meeting Am. Inst. Chem. Eng., Philadelphia, PA (June 7, 1978).
- 22- T.E. Muller "Energy and Chemical Requirements for the Manufacture of Chemical Cellulose from Wood, HWM Rayon Staple Fiber and Polyester Staple Fiber", Comite International de la Rayonne et des Fibres Synthetiques, Paris, France (Oct. 1978).
- 23- T.E. Muller "Cellulosics", Seminars Presented for Chinese Industry, Shanghai, China (May 20-21, 1979).
- 24- T.E. Muller "High Wet Modulus Rayon Fiber (Prima)", Industrial Research IR-100 Award (Oct., 1979).
- 25- T.E. Muller "New Cellulose Fibers and Processes", Eighteenth International Man-Made Fibre Conference, Dornbirn, Austria (June 20, 1979); Lenzinger Berichte 48, 87 (March, 1980).
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- 26- T.E. Muller "Developments in the Manufacture of Regenerated Cellulose Fibers and Films", Chairman, TAPPI Dissolving Pulps Conference, Vienna, Austria (Oct. 9, 1980).
- 27- H.O. Jauregui, C. J-P. Mullon, T.E. Muller and B.A. Solomon "Hollow Fiber Liver Support System", Am. Inst. Chem. Eng. Annual Meeting, San Francisco, CA (Nov. 5-10, 1989).
- 28- T.E. Muller, B.A. Solomon, T. Maki, S.J. Sullivan, K.M. Borland, A.P. Monaco and W.L. Chick "The Hybrid Perfused Pancreas: Successful Treatment of Severely Diabetic Pancreatectomized Dogs", Tenth Workshop of the European Association for the Study of Diabetes, Amsterdam, The Netherlands (Jan. 27-29, 1991).
- 29- Thomas E. Muller "Maintenance of Normoglycemia in Diabetic Dogs with an Artificial Pancreas", Presented at Swiss Federal Institute of Technology (ETH), Zurich, Switzerland (Jan. 31, 1991).
- 30- T. Maki, C.S. Ubhi, H. Sanchez-Farpon, S.J. Sullivan, K. Borland, T.E. Muller, B.A. Solomon, W.L. Chick and A.P. Monaco "The Biohybrid Artificial Pancreas for Treatment of Diabetes in Totally Pancreatectomized Dogs", XIII Int. Congress of the Transplantation Society (August 19-24, 1990) San Francisco, CA; Transplantation Proceedings 23 (1), 754-755 (1991).
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- 31- W.L. Chick, S.J. Sullivan, K.M. Borland, J.M. Harvey, T.E. Muller, K.E. Dunleavy, D.P. King, E.J. Doherty, B.A. Solomon and A.L. Foley "Artificial Pancreatic Perfusion Device", U.S. Patent 5,002,661 (March 26, 1991).
- 32- Susan J. Sullivan, Takashi Maki, Kermit M. Borland, Michelle D. Mahoney, Barry A. Solomon, Thomas E. Muller, Anthony P. Monaco, and William L. Chick "Biohybrid Artificial Pancreas: Long-Term Implantation Studies in Diabetic, Pancreatectomized Dogs", Science 252, 718 (1991).

- 33- H. Ohzato, M. Carretta, T. Maki, S.J. Sullivan, K. Borland, T.E. Muller, B.A. Solomon, W.L. Chick and A.P. Monaco "Use of Xenogeneic Islets in Hybrid Artificial Pancreas for Treatment of Diabetes Without Immunosuppression", First International Congress of Xenotransplantation, Minneapolis Transplant Congress, Minneapolis, MN, August 25-28, 1991; Transplantation Proceedings 24 (2) 661-662 (1992).
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- 34- Takashi Maki, Mauro Carretta, Hiroki Ohzato, Susan J. Sullivan, Robert P. Lanza, Kermit M. Borland, Thomas E. Muller, Barry A. Solomon, William L. Chick and Anthony P. Monaco "Islet Xenotransplantation Without Immunosuppression Utilizing the Hybrid Artificial Pancreas", Third International Symposium on Islet Transplantation, Perugia, Italy, (Sept. 26-29, 1991); Diab. Nutr. Metab. (in Press).

- 35- Anthony P. Monaco, Takashi Maki, Hiroki Ohzato, Mauro Carretta, Susan J. Sullivan, Kermit M. Borland, Michelle D. Mahoney, Thomas E. Muller, Jacqueline M. Wolfrum, Barry A. Solomon and William L. Chick "Transplantation of Islet Allografts and Xenografts in Totally Pancreatectomized Diabetic Dogs Using the Hybrid Artificial Pancreas", *Annals of Surgery*, 214 (3), 339-362 (1991).

- 36- Takashi Maki, Charanjeit S. Ubhi, Herminio Sanchez-Farpon, Susan J. Sullivan, Thomas E. Muller, Barry A. Solomon, William L. Chick and Anthony P. Monaco "Successful Treatment of Diabetes with the Biohybrid Artificial Pancreas in Dogs", 16th Annual Meeting American Society of Transplant Surgeons, Chicago, IL (May 30-June 1, 1990); *Transplantation* 51, 43-51, (1991).
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- 37- R.P. Lanza, D.H. Butler, K.M. Borland, J.E. Staruk, D.L. Faustman, B.A. Solomon, T.E. Muller, R.G. Rupp, T. Maki, A.P. Monaco and W.L. Chick "Xenotransplantation of Canine, Bovine, and Porcine Islets in Diabetic Rats Without Immunosuppression", *Proc. Natl. Acad. Sci. USA*, Acad. Sci. USA, 88--11100-11104 (1991).
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- 38- T.E. Muller, B.A. Solomon, A.P. Monaco, T. Maki, W.L. Chick, and S.J. Sullivan "Maintenance of Normoglycemia in Diabetic Dogs with an Artificial Pancreas", Study Group of the European Association for the Study of Diabetes, Igls, Austria (Jan. 26-28, 1992).
- 39- Hugo O. Jauregui and Thomas E. Muller "Long-Term Cultures of Adult Mammalian Hepatocytes in Hollow Fibers as the Cellular Component of Extracorporeal (Hybrid) Liver Assist Devices", *Artif. Organs* 16 (2), 209-212 (1992).
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- 40- S.J. Sullivan, T. Maki, M. Carretta, H. Ohzato, M.D. Mahoney, B.A. Solomon, T.E. Muller, A.P. Monaco and W.L. Chick "Implantation of the Biohybrid Pancreas in Diabetic Dogs", Third International Congress on Pancreatic and Islet Transplantation Symposium on Artificial Insulin Delivery System, Lyon, France, (June 6-8, 1991); *Transplantation Proceedings* 24 (3), 942-944 (1992).
- 41- S.J. Sullivan, T. Maki, M. Carretta, H. Ohzato, K. Borland, M.D. Mahoney, T.E. Muller, B.A. Solomon, A.P. Monaco and W.L. Chick "Evaluation of the Hybrid Artificial Pancreas in Diabetic Dogs", *ASAIJ Journal Transactions on Hybrid Organs and Cell Therapy* 38 (1), 29 (1992).
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- 42- R.P. Lanza, D.H. Butler, K.M. Borland, J.M. Harvey, D.L. Faustman, B.A. Solomon, T.E. Muller, R.G. Rupp, T. Maki, A.P. Monaco and W.L. Chick "Successful Xenotransplantation of a Diffusion-Based Biohybrid Artificial Pancreas: A Study Using Canine, Bovine, and Porcine Islets", First International Congress on Xenotransplantation, Minneapolis Transplant Congress, Minneapolis, MN, (August 25-28, 1991); *Transplantation Proceedings* 24, 669-671 (1992).
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- 43- Thomas E. Muller "Combination Medical Products", Presented at the Joint FDA-HIMA Conference, Washington, DC (February 11-12, 1992).
- 44- S. Sullivan, R. Lanza, K. Borland, T. Maki, M. Carretta, H. Ohzato, P. Lodge, T. Muller, A. Monaco, B. Solomon and W. Chick "Pancreatic Islet Transplantation Using an Immunoprotective Membrane", 38th Annual Meeting of the ASATO Nashville, TN (May 7-9, 1992).
- 45- Robert P. Lanza, Kermit M. Borland, Susan J. Sullivan, Samuel A. Clark, Peter Lodge, Mauro Carretta, Thomas E. Muller, Barry A. Solomon, Takashi Maki, Anthony P. Monaco and William L. Chick "Pancreatic Islet Transplantation Using Membrane Diffusion Chambers", First Int. Congress Cell Transplant Society, Pittsburgh, PA (May 31-June 3, 1992); Transplantation Proceedings 24 (6) 2935-2936 (1992).
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- 46- S. Sullivan, K. Borland, T. Maki, M. Carretta, H. Ohzato, P. Lodge, T. Muller, A. Monaco, B. Solomon and W. Chick, "Islet Transplantation Using an Immuno-protective Vascular Device", First Int. Congress Cell Transplant Society, Pittsburgh, PA, (May 31-June 3, 1992).
- 47- H.O. Jauregui, D. Trenkler, S. Naik, B. Monfils, C. Mullon, T. Muller and B. Solomon "Use of Artificial (Hybrid) Liver Support System to Treat the Galactosamine Rabbit Model of Hepatic Encephalopathy", International Association for the Study of the Liver Biennial Scientific Meeting, Brighton, England (June 3-6, 1992).
- 48- R.P. Lanza, K.M. Borland, S.J. Sullivan, P. Lodge, M. Carretta, T.E. Muller, B.A. Solomon, T. Maki, A.P. Monaco and W.L. Chick, "Treatment of Severely Diabetic, Pancreatectomized Dogs Using a Diffusion-based Hybrid Artificial Pancreas", 16th Annual Meeting of American Diabetes Association, San Antonio, TX, (June 20-23, 1992); Diabetes 41, 886-89 (1992).
- 49- R.P. Lanza, P. Lodge, K.M. Borland, M. Carretta, S.J. Sullivan, A.M. Beyer, T.E. Muller, B.A. Solomon, T. Maki, A.P. Monaco and W.L. Chick "Transplantation of Islet Allografts Using a Diffusion-Based Biohybrid Artificial Pancreas: Long-Term Studies in Diabetic, Pancreatectomized Dogs", XIVth International Congress of the Transplantation Society, Paris, France (August 16-21, 1992); Transplantation Proceedings 25 (1), 978-980 (1993).
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- 50- Thomas E. Muller "New Combination Therapies", Inst. International Res. Seminar, Washington, DC, January 25-27 (1993).
- 51- Thomas E. Muller "Medical Therapies Based on Advanced Biomedical Engineering Technologies", Visiting Professor Lecture, INFA (International Faculty of Artificial Organs) Symposium, Univ. Gent. Belgium (Oct. 1, 1993).

- 52- R.P. Lanza, K.M. Borland, J.E. Staruk, B.A. Solomon, T.E. Muller, B.A. Solomon, T. Maki, A.P. Monaco and W.L. Chick "Transplantation of Canine Islets Into Spontaneously Diabetic BB/Wor Rats Without Immunosuppression", Endocrinology (in Press).

- 53- Hugo O. Jauregui, Claudy J. Mullon, Donna M. Trenkler, Sharda Naik, Henry A. Santangini, Philip J. Press, Thomas E. Muller and Barry A. Solomon "Hollow Fiber Liver Assist Device for Extracorporeal Treatment of Experimental Fulminant Hepatic Failure", Proceedings of the National Academy of Sciences (Submitted).

EMPLOYMENT AGREEMENT

This Employment Agreement (the "Agreement") is entered into as of 26 October 1995, by and between AASTROM BIOSCIENCES, INC., a Michigan corporation ("Employer") and ALAN K. SMITH ("Employee").

NOW, THEREFORE, the parties agree as follows:

1. **EMPLOYMENT** Employer hereby engages Employee, and Employee hereby accepts such engagement, upon the terms and conditions set forth herein.

2. **DUTIES** Employee is engaged as a Vice President Research. Employee shall perform faithfully and diligently the duties customarily performed by persons in the position for which employee is engaged, together with such other reasonable and appropriate duties as Employer shall designate from time to time. Employee shall devote Employee's full business time and efforts to the rendition of such services and to the performance of such duties. As a full-time employee of Employer, Employee shall not be entitled to provide consulting services or other business or scientific services to any other party, without the prior written consent of Employer.

3. **COMPENSATION**

3.1 **BASE SALARY** During the term of this Agreement, as compensation for the proper and satisfactory performance of all duties to be performed by Employee hereunder, Employer shall pay Employee at an annual salary rate of One Hundred Twenty Two Thousand Five Hundred Dollars (\$122,500), payable in arrears in equal bi-weekly installments, less required deductions for state and federal withholding tax, Social Security and all other employee taxes and payroll deductions. The base salary shall be subject to review and adjustment on an annual basis.

4. **TERM**

4.1 **COMMENCEMENT** The employment relationship pursuant to this Agreement shall commence November 13, 1995.

4.2 **TERMINATION AT WILL** Although Employer and Employee anticipate a long and mutually rewarding employment relationship, either party may terminate this Agreement, without cause, upon fourteen (14) days' prior written notice delivered to the other. It is expressly understood and agreed that the employment relationship is "at will", and with no agreement for employment for any specified term, and with no agreement for employment for so long as Employee performs satisfactorily. Provided, however, before Employer exercises this right of termination at will, Employer shall first either (i) discuss with Employee the needs of Employer and why Employee no longer meets those needs, or (ii) discuss with Employee any concerns or dissatisfactions which

Employer has with Employee's performance, and give to Employee a reasonable opportunity to remedy those concerns or dissatisfactions, to the reasonable satisfaction of Employer. Should, for some reason, Employee's involuntary termination without cause be necessary, severance compensation equal to four (4) months' salary will be paid, along with compensation for any accumulated vacation time.

4.3 TERMINATION FOR CAUSE Either party may terminate this employment relationship immediately upon notice to the other party in the event of any good cause, such as a default, dishonesty, neglect of duties, failure to perform by the other party, or death or disability of Employee.

4.4 PAYMENT OF COMPENSATION UPON TERMINATION Upon termination for cause, Employee shall be entitled to the compensation set forth as "base salary" herein, prorated to the effective date of such termination as full compensation for any and all claims of Employee under this Agreement.

5. FRINGE BENEFITS

5.1 CUSTOMARY FRINGE BENEFITS Employee shall be entitled to such fringe benefits as Employer customarily makes available to employees of Employer engaged in the same or similar position as Employee ("Fringe Benefits"). Such Fringe Benefits may include vacation leave, sick leave, and health insurance coverage. Employer reserves the right to change the Fringe Benefits on a prospective basis, at any time, effective upon delivery of written notice to Employee.

5.2 ACCUMULATION Employee shall not earn and accumulate unused vacation in excess of Fifteen (15) days. Employee shall not earn and accumulate sick leave or other Fringe Benefits in excess of an unused amount equal to twice the amount earned for one year. Further, Employee shall not be entitled to receive payments in lieu of said Fringe Benefits, other than for unused vacation leave earned and accumulated at the time the employment relationship terminates.

6. INVENTIONS, TRADE SECRETS AND CONFIDENTIALITY

6.1 DEFINITIONS

6.1.1 Invention Defined. As used herein "Invention" means inventions, discoveries, concepts, and ideas, whether patentable or copyrightable or not, including but not limited to processes, methods, formulas, techniques, materials, devices, designs, programs (including computer programs), computer graphics, apparatus, products, as well as improvements thereof or know-how related thereto, relating to any present or anticipated business or activities of Employer.

6.1.2 Trade Secret Defined. As used herein "Trade Secret" means, without limitation, any document or information relating to Employer's

products, processes or services, including documents and information relating to Inventions, and to the research, development, engineering or manufacture of Inventions, and to Employer's purchasing, customer or supplier lists, which documents or information have been disclosed to Employee or known to Employee as a consequence of or through Employee's employment by Employer (including documents, information or Inventions conceived, originated, discovered or developed by Employee), which is not generally known in the relevant trade or industry.

6.2 INVENTIONS

6.2.1 Disclosure. Employee shall disclose promptly to Employer each Invention, whether or not reduced to practice, which is conceived or learned by Employee (either alone or jointly with others) during the term of his employment with Employer. Employee shall disclose in confidence to Employer all patent applications filed by or on behalf of Employee during the term of his employment and for a period of three (3) years thereafter. Any disclosure of an Invention, or any patent application, made within one (1) year after termination of employment shall be presumed to relate to an Invention made during Employee's term of Employment with Employer, unless Employee clearly proves otherwise .

6.2.2 Employer Property; Assignment. Employee acknowledges and agrees that all Inventions which are discovered, conceived, developed, made, produced or prepared by Employee (alone or in conjunction with others) during the duration of Employee's employment with Employer shall be the sole property of Employer. Said property rights of Employer include without limitation all domestic and foreign patent rights, rights of registration or other protection under the patent and copyright laws, and all other rights pertaining to the Inventions. Employee further agrees that all services, products and Inventions that directly or indirectly result from engagement with Company shall be deemed "works for hire" as that term is defined in Title 17 of the United States Codes, and accordingly all rights associated therewith shall vest in the Company. Notwithstanding the foregoing, Employee hereby assigns to Employer all of Employee's right, title and interest in any such services, products and Inventions, in the event any such services, products and Inventions shall be determined not to constitute "works for hire."

6.2.3 Exclusion Notice. The Assignment by Employee of Inventions under this Agreement does not apply to any Inventions which are owned or controlled by Employee prior to the commencement of employment of Employee by Employer (all of which are set forth on Exhibit "A" hereto). Additionally, Employee is not required to assign an idea or invention where the invention or idea meets all of the following criteria; namely if the invention or idea: (i) was created or conceived without the use of any of Employer's equipment, supplies, facilities, or trade secret information, and (ii) was developed entirely on Employee's own time, and (iii) does not relate to the business of Employer, and (iv) does not relate to Employer's actual or demonstrably anticipated research or development, and (v) does not result from any work performed by Employee for Employer.

6.2.4 Patents and Copyrights; Attorney-in-Fact. Both before and after termination of this Agreement (and with reasonable compensation paid by Employer to Employee after termination), Employee agrees to assist the Employer to apply for, obtain and enforce patents on, and to apply for, obtain and enforce copyright protection and registration of, the Inventions described in Section 6.2.2 in any and all countries. To that end, Employee shall (at Employer's request) without limitation, testify in any proceeding, and execute any documents and assignments determined to be necessary or convenient for use in applying for, obtaining, registering and enforcing patent or copyright protection involving any of the Inventions. Employee hereby irrevocably appoints Employer, and its duly authorized officers and agents, as Employee's agent and attorney-in-fact, to act for and in behalf of Employee in filing all patent applications, applications for copyright protection and registration, amendments, renewals, and all other appropriate documents in any way related to the Inventions described in Section 6.2.2.

6.3 TRADE SECRETS

6.3.1 Acknowledgment of Proprietary Interest. Employee recognizes the proprietary interest of Employer in any Trade Secrets of Employer. Employee acknowledges and agrees that any and all Trade Secrets of Employer, whether developed by Employee alone or in conjunction with others or otherwise, shall be and are the property of Employer.

6.3.2 Covenant Not to Divulge Trade Secrets. Employee acknowledges and agrees that Employer is entitled to prevent the disclosure of Trade Secrets of Employer. As a portion of the consideration for the employment of Employee and for the compensation being paid to Employee by Employer, Employee agrees at all times during the term of the employment by Employer and thereafter to hold in strictest confidence, and not to use, disclose or allow to be disclosed to any person, firm, or corporation, Trade Secrets of Employer, including Trade Secrets developed by Employee, other than disclosures to persons engaged by Employer to further the business of Employer, and other than use in the pursuit of the business of Employer.

6.3.3 Confidential Information of Others. Employee represents and warrants that if Employee has any confidential information belonging to others, Employee will not use or disclose to Employer any such information or documents. Employee represents that his employment with Employer will not require him to violate any obligation to or confidence with any other party.

6.4 NO ADVERSE USE Employee will not at any time use Employer's Trade Secrets or Inventions in any manner which may directly or indirectly have an adverse effect upon Employer's business, nor will Employee perform any acts which would tend to reduce Employer's proprietary value in Employer's Trade Secrets or Inventions.

6.5 RETURN OF MATERIALS AT TERMINATION In the event of any termination of Employee's employment, Employee will promptly deliver to Employer all materials, property, documents, data, and other information belonging to Employer or pertaining to Trade Secrets or Inventions. Employee shall not take any materials, property, documents or other information, or any reproduction or excerpt thereof, belonging to Employer or containing or pertaining to any Trade Secrets or Inventions.

6.6 REMEDIES UPON BREACH In the event of any breach by Employee of the provision in this Section 6, Employer shall be entitled, if it so elects, to institute and prosecute proceedings in any court of competent jurisdiction, either in law or in equity, to enjoin Employee from violating any of the terms of this Section 6, to enforce the specific performance by Employee of any of the terms of this Section 6, and to obtain damages for any of them, but nothing herein contained shall be construed to prevent such remedy or combination of remedies as Employer may elect to invoke. The failure of Employer to promptly institute legal action upon any breach of this Section 6 shall not constitute a waiver of that or any other breach hereof.

7. COVENANT NOT TO COMPETE Employee agrees that, during Employee's employment, Employee will not directly or indirectly compete with Employer in any way, and that Employee will not act as an officer, director, employee, consultant, shareholder, lender or agent of any other entity which is engaged in any business of the same nature as, or in competition with, the business in which Employer is now engaged, or in which Employer becomes engaged during the term of Employee's employment, or which is involved in science or technology which is similar to Employer's science or technology.

8. GENERAL PROVISIONS

8.1 ATTORNEYS' FEES In the event of any dispute or breach arising with respect to this Agreement, the party prevailing in any negotiations or proceedings for the resolution or enforcement thereof shall be entitled to recover from the losing party reasonable expenses, attorneys' fees and costs incurred therein.

8.2 AMENDMENTS No amendment or modification of the terms or conditions of this Agreement shall be valid unless in writing and signed by both parties hereto. There shall be no implied-in-fact contracts modifying the terms of this Agreement.

8.3 ENTIRE AGREEMENT This Agreement constitutes the entire agreement between the parties with respect to the employment of Employee. This Agreement supersedes all prior agreements, understandings, negotiations and representation with respect to the employment relationship.

8.4 SUCCESSORS AND ASSIGNS The Rights and obligations of Employer under this Agreement shall inure to the benefit of and shall be

binding upon the successors and assigns of Employer. Employee shall not be entitled to assign any of Employee's rights or obligations under this Agreement.

8.5 WAIVER Either party's failure to enforce any provision of this Agreement shall not in any way be construed as a waiver of any such provision, or prevent that party thereafter from enforcing each and every other provision of this Agreement.

8.6 SEVERABLE PROVISIONS The provisions of this Agreement are severable, and if any or more provisions may be determined to be judicially unenforceable, in whole or in part, the remaining provisions shall nevertheless be binding and enforceable.

9. EMPLOYEE'S REPRESENTATIONS Employee represents and warrants that Employee (i) is free to enter into this Agreement and to perform each of the terms and covenants contained herein, (ii) is not restricted or prohibited, contractually or otherwise, from entering into and performing this Agreement, and (iii) will not be in violation or breach of any other agreement by reason of Employee's execution and performance of this Agreement.

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date set forth above.

EMPLOYER:

Aastrom Biosciences, Inc.

By: /s/ R. DOUGLAS ARMSTRONG

R. Douglas Armstrong, Ph.D.
President and CEO

EMPLOYEE:

/s/ ALAN K. SMITH 10/26/95

Alan K. Smith

Address: 6964 Corte Antonio
Pleasanton, CA 94566

Exhibit A

List of Prior Inventions
(Section 6.2.3)

None, other than the following:

See Attached list.

In addition, have two potential applications pending:

(1) Implantation of microcarrier bound packaging cell lines capable of
performing in situ gene therapy.

(2) Identification and use of a specific T-cell subset to facilitate allogeneic
bone marrow transplantation.

PATENTS:

- - - - -

Kabori, Deans, Al-Abdaly, Smith, Guillermo, Angal, "Methods for Identification of Peptides for Release of Selected Cells" (patent pending, submitted 1994)

AL-Abdaly, Guillermo and Smith, "Positive Selection of Human CD34+ Cells Using Cell Specific Antibody-Desthiobiotin Conjugate/Anti-biotin Antibody Coated Paramagnetic Beads" (patent pending, submitted 1993)

Y. A. Chang, A. Gee, A. Smith, W. Lake, "Activation of Hydroxyl Groups of Polymeric Carriers Using 4-Fluorobenzenesulfonyl Chloride", European Patent #91915059.9- (Issued 1992).

A. K. Smith, "Iron supplementation of Calf Serum" U. S. Patent (Issued 1987)

Jarrett, McCain, Vickers and Smith, "Development of a Biocompatible Polymer Using Methyl Acrylamidoglycolate Methyl Ether"

Hardwick, Smith, Lake and Chenoweth, U. S. Patent for "Method and Useful Apparatus for Preparing Pharmaceutical Compositions" (Issued 1991)

PROMISSORY NOTE

\$120,000

Ann Arbor, Michigan
November 18, 1993
11/96

1. As repayment for a cash loan made by Aastrom Biosciences, Inc., a Michigan Corporation ("AASTROM"), to R. Douglas Armstrong ("Maker"), Maker hereby promises to pay to the order of AASTROM, at Ann Arbor, Michigan, or at such other place as AASTROM may direct in writing, the principal amount of \$120,000, together with interest on the outstanding principal balance owing from time to time at the rate of four percent (4%) per annum.

2. Accrued interest shall be payable on each anniversary date of this Note.

3. The principal and all unpaid accrued interest owing on this Note shall mature and be fully due and payable on the third anniversary of the date of this -----
Note. Maker may prepay any or all of the principal and interest owing on this Note at any time without penalty or premium.

4. If any installment of interest owing on this Note is not paid within ten (10) days after Maker receives a written notice of default, then Aastrom may accelerate the maturity date and declare all sums of principal and accrued interest immediately due and payable.

5. If this Note is not paid when due, Maker promises to pay all costs incurred by Aastrom in collecting amounts due on this Note, including reasonable attorney's fees.

6. Payments owing on this note shall be payable (i) in lawful money of the United States of America or, (ii) at the option of Maker, by Maker's surrender of common stock of Aastrom owned by Maker, with said common stock being valued at the public trading price for Aastrom's common stock on the date the stock is surrendered, if Aastrom's common stock is publicly traded; or if Aastrom's common stock is not publicly traded, then the value of the stock shall be the fair market value of the common stock as determined by the Board of Directors of Aastrom, or (iii) at the option of Maker, by Maker's surrender of vested stock options to purchase common stock of Aastrom, with said stock options valued at the "spread" between the then current fair market value of the stock (as determined above) and the option exercise price.

7. This Note has been executed and delivered by Maker in the State of Michigan, and shall be governed by and construed in accordance with the laws of the State of Michigan.

8. Maker acknowledges that Maker has personal liability on this Note, and that this Note is a "full recourse" note.

MAKER:

/s/ R. DOUGLAS ARMSTRONG

R. Douglas Armstrong, Ph.D.

FIRST AMENDMENT TO PROMISSORY NOTE

This Amendment (the "Amendment") to the Promissory Note (the "Note") dated November 18, 1993, payable to Aastrom Biosciences, Inc., a Michigan corporation (the "Company"), executed by R. Douglas Armstrong ("Maker"), is dated as of October 30, 1996.

WHEREAS, Section 3 of the Note provides that all principal and accrued but unpaid interest is due and payable on the third anniversary of the date of the Note (i.e. November 18, 1996).

WHEREAS, the Company desires to amend the Note to provide that all principal and accrued but unpaid interest shall be due and payable on June 30, 1997.

NOW, THEREFORE, the Company hereby amends the Note as follows:

1. Section 3 of the Note is hereby amended to read in its entirety as follows:

"The principal and all unpaid accrued interest owing on this Note shall mature and be fully due and payable on June 30, 1997. Maker may prepay any or all of the principal and interest owing on this Note at any time without penalty or premium."

2. All other provisions of the Note shall remain in full force and effect.

IN WITNESS WHEREOF, the undersigned has caused this Amendment to be executed by its duly authorized officer as of the date set forth above.

AASTROM BIOSCIENCES, INC.

By: /s/ Todd E. Simpson

Todd E. Simpson, Vice President, Finance and
Administration

PROMISSORY NOTE

Ann Arbor, Michigan

\$47,303

Date: 10/20/93

1. As payment for the purchase of common stock in Aastrom Biosciences, Inc., a Michigan corporation ("Aastrom"), the undersigned, Stephen G. Emerson ("Maker"), hereby promises to pay to the order of Aastrom, at Ann Arbor, Michigan, or at such other place as Aastrom may direct in writing, the principal amount of Forty Seven Thousand Three Hundred Three dollars (\$47,303), together with interest on the outstanding principal balance owing from time to time at the rate of six percent (6%) per annum.
2. Accrued interest shall be payable on each anniversary date of this Note.
3. The principal and all unpaid accrued interest owing on this Note shall mature and be fully due and payable on the third anniversary of the date of -----
this Note. Maker may prepay any or all of the principal and interest owing on this Note at any time, without penalty or premium.
4. If any installment of interest owing on this Note is not paid within ten (10) days after Maker receives a written notice of default, then Aastrom may accelerate the maturity date and declare all sums of principal and accrued interest immediately due and payable.
5. If this Note is not paid when due, Maker promises to pay all costs incurred by Aastrom in collecting amounts due on this Note, including reasonable attorney's fees.
6. Payments owing on this Note shall be payable in lawful money of the United States of America. This Note has been executed and delivered by Maker in the State of Michigan, and shall be governed by and construed in accordance with the laws of the State of Michigan.
7. As collateral security for the performance of maker's obligation to pay this Note, Maker hereby grants to Aastrom a security interest in the shares of common stock in Aastrom which Maker is purchasing with this Note, namely 388,031 shares of common stock (the "Shares"). As the secured party having a security interest in the Shares, Aastrom shall have all rights of a secured party pursuant to the Michigan Uniform Commercial Code. To perfect Aastrom's security interest in the Shares, Maker hereby authorizes Aastrom to retain physical possession of the Certificate evidencing the Shares, and Maker hereby delivers to Aastrom a "Stock Assignment Separate from Certificate" signed by Maker, and Aastrom is authorized to utilize said Assignment if, and only if, there is a default on this Note and Aastrom pursues its remedies to foreclosure upon its security interest in the Shares in accordance with applicable law. In the event Maker desires to sell some of the Shares prior to Maker's paying off this Note, Maker must use all of the proceeds of such a sale (up to the outstanding balance owing on this Note) to make payments on this Note; and Maker shall be entitled to a partial release of Aastrom's security interest in the Shares to permit such a sale.
8. Full Recourse Note. Maker acknowledges that Maker has personal liability -----
on this Note, that this Note is a "full recourse" note, and that Maker's liability on this Note is not limited to the value of the Shares.

MAKER:

/s/ STEPHEN G. EMERSON

Stephen G. Emerson

FIRST AMENDMENT TO PROMISSORY NOTE

This Amendment (the "Amendment") to the Promissory Note (the "Note") dated October 20, 1993, payable to Aastrom Biosciences, Inc., a Michigan corporation (the "Company"), executed by Stephen G. Emerson ("Maker"), is dated as of October 30, 1996.

WHEREAS, Section 3 of the Note provides that all principal and accrued but unpaid interest is due and payable on the third anniversary of the date of the Note (i.e. October 20, 1996).

WHEREAS, the Company desires to amend the Note to provide that all principal and accrued but unpaid interest shall be due and payable on June 30, 1997.

NOW, THEREFORE, the Company hereby amends the Note as follows:

1. Section 3 of the Note is hereby amended to read in its entirety as follows:

"The principal and all unpaid accrued interest owing on this Note shall mature and be fully due and payable on June 30, 1997. Maker may prepay any or all of the principal and interest owing on this Note at any time without penalty or premium."

2. All other provisions of the Note shall remain in full force and effect.

IN WITNESS WHEREOF, the undersigned has caused this Amendment to be executed by its duly authorized officer as of the date set forth above.

AASTROM BIOSCIENCES, INC.

By: /s/ R. Douglas Armstrong

R. Douglas Armstrong,
President and CEO

CONSULTING AGREEMENT

This Consulting Agreement (the "Agreement") is entered into as of July 1, 1995, by and between AASTROM BIOSCIENCES, INC., a Michigan corporation ("Company") and STEPHEN G. EMERSON, M.D., Ph.D. ("Consultant"), with respect to the following facts:

RECITALS

- A. Consultant is an employee of the University of Pennsylvania ("Employer").
- B. Company desires to obtain the consulting services of Consultant, and Consultant desires to provide such consulting services, as set forth in this Agreement.

AGREEMENT

NOW, THEREFORE, the parties agree as follows:

- 1. ENGAGEMENT. Company hereby appoints Consultant, and Consultant hereby accepts such appointment, upon the terms and conditions set forth herein.
- 2. ASSIGNMENT. Consultant is engaged as a consultant for the following described assignments:
 - 2.1 Assist Company in the planning, design, direction, supervision and implementation of Company's research programs and clinical trials.
 - 2.2 Assist Company with investor relations, financing and other needed presentations.
 - 2.3 Assist Company in such other matters and areas as may be mutually approved by Consultant and Company.

Consultant shall perform such consulting services at times and places which are mutually convenient to Company and Consultant, with Consultant making himself available for at least approximately eight (8) hours per month at Company's facility.

- 3. RESTRICTIONS. Consultant shall not perform any consulting or other services for any other commercial party which is engaged in research, development, technology, or products which are similar to or competing with that of Company.

4. **COMPENSATION.** As compensation for Consultant performing the consulting services pursuant to this Agreement, Company shall pay to Consultant a consulting fee of \$3,125 (Three Thousand One Hundred Twenty Five Dollars) per calendar quarter, payable quarterly in arrears, as of the last day of the months of September, December, March and June. Consultant shall be entitled to reimbursement for necessary out-of-pocket expenditures incurred in the performance of his consulting services, but subject to Consultant's obtaining the preapproval of Company prior to Consultant incurring said expenditures.
5. **TERM.** The term of this Agreement shall commence on July 1, 1995, and shall continue until June 30, 1996, unless sooner terminated in accordance with the provisions hereof.
6. **TERMINATION.**
 - 6.1 **Termination Without Cause.** Either party may terminate this Agreement without cause upon not less than thirty (30) days' prior written notice delivered to the other. The death of Consultant shall automatically terminate this Agreement.
 - 6.2 **Termination for Cause.** The non-defaulting party shall have the right to terminate this Agreement upon the occurrence of any of the following events, and the expiration of any applicable period of cure: (a) the failure of Company to make any payment within ten (10) days after the date of receipt of a written notice from Consultant stating that a payment is past due; (b) the failure of Consultant to perform the assignment to the reasonable satisfaction of Company; (c) the failure of a party to comply with any other term or condition of this Agreement, and the expiration of ten (10) days after written notice thereof, specifying the nature of such default, without cure; and (d) any attempt by Consultant to assign or otherwise transfer Consultant's rights hereunder.
7. **INDEPENDENT CONTRACTOR.** The parties expressly intend and agree that Consultant is acting as an independent contractor and not as

an employee of Company. Consultant retains sole and absolute discretion, control, and judgment in the manner and means of carrying out the assignment, except as to the policies and procedures set forth herein. Consultant understands and agrees that Consultant shall not be entitled to any of the rights and privileges established for Company's employees (if any), including but not limited to

the following: retirement benefits, medical insurance coverage, life insurance coverage, disability insurance coverage, severance pay benefits, paid vacation and sick pay, overtime pay, or any of them. Consultant understands and agrees that Company will not pay or withhold from the compensation paid to Consultant pursuant to this Agreement any sums customarily paid or withheld for or on behalf of employees for income tax, unemployment insurance, social security, workers' compensation or any other withholding tax, insurance, or payment pursuant to any law or governmental requirement, and all such payments as may be required by law are the sole responsibility of Consultant. Consultant agrees to hold Company harmless against and indemnify Company for any of such payments of liabilities for which Company may become liable with respect to such matters. This Agreement shall not be construed as a partnership agreement. Company shall have no responsibility for any of Consultant's debts, liabilities or other obligations or for the intentional, reckless or negligent acts or omissions of Consultant or Consultant's employees or agents.

8. CONFIDENTIALITY.

8.1 Acknowledgment of Proprietary Interest. Consultant recognizes the proprietary interest of Company in any Trade Secrets of Company. As used herein, the term "Trade Secrets" includes all of Company's confidential or proprietary information, including without limitation any confidential information of Company encompassed in any reports, investigations, experiments, research or developmental work, inventions, technology, experimental work, work in progress, drawings, designs, plans, proposals, codes, marketing and sales programs, financial projections, cost summaries, pricing formula, and all concepts or ideas, materials or information related to the business, products or sales of the Company or the Company's customers which has not previously been released to the public at large by duly authorized representatives of the Company, whether or not such information would be enforceable as a trade secret or the copying of which would be enjoined or restrained by a court as constituting unfair competition. Consultant acknowledges and agrees that any and all Trade Secrets of Company, learned by Consultant during the course of the engagement by Company or otherwise, whether developed by Consultant alone or in conjunction with others or otherwise, shall be and is the property of Company.

- 8.2 Ownership of Work. All inventions, patents, discoveries, reports and ideas arising from Consultant's services to Company hereunder shall be the sole property of Company and shall be Company's Trade Secrets. Consultant agrees to assign and hereby assigns to Company, its successors or assigns, all Consultant's right, title and interest in and to said Trade Secrets, inventions or discoveries and any patent application or letters patent thereon. Consultant agrees to reasonably cooperate with Company, at no expense to Consultant, to effect such ownership rights. Consultant hereby irrevocably appoints Company and its officers as his agent and attorney-in-fact to execute and file any patent applications and related documents pertaining to said Trade Secrets if he is deemed to be an "inventor" of an invention which is part of Company's Trade Secrets.
- 8.3 Publication. Any publications and reports by Consultant concerning Consultant's scientific work may be released in accordance with Employer's customary practices, policies and agreements. Provided, however, Consultant shall not publish any manuscript or other document, solely or in co-authorship with others, pertaining to Company's Trade Secrets or Company's other information attributable to any project undertaken by Company, without Company's prior written consent.
- 8.4 Covenant Not to Divulge Trade Secrets. Consultant acknowledges and agrees that Company is entitled to prevent the disclosure of Trade Secrets of Company. As a portion of the consideration for the appointment of Consultant and for the compensation being paid to Consultant by company, Consultant agrees at all times during the term of the engagement with Company and thereafter to hold in strictest confidence, and not to disclose or allow to be disclosed to any person, firm or corporation, other than to persons engaged by Company to further the business of Company, and not to use except in the pursuit of the business of Company, Trade Secrets of Company, without the prior written consent of Company, including Trade Secrets developed by Consultant.

- 8.5 Return of Materials at Termination. In the event of any termination of Consultant's appointment, with or without cause, Consultant will promptly deliver to Company all materials, property, documents or other information, or any reproduction or excerpt thereof, belonging to Company or containing or pertaining to any Trade Secrets.
- 8.6 Remedies Upon Breach. In the event of any breach of this Agreement by Consultant, Company shall be entitled, if it so elects, to institute and prosecute proceedings in any court of competent jurisdiction, either in law or in equity, to enjoin Consultant from violating any of the terms of this Agreement, to enforce the specific performance by Consultant of any of the terms of this Agreement, and to obtain damages, or any of them, but nothing herein contained shall be construed to prevent such remedy or combination of remedies as Company may elect to invoke. The failure of Company to promptly institute legal action upon any breach of this Agreement shall not constitute a waiver of that or any other breach hereof.

9. MISCELLANEOUS.

- 9.1 Governing Law. This Agreement shall be interpreted, construed, governed and enforced according to the laws of the State of Michigan.
- 9.2 Attorneys' Fees. In the event of any litigation concerning any controversy, claim or dispute between the parties hereto, arising out of or relating to this Agreement or the breach hereof, or the interpretation hereof, the prevailing party shall be entitled to recover from the losing party reasonable expenses, attorneys' fees, and costs incurred therein or in the enforcement or collection of any judgment or award rendered therein.
- 9.3 Amendments. No amendment or modification of the terms or conditions of this Agreement shall be valid unless in writing and signed by the parties hereto.
- 9.4 Successors and Assigns. The rights and obligations of Company under this Agreement shall inure to the benefit of and shall be binding upon the successors and assigns of Company. Consultant shall not be

entitled to assign any of Consultant's rights or obligations under this Agreement.

9.5 Entire Agreement. This Agreement constitutes the entire agreement between the parties with respect to the appointment of Consultant.

9.6 Employer Policies. Consultant represents, warrants and covenants that Consultant's performance of the obligations under this Agreement does not and will not violate the terms of any of Consultant's agreements with Employer or any other party.

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date set forth above.

COMPANY:

CONSULTANT:

AASTROM BIOSCIENCES, INC.

By: /s/ R. DOUGLAS ARMSTRONG

/s/ STEPHEN G. EMERSON

R. Douglas Armstrong, Ph.D.
President and CEO

Stephen G. Emerson, M.D., Ph.D.

CLINICAL TRIAL AGREEMENT

This Clinical Trial Agreement ("Agreement") is entered into as of the 28 day of August, 1996 (the "Effective Date"), by and among Aastrom Biosciences, Inc. ("Aastrom"), located at 24 Frank Lloyd Wright Dr., Lobby L, Ann Arbor, MI 48105, and Loyola University Medical Center Cancer Center (the "Institution"), located at 2160 South First Avenue, Maywood, IL 60153. Definitions shall have the meaning as set forth in Exhibit A.

RECITALS

WHEREAS, Aastrom is the developer, manufacturer and/or licensee of medical devices and materials, such as a Cell Production System ("CPS") device and related materials and device, which have potential medical application for use in subjects care and research;

WHEREAS, Aastrom desires to conduct a human clinical trial ("Study") of the CPS in subjects in accordance with a protocol entitled "A Pilot Trial of Autologous Transplantation For Patients With Advanced Breast Cancer Using Marrow Cells Expanded Ex Vivo" ("Protocol") which is incorporated herein by reference as Exhibit B attached hereto;

WHEREAS, the Institution has research, clinical and medical facilities, technical capabilities and expertise in order to conduct the Study in accordance with the Protocol;

WHEREAS, the Study contemplated by this Agreement is of mutual interest and benefit to the Institution and to Aastrom such that the parties hereto desire to have the Institution conduct the Study under the qualified direction of Patrick J. Stiff, M.D. (the "Principal Investigator"); and

WHEREAS, Aastrom and the Institution agree to conduct the Study in accordance with the terms and conditions hereinafter set forth.

AGREEMENT

I. CLINICAL TRIAL DESCRIPTION

The Institution agrees to undertake and complete the Study described in the Protocol (Exhibit B) in compliance with all applicable laws, rules and regulations relating to the Study, including without limitation, all laws, rules and regulations concerning or promulgated by the Food and Drug Administration ("FDA").

Aastrom agrees to provide the Institution the laboratory and clinical equipment listed in the Schedule of Laboratory and Clinical Equipment on Exhibit C which are reasonably necessary for the Institution to conduct the Study. Aastrom shall retain title to all such equipment which shall promptly be returned to Aastrom upon request by Aastrom.

II. FUNDING

Aastrom shall provide payments to the Institution in accordance with the terms contained in the Clinical Trial Budget (Exhibit D) and the Schedule of Clinical Trial Milestone Payments (Exhibit D) incorporated herein.

III. CONDUCT OF STUDY

A. Facilities -----

The Study shall be conducted only at the following locations: Loyola University Medical Center Cancer Center, 2160 South First Avenue, Maywood, IL 60153. The CPS and other Study materials may not be transferred to any other location or to any third party without the prior written consent of Aastrom.

B. Investigator -----

The Institution agrees that the Study will be conducted under the direction of the Principal Investigator in accordance with the Protocol and the Investigator Agreement (see Section 13.0 of the Clinical Protocol) and incorporated herein by reference. The Principal Investigator may, subject to the prior written consent of Aastrom, designate a clinical coordinator and one or more subinvestigators to assist in conducting the Study. The Institution acknowledges that the Principal Investigator and subinvestigators have each executed an Investigator Agreement, copies of which are included in Exhibit E. In the event that additional subinvestigators are added to the Study, such subinvestigators must execute and deliver an Investigator Agreement which shall be deemed incorporated by reference into this Agreement. In the event the Principal Investigator can no longer function in such capacity, then Aastrom and the Institution shall attempt to agree on a replacement. If a mutually acceptable replacement cannot be agreed upon, this Agreement and the Study at the Institution shall terminate. The Institution agrees that it will use its best efforts to recruit qualified subjects for enrollment in the Study consistent with the guidelines contained in the Protocol and the best interest of the subject; however, no subjects shall be enrolled in the Study if they are currently enrolled in another investigational study without the prior written consent of Aastrom.

C. Compliance with Protocol -----

Any changes to the Protocol may only be made with the prior written agreement of Aastrom; provided that during the Study, if the Principal Investigator feels that it is necessary to deviate from the Protocol in order to protect the life or physical well-being of a Study subject before written approval can be obtained, he/she may do so in accordance with the procedures detailed in the Protocol.

D. Institutional Review Board Approval and Informed Consent -----

The Institution will obtain: (i) the approval of the governing Institutional Review Board ("IRB") prior to initiating the Study and thereafter as required by applicable laws, rules and regulations; and (ii) prior written informed consent of all subjects and/or their legal guardians in a form that is substantially the same as provided in the Protocol and satisfactory to both the governing IRB and Aastrom and in compliance with applicable laws, rules and regulations.

E. Adverse Events -----

The Institution shall immediately notify Aastrom (Thomas E. Muller, Ph.D., Vice President Regulatory Affairs at 313/930-5555 and/or by fax at 313/930-5520) of any unanticipated adverse effect, whether ascribed to the investigational device or not, in accordance with the instructions provided in the Protocol.

IV. STUDY MONITORING AND ACCESS TO FACILITIES

Aastrom's designated representatives and/or authorized representatives of regulatory agencies may, at all reasonable times, visit the Institution in order to: (i) determine the adequacy of the facilities, (ii) validate case reports against original data in the subject medical records and the files of the Principal Investigator, and (iii) monitor the conduct of the Study to determine whether the Study is being conducted in compliance with the Protocol and all applicable laws, rules and regulations. The Institution agrees to obtain any required subject release(s) to allow Aastrom's designated representatives, and/or authorized representatives of regulatory agencies, to conduct such review prior to enrolling each subject in the Study.

V. REPORTS

The Institution agrees to have the Principal Investigator submit reports to Aastrom and the reviewing IRB in accordance with the Protocol and all applicable laws, rule and regulations.

VI. PROPRIETARY RIGHTS

A. Data and Materials

The Institution understands and agrees that the underlying rights to the CPS and other intellectual property and materials which are the subject of the Protocol belong to Aastrom. The parties agree that the Institution shall retain control over the CPS and Study materials, and further agree not to allow access to, disclose the existence or nature of, or transfer the CPS or Study materials to third parties without advance written approval of Aastrom. Aastrom reserves the right to distribute the CPS and Study materials to others and to use them for its own purposes. Title to the CPS and Study materials shall remain with Aastrom. Further, the Institution agrees that data and materials derived as a direct result of the Study described in the Protocol (hereinafter referred to as "Clinical Trial Information") whether generated by the Institution, the Principal Investigator, and/or their agents or employees, either solely or jointly with others, is the property of Aastrom; provided that the Institution and the Principal Investigator may utilize the Clinical Trial Information in furtherance of academic publications authorized by this Agreement and for subject care purposes.

B. Patent Ownership and Related Matters

The Institution agrees that the Study results and any inventions or discoveries by the Institution, the Principal Investigator or their agents or employees during the Study that are modifications, improvements or new uses applicable to the CPS or that are a direct result of the performance of the Study in accordance with the detailed testing Protocol provided by Aastrom to Institution and which are dependent on, or relate to, the Study, the claims of Aastrom's patentable inventions, the use of the cells processed through the CPS or Aastrom's Confidential Information shall be the property of Aastrom. Any invention arising out of the work performed under this Study solely by the Institution and not covered in the previous sentence shall be the exclusive property of the Institution (the "Institution Invention") and shall not be considered a part of Aastrom's Confidential Information. The Institution shall promptly disclose each such Institution Invention and the terms under which the Institution would be prepared to license it. Aastrom shall have a right of first refusal to exclusively develop, license and commercialize such Institution Invention. Aastrom shall have sixty (60) days after receipt of such disclosure to exercise its right of first refusal, and if so exercised, the parties shall thereafter negotiate a mutually acceptable licensing agreement in good faith. If the Institution at any time

offers such Institution Invention on terms different than those disclosed to Aastrom, the Institution shall offer such Institution Invention to Aastrom on such different terms in accordance with the first right refusal herein. The Institution and Principal Investigator shall not obtain, or attempt to obtain, patent coverage on the CPS or its use without the express written consent of Aastrom. The Institution and the Principal Investigator shall assist Aastrom in prosecuting any Aastrom patent applications and shall execute and deliver any and all instruments necessary to make, file and prosecute all such applications, divisions, continuations, continuations-in-part or reissues thereof.

VII. WARRANTIES AND REPRESENTATIONS

A. No Warranties

It is understood that the CPS is experimental in nature, has not been approved for commercial distribution and is provided hereunder for investigational purposes only. NEITHER THE INSTITUTION NOR AASTROM MAKES ANY REPRESENTATIONS OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING ANY REPRESENTATION WITH RESPECT TO SAFETY, EFFICACY, MERCHANTABILITY, FITNESS FOR ANY PURPOSE OR NON-INFRINGEMENT OF ANY INTELLECTUAL PROPERTY RIGHTS, WITH RESPECT TO THE PRODUCT OR INFORMATION PROVIDED TO THE OTHER HEREUNDER.

B. Representations of the Parties

Each party hereto represents that it has right to enter into and perform its respective obligations under this Agreement.

C. Representations by the Institution and the Principal Investigator

The Institution represents that: (i) it has adequate facilities and staff to conduct the Study in accordance with the Protocol; (ii) the governing IRB is qualified to review and approve the Study; and (iii) the Principal Investigator is qualified by education and training to conduct the Study and has not been disqualified, or otherwise limited, as a clinical investigator by the FDA or any other regulatory or administrative body. The Institution represents that the Principal Investigator and all other investigators and personnel that may perform services hereunder are its employees and shall abide by the terms and conditions of this Agreement as if each were a party hereto.

VIII. LIMITATIONS OF LIABILITY

In no event shall any party be liable to the other party hereto for any incidental, special or consequential damages.

IX. INDEMNIFICATION

A. Indemnification of Aastrom

Aastrom agrees to indemnify, defend and hold harmless the Institution, the Loyola University System, and their Regents, officers, agents and employees from and against any and all claims, suits, and liabilities (collectively "Liabilities") arising out of or resulting from the activities to be carried out pursuant to the obligations of this

Agreement, including but not limited to the use by Aastrom of the results of the Study; provided that such Liabilities do not arise from:

- i. a failure to adhere to the Protocol or written instructions relative to use of the CPS of other materials utilized in the Study;
- ii. a failure to comply with any applicable law, rule or regulation relating to the Study, including without limitation, all FDA regulations or other governmental requirements; or
- iii. the negligence or willful misconduct by the regents, officers, agents or employees of the Institution or the Loyola University System.

B. Indemnification by the Institution

The Institution agrees, to the extent allowed by the Constitution and the laws of the State of Illinois, to indemnify, defend and hold harmless Aastrom and its directors, officers, agents and employees from and against any and all Liabilities they may suffer in connection with the Study which arise out of the negligent acts or omissions of the Institution, its employees or agents pertaining to the activities to be carried out pursuant to the obligations of this Agreement; provided, however, that Institution shall not hold Aastrom harmless from claims arising out of the negligence or willful malfeasance of Aastrom, its directors, officers, agents or employees, or any person or entity not subject to Institution supervision or control.

C. Notification

The Institution and Aastrom each agree to notify the other in writing as soon as they become aware of a claim or action and to, subject to the statutory duties of the Illinois Attorney General, cooperate with the management and defense of such claim or action. The indemnifying party agrees, at its own expense, subject to the statutory duties of the Illinois Attorney General, to provide attorneys of its own selection to defend against any actions brought or filed against the indemnified party with respect to the subject of indemnity contained herein. The indemnifying party shall, subject to the statutory duties of the Illinois Attorney General, control the defense of any action; however the indemnified party may, at its own expense, participate by providing attorneys of its own selection. No indemnified party shall compromise or settle any claim of action without the prior written approval of the indemnifying party.

X. RESTRICTIONS ON USE; COMPLIANCE WITH LAWS

The Institution and the Principal Investigator agree that the CPS will be used for clinical research purposes only in connection with the Study by the Principal Investigator and his/her subinvestigators at the facility(ies) described in Section III.A. under suitable containment conditions. Neither the Institution nor the Principal Investigator shall use the CPS for any commercial purposes, including screening, production or sale. The CPS will not be used in the treatment or diagnosis of human or animals except for the purpose of conducting the Study as described in the Protocol. The Institution agrees to comply with all laws, rules and regulations applicable to the Study and the handling, use and disposal of any Study materials. The CPS is to be used with caution and prudence since all of its characteristics are not known.

XI. CONFIDENTIALITY

A. Treatment of Confidential Information

The Institution agrees that it will not disclose or use Confidential Information for any purpose other than the purpose of conducting the Study, obtaining any required review of the Protocol or its conduct, or ensuring proper medical treatment of any subject or subjects. The Institution agrees to limit distribution of Aastrom's Confidential Information to Institution personnel on a need-to-know basis. The Institution agrees to ensure that its personnel abide by the confidentiality obligations as set forth herein in accordance with Section VII.C. The obligations set forth in this Section XI.A. shall survive for a period of five (5) years following the termination or expiration of this Agreement.

The term "Confidential Information" shall mean any and all oral, written or tangible proprietary or confidential ideas, inventions, information, data, plans, materials and know-how or the like owned, controlled or developed by Aastrom or developed under the Agreement and disclosed to Institution. Aastrom shall attempt to identify the confidential status of Confidential Information disclosed hereunder, but the failure to so mark or identify shall not destroy the confidential nature of such Confidential Information. Without limiting the generality of the foregoing, Confidential Information shall include, without limitation, all clinical trial plans, protocols, information, data analyses, proprietary equipment, and materials related to the Confidential Information. Confidential Information shall not include any information which the Institution can demonstrate:

- i. Was known to the Institution prior to receipt from Aastrom, provided that the Institution promptly notifies Aastrom in writing of the same promptly after disclosure by Aastrom;
- ii. Is or becomes part of the public domain through no act by or on behalf of the Institution;
- iii. Was lawfully received by the Institution or the Principal Investigator from a third party who had a legal right to disclose the same; or
- iv. Is required by law or regulation to be disclosed.

In the event that Confidential Information is required to be disclosed pursuant to subsection iv., the Institution will notify Aastrom to allow Aastrom to assert whatever exclusions or exemptions may be available to it under such law or regulation.

B. Publicity

No publicity, new releases, or other public announcement, written or oral, relating to the Agreement, to any amendment hereto or to performance hereunder or to the existence of an arrangement between the parties, shall be originated by either party without the prior written approval, such approval not to be unreasonably withheld, of the other party except as shall be required by law.

C. Use of Name

No Party shall use or publicly disclose the name of another party hereto without the prior written consent, such consent not to be unreasonably withheld, of such other party except that the name of a party may be disclosed to regulatory bodies such as the FDA, Securities and Exchange Commission or as required by law.

XII. PUBLICATION RIGHTS

At least thirty (30) days prior to submission for publication, the Institution agrees to provide Aastrom a final draft of any manuscript describing the results obtained by the Institution from the Study. Aastrom shall be permitted to advise as to the implications of such manuscripts upon patentability of any inventions or the potential effects on commercialization. The Institution shall, upon Aastrom's request, delete any of Aastrom's Confidential Information and shall consider all reasonable editorial suggestions based on sound scientific and clinical judgment, Aastrom acknowledges that Institution shall have the final authority to determine the scope and content of any publication, provided that such authority shall be exercised with reasonable regard for the commercial interests of Aastrom. Subject to Aastrom's right to delete such Confidential Information and to propose mutually agreeable modification of such manuscripts, the Institution shall have the right to submit the manuscript for publication. However, if Aastrom determines that any invention disclosed therein is patentable and that a patent application should be filed on such invention, Aastrom shall notify the Institution in writing and the Institution shall postpone publication for a period not to exceed sixty (60) days from said notice (unless otherwise mutually agreed in writing) to provide time for patent applications to be filed.

XIII. TERM AND TERMINATION

A. Term

Except as otherwise provided in this section, this Agreement shall commence on the Effective Date hereof and continue for the period necessary to satisfy the requirements of the Protocol.

B. Termination

Aastrom and the Institution shall have the right to terminate this Agreement at any time without cause upon thirty (30) days prior written notice. Any party may terminate the Study at any time if, in its opinion, it is in the best interest of the Study subjects.

C. Termination Obligations

Any termination of this Agreement shall not relieve any party hereto of any obligation or liability accrued hereunder prior to such termination, or rescind or give rise to any right to rescind anything done hereunder prior to the time such termination becomes effective; nor shall such termination relieve any party from any obligation which, by its nature, survives termination including the obligations set forth in Articles IV through IX and X.D.

The parties further agree that all Study data and used and unused Study equipment, materials and supplies, including the CPS, provided to the Institution by Aastrom for the purpose of this Study will be returned to Aastrom promptly upon request by Aastrom.

XIV. MISCELLANEOUS

A. Independent Contractor

The Institution recognizes and agrees that it is operating as an independent contractor and not as an agent of Aastrom. The Agreement shall not constitute a partnership or joint venture, and no party may be bound by the other to any contract, or make any representations or warranties, express or implied, on behalf of another party, or otherwise create any liability against another party in any way for any purpose.

B. Assignment

The rights and obligations of the parties under this Agreement shall bind and inure to the benefit of the successors, assigns and transferees of the parties; provided, however, this Agreement shall not be assignable by either party without the prior written consent of the other party.

C. Governing Law

This Agreement shall be construed and interpreted in accordance with and governed by the laws of the State of Illinois.

D. Alternative Dispute Resolution

Any controversy or claim arising out of or relating to this Agreement or the breach thereof, including, without limitation, disputes relating to patent validity or infringement arising under this Agreement, shall be settled through use of an appropriate method of Alternative Dispute Resolution, including, without limitations, by arbitration in accordance with the rules of the American Arbitration Association, and judgment upon an award rendered may be entered in any court having jurisdiction thereof. Notwithstanding the foregoing, the parties shall be entitled to petition any court of competent jurisdiction in the event of any alleged breach of Article XI.

E. Entire Agreement: Modification

This Agreement contains the entire agreement and understanding between the parties and supersedes all prior agreements and understandings between them relating to the subject matter hereof.

F. Headings

The headings of this Agreement are to facilitate reference only, do not form a party of this Agreement and shall not effect the interpretation thereof.

G. Severability

If any provision of this Agreement or portion of this Agreement is construed or declared to be invalid, such provision or portion shall be deemed reformed to become valid in a manner consistent with the parties' intentions under this Agreement, and the validity of the remaining portions and provisions of this Agreement shall not be affected thereby and shall remain in full force and effect.

H. No Waiver

No waiver of a breach by a party of any provision of this Agreement shall be construed to be a waiver of any other breach of the same of any other provision.

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IN WITNESS WHEREOF, the parties hereto have caused this Agreement to be duly executed as of the date and year first above written.

INSTITUTION:	AASTROM:
LOYOLA UNIVERSITY MEDICAL CENTER	AASTROM BIOSCIENCES, INC.

By: /s/ -----	By: /s/ R. DOUGLAS ARMSTRONG, PH.D. ----- Name: R. Douglas Armstrong, Ph.D. Title: President and Chief Executive Officer
------------------	-----------------------------------------------------------------------------------------------------------------------------------

Date: 9/19/96 -----	Date: 9/3/96 -----
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I have read this agreement and
understand my obligations hereunder:

By: /s/ PATRICK J. STIFF, M.D.

Patrick J. Stiff, M.D.
Principal Investigator
Associate Professor of Medicine
Director, Bone Marrow Transplantation Program

EXHIBIT A

DEFINITIONS

1. Aastrom. Aastrom shall have the meaning as set forth in the first

paragraph of this Agreement.
2. Clinical Trial Information. Clinical Trial Information shall have the

meaning as set forth in Section VI.A. of this Agreement.
3. Confidential Information. Confidential Information shall have the meaning

as set forth in Section XI.A.
4. CPS. The CPS means the Cell Production System developed by Aastrom for the

ex vivo growth and expansion of human stem and hematopoietic progenitor
cells. The CPS consists of: (a) a single use Cell Cassette in which the
growth and expansion of cells takes place; (b) dedicated laboratory
instruments to facilitate the cell culture process and associated cell
inoculation and harvest procedures; (c) single use growth medium required
for the cell culture to which specified growth factors and glutamine are
added; and (d) single use harvest reagents which facilitate the removal of
the expanded cells from the Cell Cassette.
5. Effective Date. The Effective Date shall have the meaning as set forth

in the first paragraph of this Agreement.
6. FDA. FDA shall have the meaning as set forth in Article 1 of this

Agreement.
7. Institution. Institution shall have the meaning set forth in the first

paragraph of this Agreement.
8. Institution Invention. Institution Invention shall have the meaning set

forth in paragraph VI.B. of this Agreement.
9. Principal Investigator. Principal Investigator shall have the meaning

set forth in the Recitals on page 1 of this Agreement.
10. Protocol. Protocol shall have the meaning as set forth in the Recitals on

page 1 of this Agreement.
11. Study. Study shall have the meaning as set forth in the Recitals on

Page 1 of this Agreement.

EXHIBIT B

LOYOLA UNIVERSITY MEDICAL CENTER

BONE MARROW TRANSPLANT PROGRAM

A PILOT TRIAL OF AUTOLOGOUS TRANSPLANTATION FOR PATIENTS WITH ADVANCED
BREAST CANCER USING MARROW CELLS EXPANDED EX VIVO.

Principal Investigator

Patrick J. Stiff, M.D.
Director, BMT Program
Loyola University Medical Center
2160 South First Avenue
Maywood, Illinois 60153
Ph: 708-327-3148
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Co-Investigators

BMT Ex Vivo Expansion Team: Robert Bayer, M.D., David Peace, M.D., Deepak
Malhotra, M.D., Bahao Chen, M.D., David Oldenberg

June 21, 1996
REVISED AUGUST 5, 1996

1.0 OBJECTIVES

- 1.1 To assess the safety of the mixture of early-, mid-, and late-stage bone marrow-derived mononuclear cells produced in the Aastrom Cell Production System (CPS) when infused into patients with breast cancer.
- 1.2 To determine the biological effect in terms of hematopoietic recovery after infusion of ex vivo-produced hematopoietic cells following high dose chemotherapy as treatment of patients with breast cancer.
- 1.3 To record the clinical disease related outcome in these patients with advanced breast cancer- clinical tumor response, duration of responses, and disease free duration post-high dose chemotherapy.

2.0 BACKGROUND

- 2.1 Ex Vivo Expansion: Current Status June 1996
Autologous bone marrow transplantation has been increasingly employed as supportive therapy for subjects undergoing high dose chemotherapy or chemoradiotherapy for malignant diseases, including lymphoma, leukemia, and breast cancer. Breast cancer is now the most frequent indication for autologous bone marrow or blood progenitor cell transplantation.

Despite the use of cytokines such as granulocyte-macrophage colony-stimulating factor (GM-CSF) and granulocyte colony-stimulating factor (G-CSF) following bone marrow reinfusion, there is an obligate period of profound pancytopenia lasting 1-3 weeks, and delayed engraftment can occur, resulting in morbidity or mortality.

The safety, comfort, and cost of stem- and progenitor cell harvest are also concerns. The standard techniques employed to harvest bone marrow involves obtaining 500-1500 mL of bone marrow from the marrow donor, usually under general anesthesia. In addition to the discomfort caused by the hundreds of marrow aspirates performed, donors are subject to the risks of general anesthesia. Finally, the bone marrow harvest procedure is expensive. Alternatively, stem- and progenitor cells can be collected from peripheral blood by apheresis, but this requires chemotherapy and/or growth factors for mobilization and multiple collections are generally necessary, which are costly.

Recently, novel technology has been developed to produce stem- and progenitor cell populations in vitro, commonly referred to as ex vivo expansion. Hematopoietic cell expansions achieved with this technology are based upon the principles of continuous perfusion culture, a bioengineered metabolic environment, augmented by hematopoietic growth factors. Through this technology, a small bone marrow or peripheral blood mononuclear cell population can be perfused ex vivo so that total cell numbers, colony forming units (CFU-S) and long term culture initiating cells (LTC-ICs) increase up to 20 fold (1-17). In a preliminary study, Brugger et al recently reported that

expanded cells alone can reconstitute hematopoiesis after high dose chemotherapy (18).

Important differences exist among approaches, systems and devices used for ex vivo expansion. This study utilizes the Aastrom CPS, which includes a cell culture device and a biological environment designed to allow the establishment of a stromal adherent layer, using constant perfusion with medium, and relatively low concentrations of hematopoietic growth factors. Preliminary studies at MD Anderson Cancer Center (DM94-127), using transplantation of ex vivo-produced cells prepared with this system, in combination with a standard autologous marrow transplant, indicate that ex vivo expansion can be performed reliably and reproducibly, and that no toxicity occurs with intravenous infusion (19). Ten patients, age 18-60 years with breast carcinoma, were entered into a study transplanting bone marrow plus ex vivo-produced cells. Bone marrow was harvested, collecting greater than 2×10^8 /nucleated cells/kg and greater than 0.5×10^6 /CD34+ cells/kg. Twelve days prior to the planned bone marrow transplant, 2.25×10^8 /mononuclear cells were inoculated into a cell culture device, part of the CPS, and continuously perfused with medium containing PIXY321 (5 ng/ml), Epo (0.1 U/ml) and hydrocortisone (5×10^{-6} M). The expansion reproducibly increased total nucleated cells, CFU-GM, and long term culture initiating cells (LTC-IC). Patients received Cyclophosphamide 2.0 g/m²/d: Thiopeta 240 mg/mi/d: BCNU 150 Mg/M²/d. Days -7, -6, -5, with reinfusion of the cryopreserved bone marrow on Day 0 plus the ex vivo-produced cells four hours later. No toxicity was observed from the expanded cell infusion. Nadir WBC was less than 0.1/ul. All patients engrafted within narrow time ranges, with median recovery of WBC greater than 200/ul on Day 8 (range 7-8) granulocytes greater than 500/ul on Day 11 (range 10-13) and platelets greater than 25,000/ul on Day 16 (range 13-21) and greater than 50,000 on Day 20 (range 18-27). A median of 4 (range 1-9) platelet and 4 (range 2-9) RBC transfusions were administered. No grade greater than 2 toxicity occurred from the chemotherapy or bone marrow infusions. Four patients had infections unrelated to the infusion of the cells produced in the CPS. These data compare favorably with 29 historical controls receiving the same chemotherapy and autoBMT without cell expansion, in which granulocytes recovered to greater than 500 on Day 11 (range 7-29) and platelets to greater than 25,000 and greater than 50,000 on Days 24 (range 9-78) and 28 (range 9-147), respectively.

A potential advantage of collecting a relatively small marrow inoculum is that the number of contaminating malignant cells is reduced: additionally, growth of breast cancer cells is not stimulated under these expansion conditions (Brugger et al).

Application of this technology to autologous bone marrow and peripheral stem cells transplant offers a potentially attractive means to increase the efficacy and safety of autologous transplantation, while reducing its complexity and cost. In particular, this technology could eliminate the need for operative bone marrow

harvests, produce more rapid recovery of hematopoiesis post-transplant, reduce the length of post-transplant hospitalization, and could increase the purity of the stem- and progenitor cells transfused. In addition, the inclusion of cytokine-primed progenitors could result in accelerated hematopoietic recoveries.

2.2 Previous Pre-Clinical Research

During hematopoietic expansion culture, total cell numbers increase 8 to 11-fold over 12 days. This includes nonadherent, loosely adherent, and tightly adherent cells. Over 80% of the nucleated cells are viable, as shown by exclusion of propidium iodine stain (4) or Trypan blue dye. These cells have the morphological distribution of normal bone marrow cells, including blast cells and maturing granulocyte precursors, maturing erythroid cells, monocytes and macrophages.

These expanded cells also show typical immunophenotype characteristics of normal granulocyte, erythroid, monocyte/macrophage megakaryocytic, and blast cells (5). Cell surface antigens identified using this technique include CD3, CD11b, CD15, CD20, CD33, CD71, and glycophorin A. While there are minor variations in staining patterns from sample to sample, the expanded cells are typically less than 3% CD3-.20-50% CD11b-, less than 1% CD19-, and 40-70% CD71-. The frequency of mature T and B lymphocytes in the expanded cell population is significantly reduced.

As shown in the experiments summarized in the Table below, it was shown by Aastrom that varying the standard growth factor combination (IL-3-GM-CSF or PIXY321, Epo, SCF and flt3L) had a direct effect on the productivity of cells in the CPS, but the relative cell mixture composition remained substantially similar. These data were obtained in 36-well plate studies. This finding provided the original justification for selecting the growth factor combination (Epo - PIXY321 - flt3L) for this study to yield the desired relative composition and mixture of early-, mid- and late-stage cells produced in the pre-clinical experiments.

Product/cm/2/

Growth Factors	CellsX10 ⁶ /	CFU-GM	LTC-IC	n
None	0.58	404	yes/3/	7
Epo, GM-CSF, IL-3, SCF	2.35	4,790	48	23
Epo, GM-CSF, IL-3	1.13	21,060	yes/3/	3
Epo, PIXY, SCF	1.72	69,960	yes/3/	4
Epo, PIXY	1.31	3,140	94	3
Epo, PXY, fit3L	1.57	10,580	11	14

/2/LTC-IC were not evaluated, but in these conditions, 24 week CFU-GM producing cultures were obtained, representing an LTC-IC proxy.

Aastrom has projected, based on this pre-clinical research, that clinical-size CPSS are expected to yield a mean of 3.0×10^9 cells, 17.7×10^6 CFU-GM and 6.4×10^5 LTC-IC per patient in this proposed clinical feasibility trial, and set the expected minimum per-patient cell yield from the CPS at 1.6×10^9 total nucleated cells and 7.0×10^{10} CFU-GM. In an average 70 kg patient, this translates to a dose of 2×10^5 CFU-GM/kg. The clinically standard ABMT engraving dose is reported to be 1×10^5 CFU-GM/kg. Therefore, using the cell dose and the CFU-GM content in the cells produced in the CPS as a key progenitor marker, along with the reliable presence of early stage cells (e.g., LTC-IC, CD34-lin-), there is an expectation that the CPS-produced cells should provide a minimum full engraving dose for these subjects, with a greater number expected for most patients. Should the minimum cell number, 1.6×10^9 , not be attained, the cryopreserved back-up cells will be reconstituted and administered to a subject on Day 0.

It is anticipated that infusion of ex vivo-produced progenitors generated with the CPS will enhance engraftment and shorten time to recovery of granulocytes and platelets and, in so doing, reduce the incidence of infections, febrile episodes and the need for blood- and platelet transfusions.

Amended August 5, 1996: In several in vitro studies using tumor cells that are easy to detect in small quantities (neuroblastoma and B-cell CLL), the expansion process appeared to passively purge tumor cells of slightly less than one log to greater than three logs. When combined with the smaller inoculum of marrow needed to initiate the bioreactors as compared to a normal marrow harvest, the depletions appear to be as high as four to five logs. It is anticipated that since the marrows must be histologically normal for patients to enter this trial, i.e., undetectable amount of breast cancer cells, that expansion of tumor cells will not be important clinically. This is especially true since there is additional in vitro data to show that the cytokines used do not stimulate the growth of tumor cells when used whether in vitro or in vivo when used in closely monitored clinical trials.

The washing of the expanded cell products eliminates the amount of the cytokines to undetectable levels using a sensitive ELISA method. Only GMP (Good manufacturing process) cytokines are used for the expansion process, making it unlikely that any adverse clinical event will occur.

Microbial contamination has not been a problem in the patients treated to date and in preliminary studies done preclinically. This is likely because of the closed system setup, growth and collection of the expanded cells, the

use of antibiotics in the growth media, and the assays done 48 hours prior to the collection of the expanded cells (day 10). In addition, all patients will be on prophylactic antibiotics at the time of the cell infusions as per routine BMTU protocols.

2.3 High Dose Chemotherapy and Autologous Bone Marrow Transplant Breast Cancer

Breast cancer is responsive to initial combination chemotherapy for metastatic disease with a 50-80% response rate and a 10-20% complete response rate, but few patients are cured and median duration of response is generally less than one year (20-24). Once patients relapse, the response to second-line therapy is 20-40% with very few complete responses (CR) and a median duration of response of 2-3 months and a median survival of 12 months.

When patients with metastatic breast cancer receive high-dose chemotherapy, there is substantially higher complete response rate than that can be achieved with conventional treatment (25-38). Peters et al (39) used a regimen of Cyclophosphamide, Cisplatin, and BCNU or Melphalan in 22 ER-negative patients without prior induction chemotherapy, and reported a 54% CR rate and an overall response rate of 73% and a median duration of response of 7 months from the time of transplant. Antman et al recently reported similar results with a combination of high-dose Carboplatin, Cyclophosphamide and Thiotepa (26); each study reported approximately 20% 5-year disease-free survival. A recently published study that compared in a randomized fashion chemotherapy at conventional doses versus high dose therapy with stem cell rescue verified that this high dose approach is superior to conventional chemotherapy as measured both by progression-free as well as overall survival. Application of the same therapy to patients with Stage II breast cancer with greater than 10 positive nodes or Stage III disease has resulted in approximately 70% 5-year disease-free survival, substantially higher than that reported with standard adjuvant therapy in such patients.

3.0 BACKGROUND DRUG AND DEVICE INFORMATION

3.1 Description of the CPS

The single-use, sealed, sterile cell culture device in the Aastrom CPS consists of three rigid plastic parts separated by a gas-permeable, water-impermeable membrane. The lower cell culture chamber is continuously perfused by growth medium. The cells expand in culture on the plastic surface of the cell culture bed. The upper cell culture chamber is provided with a constant flow of gas, such that oxygenation of the cell culture bed is accomplished by diffusion across the membrane and through the culture medium. Carbon dioxide is removed by the same mechanism. The medium used to perfuse the cultured

cells is stored in a closed vessel in an adjacent refrigerator at 4 degrees C whose only external connection is by medical grade tubing. A "Y" connector, attached to the effluent line, allows sampling of the cell product prior to harvest, to test for bacterial and fungal contaminants. A detailed device description is provided in the Operators Manual provided by Aastrom. The system to be used will include dedicated Aastrom instruments, the Processor and incubators which replace standard laboratory equipment and perform all of the steps in the cell production automatically and more importantly sterily, and in a close system manner, after the initial inoculation of the cells into the CPS. The incubator contains a cold compartment for media storage for perfusion during the 12 day culture (perfusion begins on Day 3), and a 37 degrees C compartment in which the Cell Cassette is placed for the duration of the culture.

3.1.1.1 Cell Culture Conditions

The hematopoietic cells are suspended in tissue culture medium composed of Iscove's Modified Dulbecco's Media supplemented with 10% fetal bovine serum, 10% horse serum, hydrocortisone (5×10^{-6} M), PIXY321 (5 ng/ml), glutamine (4 mM), Erythropoietin (Epo 0.1 U/ml), flt3L (5 ng/ml), gentamicin sulfate (5 Fg/ml), vancomycin (20 Fg/ml), sterile water for injection, and are inoculated into the CPS, starting after Day 3. The cells are cultured in the CPS for 12 days at 37 degrees C with the tissue culture medium continuously replaced with fresh medium. Sampling of the culture medium is carried out 48 hours prior to harvest, to allow testing for bacterial and fungal contaminants.

The cell harvest is performed automatically, by a programmed schedule with the Processor. In this process, the non-adherent fraction is removed from the cell culture device by draining the growth medium from the cell culture device into the harvest bag. The chamber is then rinsed with 50 ml of Hank's Balanced Salt solution (HBSS). This is followed by agitation of the cell culture device and collection of the rinse into the harvest bag. The adherent layer is detached from the cell culture bed surface by injection of 50 ml of Trypsin-EDTA solution. This is also followed by agitation of the cell production device and collection of the rinse into the harvest bag. The chamber is then given a final rinse by injecting 50 ml of HBSS. This is followed by agitation of the cell production device and collection of the rinse into the harvest bag. Again this is done automatically, sterily in a closed system fashion.

Following collection, the cells are washed free of culture medium as detailed in the Operator's Manual. The final product is suspended in appropriate media for immediate infusion.

3.1.2 Cell Culture Media Information

Studies by Aastrom and the University of Michigan have shown that, after the cell washing regimen, the added growth factors and other reagents are below detectable limits, using a very sensitive ELISA assay (R&D Systems, Minneapolis, MN, and Immunex Research Corporation, Seattle, WA). These levels are well below the level of biological activity. The horse and fetal calf sera are tested preclinically for contamination for bacteria, fungi, mycoplasma, endotoxin, and viruses. The expanded cell product is washed (See Operators Manual) prior to transfusion. Nonetheless, the human toxicities and contraindications identified for these drugs are included below:

3.1.2.1 Recombinant Human Epo

Recombinant Human Erythropoietin: Epoetin Alfa, Procrit, NOC 0062-7402-01 Amgen, Thousand Oaks, CA.

Human Toxicity: Toxicities have included hypertension, headache, fever, seizures, and skin rash. The majority of these subjects had chronic renal failure, and these adverse events are frequent sequelae of chronic renal failure and were not necessarily attributable to Epo.

Contraindications: Epo is contraindicated in subjects with: uncontrolled hypertension, known hypersensitivity to mammalian-derived products, and known sensitivity to human albumin.

3.1.2.2 PIXY321

PIXY321 is a fusion protein of granulocyte-macrophage colony-stimulating factor (GM-CSF) and interleukin 3 (IL-3).

3.1.2.3 Recombinant GM-CSF

Human Toxicity: Specific Toxicities include peripheral edema, pleural and/or pericardial effusions, fluid retention, sequestration of granulocytes in the lung, supraventricular arrhythmia, elevation of serum creatinine, and elevation of hepatic enzymes.

Contraindications: GM-CSF is contraindicated in subjects with excessive leukemic blasts in the bone marrow or peripheral blood (greater than 10%), or with known hypersensitivity to GM-CSF, yeast-derived products, or any component of the product.

3.1.2.4 Flt3 Ligand (flt3L)

The manufacturer of flt3L, Immunex Research and Development Corporation, Seattle, WA, has advised that a biologic Master File is in preparation for clinical, in vivo grade flt3L, and that the Master File will be submitted to the FDA in 1996, and will be available as reference for the purposes of this clinical feasibility trial (Letter, Immunex to Aastrom, December 11, 1995).

Immunex has also advised that flt3L appeared to be well tolerated when administered to mice and monkeys for 14 days, at doses up to 4000g/kg/day. Based on the safety profile established by Immunex, including the animal data generated to-date, flt3L has no apparent toxicities, and does not stimulate the proliferation and detrimental activation of mast cells.

As indicated above, the cells produced in the CPS are washed four times, resulting in a 5-log reduction in the presence of media components, to levels below detectable limits. An ELISA, supplied by Immunex, is used to determine residual flt3L levels subsequent to cell washing.

3.1.2.5 Horse Serum

Contraindications: Known hypersensitivity to horse serum.

3.1.2.6 Fetal Calf Serum

Contraindications: Known hypersensitivity to bovine serum.

3.2 CHEMOTHERAPY AGENTS AND CYTOKINES

rhG-CSF (Filgrastim: NSC-614629)

3.2.1 Chemistry: rhG-CSF is a protein produced in E. Coli into which the gene synthesized for high expression in E Coli has been inserted. The 175 amino acid protein has a molecular weight of about 18,800 daltons. rhG-CSF differs from the natural protein (M.W. 19,600 daltons) in that the N-terminal amino acid is a methionine and is not O-glycosylated.

3.2.2 Mechanism of Action: rhG-CSF is a hematopoietic regulator which has the ability to modulate the growth and maturation of myeloid cells, and in particular the proliferation and differentiation of granulocytes both in vitro and in vivo.

3.2.3 Human toxicity: Specific toxicities include medullary bone pain.

musculoskeletal symptoms (muscle cramps, back and or leg pain); exacerbation of preexisting inflammatory conditions (psoriasis, arthritis, vasculitis); splenomegaly and hair thinning with prolonged administration. Elevated leukocyte alkaline phosphatase, uric acid, and lactate dehydrogenase. Progression of patients with myelodysplasia to acute myeloid leukemia occurred rarely during treatment with this agent.

- 3.2.4 Pharmaceutical Data: rhG-CSF is supplied in colorless, glass, single use vials containing 1.6 ml of buffered solution at a concentration of 0.3 mg/ml. It is formulated as a sterile, colorless liquid in a 10 mM sodium acetate buffer at pH 4.0.

Administration: rhG-CSF will be administered in this study subcutaneously. It will be undiluted and be drawn into 3 cc syringes. To reduce the possibility of bacterial contamination in this product which contains no preservatives, the syringes should be stored at 2-8 degrees C and used within 24 hours of preparation, rhG-CSF should not be frozen and vials or syringes that have been frozen should not be used.

- 3.2.5 Supplier: This agent will be supplied through AMGEN for the trial free of charge to the patients.

3.3 Carboplatin (NSC-241240) (CBDCA)

- 3.3.1 Human Toxicity: Side effects of Carboplatin (CBDCA) include myelosuppression, nausea, vomiting, loss of appetite. Rare toxicities include gross hematuria, hyponatremia, ageusia, allergic reaction, peripheral neuropathy, veno-occlusive disease, loss of hair, liver damage, kidney damage, hearing loss, dizziness and blurred vision. Two cases of optic neuritis have been reported in patients receiving carboplatin which were thought to be possible drug-related events. A single case of severe pulmonary toxicity has been reported.

- 3.3.2 Pharmaceutical Data: Formulation: CBDCA is supplied as a sterile lyophilized powder available in single-dose vials containing 50 mg, 150 mg and 450 mg of Carboplatin for administration by intravenous injection. Each vial contains equal parts by weight of Carboplatin and mannitol. Immediately before use, the content of each vial must be reconstituted with either Sterile Water for Injection, USP, 5% Dextrose in Water, or 0.9% Sodium Chloride Injection, USP, according to the insert.

Diluent Volume

50 mg 5 mL

150 mg	15 mL
450 mg	45 mL

These dilutions all produce a Carboplatin concentration of 10 mg/ml. CBDCA can be further diluted to concentrations as low as 0.5 mg/ml with 5% Dextrose in Water or 0.9% Sodium Chloride Injection, USP (NS).

3.3.3 Storage & Stability: Unopened vials of CBDCA for injection are stable for the life indicated on the package when stored at controlled room temperature 150 - 300 C. and protected from light. When prepared as directed, CBDCA solutions are stable for 8 hours at room temperature. Since no anti-bacterial preservative is contained in the formulation, it is recommended that CBDCA solutions be discarded 8 hours after dilution. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

3.3.4 Administration: Intravenous.

3.3.5 Supplier: CBDCA is commercially available and will be purchased through third party payers.

3.4 Cyclophosphamide (NSC-26271)

3.4.1 Mechanism of Action: Cyclophosphamide is a very weak alkylating agent, but enzymatic oxidation and a series of undefined subsequent reactions produce one or more molecules with alkylating activity. In experimental animals, the first step of activation occurs more extensively in the liver than in the neoplasm or other tissues of the host.

3.4.2 Toxicities: Human toxicity includes alopecia, nausea and vomiting, stomatitis, leukopenia, anemia, thrombocytopenia, sterility or decreased gonadal function, hemorrhagic cystitis and fibrosis of the bladder.

3.4.3 Pharmaceutical Data: Formulation: Cyclophosphamide is supplied in 100, 200, and 500 mg ampules containing white powder. The drug can be reconstituted in normal saline or 5% dextrose and water.

3.4.4 Stability: Store at room temperature. Do not store at temperatures above 90 degrees F.

3.4.5 Supplier: This drug is commercially available for purchase by the third party.

3.5 Thiotepea (Triethylene-thiophosphoramide) (NSC-6369)

- 3.5.1 Mechanism of Action: Thiotepea is a cytotoxic agent of the polyfunctional alkylating type related chemically and pharmacologically to nitrogen mustard. On the basis of tissue concentration studies, it is reported that Thiotepea has no differential affinity for neoplasms. Most of the drug appears to be excreted unchanged in the urine.
- 3.5.2 Human Toxicology: The major side effects of Thiotepea are pain at the site of injection, nausea and vomiting, anorexia, dizziness, headache, amenorrhea and interference with spermatogenesis. Febrile reaction and weeping from a subcutaneous lesion may occur as the result of a breakdown of tumor tissue. Allergic reactions are rare, but hives and skin rash have been noted occasionally. The serious complication of excessive Thiotepea therapy, or sensitivity to the effects of this agent, is bone marrow depression. If proper precautions are not observed, it may cause leukopenia, thrombocytopenia and anemia. The most reliable guide to Thiotepea toxicity is the white blood count.
- 3.5.3 Pharmaceutical Data: Formulation: Thiotepea is available in a powder form in 15 mg vials. The powder should be reconstituted in sterile water for injection.
- 3.5.4 Storage and Stability: Reconstituted solutions may be kept for five days in a refrigerator without a substantial loss of potency. Vials containing Thiotepea should be stored at 2-8 degrees C (35-46 degrees F).
- 3.5.5 Administration: The amount of diluent most often used is 1.5 ml resulting in a drug concentration of 5 mg in each 0.5 ml of solution. Thiotepea may be given by rapid intravenous administration or via continuous intravenous infusion.
- 3.5.6 Supplier: This drug is commercially available for purchase by the third party.

3.6 Intended Use

The intended use of the CPS is to produce human stem- and hematopoietic progenitor cells to support subjects with compromised hematopoietic systems. A per-patient cell production procedure, beginning with 2.25×10^8 nucleated bone marrow cells per device, will yield at least 1.6×10^9 cells. The cells will not be infused if the cell yield is below this level; the back-up cells will be infused in such a case.

4.0 PATIENT ELIGIBILITY

- 4.1 Patients with histologically confirmed breast cancer with advanced disease as defined as high risk Stage II (greater than 10 LN), Stage III or stage IV (inflammatory, fixed to chest wall, or fixed axillary lymph nodes) or recurrent or metastatic disease.
- 4.2 Patients with measurable disease must have disease which is responsive to standard dose systemic chemotherapy administered prior to enrollment on study. Patients may have a maximum of two prior chemotherapy regimens for their disease. Patients with metastatic disease (beyond draining lymph nodes) with no evaluable or measurable disease following surgical resection, radiotherapy, or chemotherapy are still eligible.
- 4.3 Patients must have a Performance status of 0-1 by SWOG criteria (see appendix). As patient weight is used to calculate the minimum safe dose of CFU-GM to accomplish a transplant, and given the production capabilities of the CPS, patients in this initial trial must be less than 90 kg of actual body weight.
- 4.4 Patients must have received a cumulative adriamycin dose of less than 350 mg/m² with no prior nitrosoureas, platinum or mitomycin C.
- 4.5 Patients must have recovered from prior therapy with at least 4 weeks since the last chemotherapy, 4 weeks since last radiotherapy, and 3 weeks since major surgery.
- 4.6 Patients must have adequate cardiac function as defined by a MUGA with an ejection fraction greater than or equal to 45%. Patients may not have active coronary disease as defined by angina or history of a myocardial infarction. In addition, patients must have no clinically apparent uncorrectable pulmonary disease such as cor pulmonale or severe COPD, or be requiring oxygen therapy for any reason.
- 4.7 Patients with a history of or any evidence for brain metastases are ineligible. Head CT or MRI scans are not required if patients are asymptomatic.
- 4.8 Patients must have adequate organ function as defined by the following: Serum creatinine less than or equal to 1.5 mg/dl or calculated Cr-CI or greater than or equal to 60 ml/min; Hepatic function as defined by Bilirubin less than or equal to 2.0 mg/dl and AST/ALT less than or equal to 2 x institutional normal values; hematologic functional as defined by WBC greater than or equal to 3400/ul. Hgb greater than or equal to 9.0 gm/dl. platelet count greater than or equal to 140,000/ul.
- 4.9 Exclusion Criteria include: History of hypersensitivity to horse serum or fetal calf serum; Concurrent involvement in any other clinical trial that affects engraftment (e.g. other hematopoietic growth factors); treatment with any growth factors within two weeks; Previous pelvic radiotherapy rendering the marrow hypocellular, any co-morbid condition which, in the view of the Principal Investigator, renders the patient at high risk from treatment complications.

- 4.10 Patients must undergo a BM biopsy and BM must be either free of disease by standard histologic exam, and a cellularity on biopsy of at least 35%.
- 4.11 Patients must be less than 65 years of age.
- 4.12 Patients must be HIV negative.
- 4.13 Pregnant or lactating women may not participate.
- 4.14 Patients with prior hemorrhagic cystitis are ineligible.
- 4.15 Patients must be free of active systemic infection at the time of initiating therapy. Patients must have had no episodes of systemic mycotic infections, nor have required Amphotericin B therapy in the previous 12 months.
- 4.16 Patients must be free of active CNS diseases (seizures, etc.)
- 4.17 Patients must have signed an IRB approved consent form prior to trial enrollment.
- 4.18 Patients may not have an active second malignancy within the previous 2 years except localized non-melanoma skin cancer or uterine cervical cancer in situ.

5.0 TREATMENT PLAN

5.1 Registration

All patients must be registered with the Data Management office at 708-327-3230 for entry on study. A total of 6-10 patients will be treated in this pilot study.

5.2 Bone Marrow Harvest

Patients will undergo back-up bone marrow harvest at any time prior to initiation of the ablative chemotherapy, with cryopreservation, using standard techniques. Patients must have greater than 2×10^8 /nucleated cells per kg harvested, including greater than 0.5×10^6 /CD34- cells/kg.

The bone marrow harvest will be performed by standard technique in an operating suite under general or epidural anesthesia. In a standard harvest, approximately 500-1500 ml of marrow is withdrawn. Patients will have the back-up bone marrow collected simultaneously with the cells for ex vivo production. If a sufficient number of cells are collected, the bone marrow collected will be processed and a small fraction utilized for the ex vivo culture described below, and the remainder of the cells will be cryopreserved per

standard technique and held as a back-up for use if the prescribed number of cells is not produced or if graft failure occurs. The cells for the expansion will be collected from the posterior iliac crest or from the sternum at the initiation of the harvest procedure. No more than 5 cc of marrow for the expansion will be aspirated from each bone puncture. Approximately 40 ml of marrow will be aspirated in this fashion.

5.3 Ex Vivo Cell Production

As mentioned in other parts of the Protocol, at the time of bone marrow harvest, all harvested marrow will be delivered to the bone marrow laboratory for processing. A portion of the harvested marrow will be used for cell production in the CPS and balance of the harvested marrow will be cryopreserved. Twelve days prior to the scheduled bone marrow transplant, 2.25×10^8 mononuclear cells from freshly collected marrow will be placed into each CPS in the presence of PIXY321 (5 ng/ml), hydrocortisone (final concentration 5×10^{-6} M), glutamine (4 mM), gentamicin sulfate (5 Fg/ml), vancomycin (20 Ff/ml), Epo (0.1 U/ml/day) and fit3L (5 ng/ml). The tissue culture medium will be supplemented with 1.0% fetal calf serum and 1.0% horse serum. All processing will be done using the dedicated CPS instrumentation. No standard laboratory equipment will be used for the expansion or processing of the cells. A sample of the harvested marrow will be sent for bacterial and fungal culture.

The cell production will be performed in the Aastrom CPS, which is operated as a stand alone, dedicated piece of validated laboratory equipment (incubator, refrigerator, gas pumps) which provide for constant temperature (37C), pH (7.2-7.4), and delivery of sterile air (5% CO₂) to the hematopoietic cells.

Two days prior to the completion of cell production, the cell culture effluent will be sampled to allow for bacterial and fungal testing including gram stain, endotoxin testing and mycoplasma. At the completion of the cell expansion process (12 days), the non-adherent fraction will be removed from the cell culture devices by draining the growth medium from the cell culture devices into the harvest bag. The devices will then be rinsed by using a syringe to inject 50 ml of an HBSS solution into an access port. This is followed by agitation of the cell culture device and collection of the rinse into the harvest bag. The adherent layer will be detached from the cell culture device surface by injection of 50 ml of Trypsin-EDTA solution via an access port. This is again followed by agitation of the cell culture device and collection of the rinse into the harvest bag. The chamber will be then given a final rinse with 50 ml of HBSS, again by injection via an access port. This is followed by agitation of the cell culture device and collection of the rinse into the harvest bag.

The expanded cells will be washed according to the procedure outlined in the Operators Manual.

All subjects will receive freshly harvested expanded cells. The expanded cells must be greater than 80% viable, as determined by Trypan blue dye, and the minimum total cell number, as

determined by an automated cell counter, will be 1.6×10^9 cells.

As part of the standard laboratory in this Study, the total cell count, CFU-GM and LTC-IC will be determined for the starting and final cell number. The pre and post expansion sample will be sent for cytology and immunocytochemistry for breast cancer cells.

Pre-transplant Evaluation of the cultured Cells: 48 hours prior to the collection of the expanded cells, the effluent from the CPS will be tested for bacterial and fungal contamination, as described above. If the bone marrow cultures are either visibly contaminated or are positively cultured for bacterial or fungal contamination, or if the cultures die, the expanded cells will not be returned to the subject, who will then simply receive her cryopreserved bone marrow.

Flow Cytometry: Aliquots of the ex vivo produced cells (approximately 10×10^6) will be removed at 12 days, placed in a tube containing sterile buffered medium, and shipped by overnight mail carrier to Aastrom Biosciences, Inc., Domino's Farms, 24 Frank Lloyd Wright Drive, Lobby L., Ann Arbor, MI, 48105. These cells will be analyzed for the presence of several cell surface markers (CD34, CD11b, CD15, CD33, CD3, CD4, CD8, CD19, CD71 and glycophorin A and other appropriate markers) in the laboratory at Aastrom as potential correlates for the cell production process. The Aastrom Laboratory operates under GLP (Good Laboratory Practices) guidelines.

Release Criteria: Cells produced in the Aastrom CPS will be considered eligible for release and reinfusion if greater than 1.6×10^6 nucleated cells/kg are recovered after the expansion period and cell washing, and if greater than 80% of the nucleated cells are viable as judged by exclusion of Trypan blue dye. Microbial contamination studies collected from the expansion on Day 10 must be negative.

If the expansion is not deemed sufficient, a patient will receive her backup marrow instead, without infusion of the expanded cells.

5.5 Transplant Regimen

5.4.1 High Dose Chemotherapy (STAMP V Regimen)

Chemotherapy will begin a minimum of 48 hours following the last pheresis. Prior to the administration of chemotherapy, patients will receive anti-emetics including ondansetron and dexamethasone. Chemotherapy will consist of the following:

Cylophosphamide 1500 mg/m² Q day by continuous infusion (CI) for 4 days (d-7 through d-4) (96 hours) Total dose 6000 mg/m²

Thiotepa 125 mg/m² Q day by CI for 4 days (d-7 through d-4) (96

hours) Total dose 500 mg/m².

Carboplatin 200 mg/m² Q day CI for 4 days (d-7 through d-4) (96 hours)
Total Dose 800 mg/m².

Supportive Issues:

All patients will receive therapy through three separate lumens. The agents can not be mixed. Vigorous hydration will be included with a minimum of 200 cc/hour of IV fluids with diuretics as needed, while the chemotherapy is infusing and continuing till stem cell infusion. Patients will receive aggressive anti-emetic therapy with ondansetron, lorazepam, dexamethasone, etc.

5.4.2 Post-Transplant Growth Factor Support

G-CSF (10 mcg/kg/d) will be administered SQ until granulocytes greater than $2.0 \times 10^9/L$ or greater than $1.0 \times 10^9/L$ for 3 days. If granulocytes fall to less than $1.0 \times 10^9/L$, hematopoietic growth factor treatment can be resumed as indicated to maintain an absolute granulocyte count greater than $1.0 \times 10^9/L$. GM-CSF 250 mg/m²/d may be used in patients intolerant to G-CSF.

Patients who require the administration of any myelosuppressive therapy in the first 7 days post transplant such as full dose Amphotericin B therapy will be required to receive the infusion of their back up marrow cells on that date.

5.4.3 Neutrophil Engraftment and Stopping Rules

Neutrophil engraftment is defined as recovery as granulocytes to $0.5 \times 10^9/L$. Back-up autologous bone marrow will be infused intravenously per the following stopping rules:

- a. Back-up cells will always be administered to subjects on Day -21 if ANC is less than $0.5 \times 10^9/L$; if back-up cells are administered to a subject on Day-21, it is reasonable to assume that an ANC level of $0.5 \times 10^9/L$ can only be reached between Day -21 and Day -25 if the cells produced in the CPS alone contribute to a subject's recovery, because the administration of back-up cells would not be expected to impact engraftment so rapidly, between Days -21 and-25. It is relevant to point out that ANC recovery in the Day -18-25 time frame is often experienced in standard bone marrow transplantation.
- b. If the ANC is greater than 500 on Day -28 but the platelet count is less than 20,000, the marrow cells will be infused on that date.
- c. If the patient is experiencing a severe infection or uncontrolled bleeding

at any point during the period of pancytopenia, the back-up cells may be administered at the discretion of the investigator.

5.4.3.1 Stopping Rules

With the above as background, stopping rules will be as follows: the trial will be stopped and reevaluated if two subjects fail to reach ANC $0.5 \times 10^9/v/1$ by Day +25, even with the administration of back-up cells on Day +21;

The trial will also be stopped and reevaluated if four of the first five subjects, or if any five of the ten total subjects, required the administration of back-up cells because they failed to reach ANC $0.5 \times 10^9/v/1$ on or before Day +21.

6.0 PRETREATMENT EVALUATION

- 6.1 Complete history and physical examination, including SWOG performance status (Appendix C)
- 6.2 CBC, diff, and platelet count
- 6.3 SMA 12 and electrolytes
- 6.4 PT, PTT
- 6.5 Cardiac ejection fraction
- 6.6 Pulmonary function - DLCO
- 6.7 HIV, hepatitis, HTLV-1 (1764 panel)
- 6.8 Pregnancy test (in fertile women)
- 6.9 Tumor staging as indicated including bone scan with X ray of hot spots. Chest X-Ray, CT scan abdomen, tumor markers, such as CEA will be assessed.
- 6.10 Bilateral bone marrow aspirate and biopsy

7.0 STUDY PROCEDURES AND EVALUATIONS

- 7.1 Interim history, physical examination and toxicity assessment daily while in hospital and at least weekly until WBC greater than 3000 and platelets greater than 100,000. Toxicity assessment will be made pre-infusion and 2 and 24 hours post-infusion of both the expanded and unexpanded bone marrow cells.

- 7.2 CBC, diff, platelet counts daily while hospitalized and at least twice per week as an outpatient until WBC greater than 3000/uL and platelets greater than 100,000/uL.
- 7.3 SMA twice per week while hospitalized. Electrolytes as indicated.
- 7.4 Tumor restaging as indicated including bone scan with X ray of hot spots, CXR, CT scan of abdomen, and CEA, at day 60. Subsequent follow up is as indicated for patients with this malignancy.
- 7.5 Criteria for discharge: A study subject will be eligible for discharge from the hospital when she meets the following criteria:
afebrile for 2 or more consecutive days, ANC greater than 500 for 3 consecutive days and SWOG status of 0, 1 or 2.

All study subjects will receive follow-up care and treatment (as appropriate) by their physician. The subjects' medical records will be available to medical study monitors should additional information be required.

8.0 DATA COLLECTION

8.1 General Information

Data will be recorded using a standard 'Therindex' reporting system at the time of each evaluation. Data must be recorded for all subjects from whom an Informed Consent is obtained.

8.2 Contents

Data to be collected at each of the study time period is as follows:

Pre-treatment Evaluation

Eligibility criteria

Demographic data

Medical history

Physical examination

Laboratory profile

Bone marrow biopsy

toxicity status

Baseline (Day 0)

Laboratory profile
Bone marrow/cultured cell profile
Transfusion record
Toxicity assessment
Vital signs
Concomitant medication(s)
Infection reporting and adverse effects greater than grade 3 -
report immediately to sponsor as event occurs.

Daily Evaluations (Post-transplant)

Laboratory profile
Transfusion record
Toxicity assessment (note preinfusion, 2 hour and 24 post infusion
toxicity assessment above)
Vital signs
Concomitant medications

Infection reporting and grade greater than 2 adverse effects - report
immediately to sponsor as event occurs.

Hospital Discharge (study completion)

Laboratory profile
Vital signs

Toxicity assessment
Concomitant medications
Infection reporting and Adverse Effects grade greater than 3 - Report
immediately to sponsor as event occurs.

Early termination or D60

Laboratory profile
Assessment of late toxicity
Transfusion record
Vital signs
Concomitant medications
Study completion questionnaire

8.3 Quality System

Quality system procedures are designed to ensure that complete, timely, and accurate data are submitted, that protocol requirements are followed, and that complications and/or adverse reactions are immediately identified.

The study monitors will promptly review all incoming data to identify inconsistent or missing data and adverse effects. Data problems will be addressed in telephone calls and correspondence to the investigational site and during site visits. Clinical monitoring procedures are described in Section 12 of this protocol. The Medical Monitor will receive immediate notification of adverse reactions Grade greater than 3. Both the site and -----

Astrom will maintain secure hard copy Case Record Forms and data files.

9.0 ADVERSE EFFECTS

All adverse effects, whether or not considered anticipated, must be recorded on the data sheets. Unanticipated effects, as defined below, must be reported promptly to the sponsor for further evaluation and adequate required reporting to IRBs and investigators.

9.1 Anticipated Adverse Effects

The preliminary clinical experience has not identified any serious adverse effects on health or safety caused by or associated with the CPS and no adverse effects related to the ex vivo use fit3 ligand are anticipated. Patients undergoing high dose chemotherapy are anticipated to experience anorexia, nausea, vomiting, mucositis, pancytopenia and associated infections while neutropenia. Some patients may develop organ toxicities from high dose therapy. The anticipated events are therefore those associated with bone marrow transplantation and/or chemotherapy.

9.2 Unanticipated Adverse Effects

An unanticipated adverse effect is:

Any serious effect on health or safety or any life-threatening problem, or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan, or any other unanticipated serious problem that relates to the rights, safety or welfare of subjects. [21 CFR 812.3 (s)]. In particular, any unexpected grade III or IV toxicities or any other serious event that might be attributable to the infusion of the expanded hematopoietic cells.

Reporting requirements:

Unanticipated adverse effects should be reported to the Aastrom Study Director, Thomas E. Muller, Ph.D., Vice President Regulatory Affairs, immediately by the Investigator and subsequently to BRI.

Aastrom requires an immediate telephone report followed by a written report within 5 days.

An investigator shall submit to Aastrom and the reviewing IRB a report of any unanticipated adverse device effect occurring as soon as possible, but no later than 10 working days after the investigator learns of the effect [21 CFR 812.150 (a) (1)]. Aastrom shall immediately conduct an evaluation and report the results of the evaluation to FDA and to reviewing IRB's and participating investigator(s) within 10 working days after the sponsor first receives the notice of the effect [21 CFR 812.150 (b) (1)]. If Aastrom determines that an unanticipated adverse effect presents an unreasonable risk to subjects, all investigations or parts of investigations presenting that risk shall be terminated as soon as possible [21 CFR 812.46 (b)].

9.3 DEPARTURE FROM PROTOCOL

When a situation occurs which requires a departure from the protocol, the Principal Investigator or other physician in attendance will contact the Medical Monitor by telephone:

Thomas E. Muller, Ph.D.
Vice President Regulatory Affairs
Aastrom Biosciences, Inc.
24 Frank Lloyd Wright, Lobby L
Ann Arbor, MI 48105
Telephone: 313-930-5555
Fax: 313-665-0485

Contact with the Medical Monitor will be made as soon as possible in order to discuss the situation and agree on an appropriate course of action. The patient's medical records and source documents will describe the departure from the protocol and the circumstance requiring it.

10.0 STATISTICAL CONSIDERATIONS AND DATA ANALYSIS

10.1 Evaluation of the Data

All subjects will be evaluated. Descriptive statistics will be presented for demographic variables and baseline characteristics such as age, sex, medical history, physical examination results, cost information (especially as this relates to morbidity).

The primary endpoint is the safety of the cells produced in the CPS. To assess the hematopoietic recovery post-infusion with ex vivo-produced cells, the day of engraftment is defined by the first day on which granulocytes less than $0.5 \times 10^9/\text{L}$ are observed. Other secondary endpoints include nadir WBC and platelet count, febrile days, treatment related complications, antitumor response, and survival.

Secondary Endpoints:

- a. The day of platelet transfusion independence with platelet count less than 20,000/MM3, 50,000/MM3 and 100,000/MM3 as defined by first of two consecutive time points on which platelet counts meet these endpoints not related to transfusion.
- b. Packed red blood cell transfusion and platelet transfusion requirements.
- c. Number of documented infections.
- d. Number of bleeding episodes.
- e. Number of days of hospitalization.

Tumor response and response duration

- a. Patient survival at 90 days post transplant.

10.2 Safety variables

Safety variables summarized will include incidence of adverse effects (including duration, severity, and outcome). Other safety variables reported will include the incidence and types of laboratory abnormalities. When the frequencies are sufficiently large, a Fishers exact test or Chi-square test may be used to compare enrolled subjects and historical controls including approximately 65 patients receiving autologous bone marrow transplants without expansion using the same preparative regimen.

10.3 Biological Effect Variables

The following biological effects will be summarized:

Incidence of febrile neutropenia
Time to platelet transfusion independence Antibiotic usage:

Number of days on antibiotics
Number of total antibiotic days (# antibiotics x days)
Number of days on antifungals
Number of days on antivirals
Number of documented infections
Time to neutrophil engraftment
Length of initial hospitalization

11.0 CLINICAL SUPPLIES

A complete CPS description is provided in the Operators Manual. 1

11.1 Materials and Supplies

11.1.1 CPS

Aastrom will supply the CPS, which includes the cell culture device. This device consists of three rigid plastic parts (top, cell bed, and base), and a gas-permeable, water-impermeable membrane. Additional components include the means to facilitate air removal, seals to maintain leak-proof integrity, and mechanical fasteners.

11.1.2 Growth Medium

The culture medium is prepared at the clinical site by supplementing a custom medium, produced to Aastrom specifications in a FDA-registered facility in compliance with GMPs (21 CFR 820), with glutamine and growth factors in accordance with a standard operating procedure. Medium components are shipped to or procured by the clinical trial site according to instructions, specifications and acceptance criteria defined by Aastrom.

11.1.3 Supporting Tubing and Materials

Aastrom will supply the supporting tubing, harvest container, and waste container. These components will be supplied in sterile packages (for single use only).

11.2 Packaging and Labeling

The package labeling includes the statement "Caution. Investigational Device-Limited by United States Law to Investigational Use," Lot Number, "Sterile unless unit package is opened or damaged," and "Manufactured for Aastrom Biosciences, Inc."

11.3 Assembly

Components of the CPS will be received at the clinical test sites in sterile packages. The elements of the system will be connected under a laminar flow hood using aseptic technique provided in the Instructions for Use. The instructions for use will be provided by Aastrom.

11.4 Storage Requirements

The devices may be stored indefinitely under typical laboratory conditions (50 degrees to 90 degrees F) and may be transported at temperatures up to 125 degrees F.

11.5 Retrieval and/or Disposal of Investigational Materials

At the completion of the cell production process and harvest, the devices will be considered biohazardous waste and disposed of in accordance with standard procedures at the test site. Record will be made of the date of disposal and initials of the individual responsible for their disposition.

12.0 STUDY MONITORING

12.1 Medical Monitor

The Medical Monitor will review the investigational plan, review adverse - reactions and/or unanticipated device effects as reported by the Investigator and interpret clinical results. The Medical Monitor for this study is:

Thomas E. Muller, Ph.D.
Vice President Regulatory Affairs
Aastrom Biosciences, Inc.

Domino's Farms
24 Frank Lloyd Wright Dr., Lobby L
Ann Arbor, MI 48105
Telephone: 313-930-5555
Fax: 313-665-0485

12.2 Clinical Monitor

Aastrom has designated BRI International, Inc., as Clinical Monitor for this study. The Clinical Monitor is qualified by training and experience to oversee the conduct of the study. The Clinical Monitor's responsibilities include maintaining regular contact with the investigational site, through telephone contact, correspondence and on-site visits, to ensure that the investigational plan and FDA regulations are followed, that complete, timely and accurate data are addressed, and that the site facilities continue to be adequate. Any questions regarding

these matters should be addressed to:

Diane Goleb, Senior Project Director
BRI International, Inc.
15825 Shady Grove Road
Rockville, MD 20850
Telephone: 301-548-0500
Fax: 301-548-0519

12.3 Monitoring Procedures

12.3.1 Preinvestigational Site Visit

The Preinvestigational Site Visit, conducted by the Clinical Monitor, will involve review of relevant FDA regulations and inspection procedures, the investigational plan, requirements for IRB review and approval, completion and submission of forms, record keeping requirements, and administrative reports.

The adequacy of the facilities, the availability of the investigators, the potential number of study participants, and the provisions for staff support will also be assessed during the Preinvestigational Site Visit.

12.3.2 Routine Monitoring Visits

Regular clinical monitoring visits to the investigational site will be conducted by Aastrom and BRI.

To ensure that the Principal Investigator and his staff understand and accept their defined responsibilities, the Clinical Monitor will maintain regular correspondence and perform periodic site visits during the course of the study to verify the continued acceptability of the facilities, compliance with the investigational plan and relevant FDA regulations, and the maintenance of complete records. Clinical monitoring will include review and resolution of missing or inconsistent results and source document checks (i.e., comparison of submitted study results to original reports) to assure the accuracy of the reported data.

The Clinical Monitor will evaluate and summarize the results of each site visit in written reports, identifying any repeated data problems with any investigator and specifying recommendations for resolution of noted deficiencies.

12.3.3 Termination/Close-out Procedures

The Clinical Monitor, BRI, will notify the investigator in writing of study completion/termination. The letter will include the reason for termination, document unresolved study discrepancies, and remind the investigator of her obligation to retain records according to FDA regulations.

BRI will be responsible for meeting the FDA regulations with regards to record keeping and records retention.

BRI will conduct a standard closure monitoring site visit. The objectives of the closing visit are:

verify compliance with protocol and FDA regulations; ensure accuracy and completeness of subject and administrative files; resolve any outstanding questions/problems; verify accountability for the test devices; ensure the proper disposition of test devices and completed case report forms; confirm the investigator's understanding of his/her regulatory obligations, including record retention requirements.

13.0 INVESTIGATOR OBLIGATIONS

13.1 Principal Investigator Responsibilities

13.1.1 Compliance

The Principal Investigator is responsible for ensuring that the study is conducted according to the signed Investigator Agreement, the investigational plan, and applicable FDA regulations for protecting the rights, safety and welfare of subjects under the Investigators care. The Principal Investigator must follow the Investigator Agreement, the investigational plan, and all conditions of FDA and IRB approval.

13.1.2 Awaiting Approval

Written confirmation of IRB approval must be provided to Aastrom prior to the start of the study. The Principal Investigator may determine whether potential subjects would be interested in participating in a study but may not request signature of the Informed Consent or allow any subject to participate until FDA and the reviewing IRB have approved the study.

13.1.3 Supervising Device Use

The Principal Investigator must supervise all use of the CPS involving human subjects and may not supply the device to any person not specifically authorized to receive it according to the investigational plan and applicable regulations.

13.1.4 Informed Consent

The Principal Investigator shall make known to each subject the nature, expected duration, and purpose of the study; the administration and hazards of treatment; and available alternative therapy. Signed, written Informed Consent must be obtained prior to treatment. The original will be kept by the Principal Investigator and will be subject to review by Aastrom. Subjects will be informed that their medical records will be subject to review by Aastrom and the FDA. Subjects shall be informed that they are free to refuse participation in this clinical investigation; and if they participate, that they may withdraw from the study at any time without prejudicing future care.

13.1.5 Device Disposal

Upon completion or termination of the study of the Principal Investigators participation in the study, or at Aastrom's request, the Principal Investigator must return to Aastrom the device(s) or otherwise dispose of the device(s) as Aastrom directs.

13.1.6 Reporting Requirements

Any life-threatening and/or unexpected serious (grade 3 or 4) toxicities will be reported immediately to the Study Chairman who, in turn, will notify the IRB (Surveillance Committee) and the study sponsor.

13.1.7 Inspections and Records

In accordance with the Investigator Agreement, the Principal Investigator shall permit authorized FDA employees to enter and inspect any site where the device or records pertaining to the device are held, and to inspect and copy all records relating to an investigation, including subject records.

13.1.8 Investigator Records

The Principal Investigator will maintain complete, accurate and current study records, including the following materials:

Correspondence with FDA, Aastrom, BRI, and the IRB; Record of receipt of the device:

Instructions for device use;
Subject Records, including Informed Consent, copies of Case Report Forms and supporting documents (laboratory reports, medical records, etc.); Log Book;
Current study protocol and a log of any significant protocol deviations (e.g., lack of informed consent or treatment of ineligible subjects);
Adverse event reports;
Certification that the investigational plan has been approved by all of the necessary approving authorities;
The approved blank informed consent form and blank subject report forms. Signed Investigator's Agreement with CV's of the Principal Investigator and all participating sub-investigators attached.

These records shall be maintained for a period of 2 years after the latter of the following two dates: the date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or notice of completion of a product development protocol.

13.1.9 Investigator Reports

The Principal Investigator will be responsible for the following reports:

13.1.9.1 Unanticipated Adverse Effects

The Investigator will report any serious adverse effect, death or life-threatening problems that may reasonably be regarded as caused by the CPS to Aastrom and the reviewing IRB as soon as possible but no later than 10 working days after the event. All anticipated serious adverse effects should be documented with an explanation of any medical treatment administered.

An unanticipated serious adverse effect is defined as any serious adverse effect on health or safety, or any life-threatening problem or death caused by, or associated with this device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in this investigational plan.

13.1.9.2 Withdrawal of IRB Approval

The Principal Investigator will immediately notify to Aastrom (within 5 working days) if, for any reason, the IRB withdraws approval to conduct the investigation.

The report will include a complete description of the

reason(s) for which approval was withdrawn.

13.1.9.3 Departure from Protocol

The Principal Investigator shall notify Aastrom and the IRB of any deviation from the investigational plan made to protect the life or physical well-being of a subject in an emergency. A full report should be made as soon as possible and in no case later than 5 working days after the emergency. NOTE: Except in such an emergency, prior approval by Aastrom is required for changes in, or deviations from, the investigational plan. If such changes or deviations may affect the scientific soundness of the plan or the rights, safety or welfare of subjects, FDA and IRB approval are also required.

13.1.9.4 Progress Reports

The Principal Investigator is required to submit progress and administrative reports to Aastrom, and to the reviewing IRB. Reports will include the number of study subjects, a summary of all adverse reactions, and a general description of the study's progress.

13.1.9.5 Final Report

The Principal Investigator will submit a final report to Aastrom within four weeks following termination of the study or that site's participation in the study, and within three months to the IRB.

13.1.9.6 Other Reports

Upon request, the Principal Investigator will provide accurate, complete, and current information to Aastrom Biosciences, Inc., the FDA, and to the reviewing IRB.

13.1.9.7 Investigator Materials Accountability

All devices received and used by the Principal Investigator will be inventoried and accounted for throughout the study. The devices will be stored in a secured area. Upon study completion, all unused devices will be returned to Aastrom. A final inventory will then be performed.

13.1.9.8 Laboratory Normal Values

The investigational site must maintain a current copy of normal values used by that site's clinical laboratory. The Principal Investigator must assess the clinical significance of all abnormal laboratory values. All clinically significant abnormalities must be characterized by the Principal Investigator as treatment-related, not treatment-related, or of uncertain etiology; all abnormalities judged treatment-related or of uncertain etiology must be repeated. Any abnormal values that persist should be followed at the Principal Investigators discretion. In some cases, significant changes within the normal range will require similar judgment.

13.1.9.9 Disclosure of Data

All information concerning this clinical study are considered confidential. The Principal Investigator agrees to use this information only to accomplish this study and will not use it for other purposes without Aastrom's written consent.

It is understood by the Principal Investigator that the information developed in the clinical study may be disclosed as required to the United States Food and Drug Administration.

In order to allow for the use of the information derived from the clinical studies, it is understood that there is an obligation to provide Aastrom with complete test results and all data developed in the study.

Aastrom has no objection to the publication of the results of this study by the investigator. However, a pre-publication manuscript must be provided to Aastrom at least 30 days before the manuscript is submitted to a publisher.

Aastrom agrees that before it publishes any results of the study, a pre-publication manuscript will be provided to the investigator for review at least 30 days prior to the submission to a publisher.

13.1.10 Records Retention and Access

FDA regulations require that, following completion of a clinical trial, a copy of all subject and administrative

records pertaining to that study be maintained by the Investigator for 2 years after FDA approval of the investigational device, or, if no application for approval is filed or intended to be filed, for 2 years after all investigations have been completed, terminated, or discontinued, whichever time period is longer.

Completed data records must be made available for review by Aastrom, the Clinical Monitor, and FDA. To ensure the accuracy of data submitted, it is mandatory that representatives of Aastrom and of the FDA have access to source documents (i.e., subject medical records, charts, laboratory reports, etc.). Subject confidentiality will be protected at all times.

Aastrom reserves the right to terminate the study for refusal of the Principal Investigator to supply source documentation of work performed in this study.

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Schedule of Laboratory and Clinical Equipment

Item	Supplier	Cat. No.	UNIT QTY:	UNIT/PKG:	PKG:	COST/PKG:	Total Cost:
EQUIPMENT:							
18 degrees C to 50 degrees C thermometer	SP		2	1	2	\$36.00	\$72.00
neg 5 degrees C to 20 degrees C thermometer	SP		2	1	2	\$21.91	\$43.82
P-1000 Pipetman	Gilson		1	1	1	\$219.50	\$219.50
P-200 Pipetman	Gilson		1	1	1	\$219.50	\$219.50
P-20 Pipetman	Gilson		1	1	1	\$219.50	\$219.50
Repeater Pipet	Eppendorf		1	1	1	\$350.00	\$350.00
CPS Processor	Aastrom		1	1	1	\$26,940.00	\$26,940.00
CPS Incubator	Aastrom		5	1	5	\$15,518.00	\$77,590.00
Interim Monitor	Aastrom		1	1	1	\$3,000.00	\$3,000.00
Gas Regulator Assembly	Aastrom		3	1	3	\$360.00	\$1,080.00
Tubing Heat Sealer	Sebra		1	1	1	\$3,298.00	\$3,298.00
Incubator Rack	Metro		2	1	2	\$346.00	\$692.00
							\$113,724.32

EXHIBIT D
SCHEDULE OF CLINICAL TRIAL BUDGET

Item	Cost per patient
- - - - -	- - - - -
Supplies	\$ 190.00
Reagents	167.52
Bone Marrow Transplant Laboratory	630.00
Other	128.00
Labor and fringes	2,454.45
	- - - - -
Subtotal	3,569.97
Indirect	680.03
	- - - - -
Total	\$4,250.00
	=====

Institution shall invoice Aastrom on a monthly basis as patient marrows are harvested and expansion is initiated.

EXHIBIT D
SCHEDULE OF MILESTONE PAYMENTS

COMPENSATION AMOUNT AND SCHEDULE

1. COMPENSATION AMOUNT

Aastrom agrees to provide, according to the terms and conditions set forth herein, and contingent upon the conducting of the Study as specified by the Protocol, a total compensation of Forty Two Thousand Five Hundred US Dollars (\$42,500), or Four Thousand Two Hundred Fifty US Dollars (\$4,250) per subject according to the compensation schedule set forth below in Section 2 of this Exhibit D. The \$4,250 per subject compensation represents any and all compensations associated with the Study. The total compensation amount is based upon the actual number of subjects to be completed and may be adjusted based upon the actual number of subjects actually completed. If a subject is removed from the Study for any reason, payment for that subject will be prorated.

2. COMPENSATION SCHEDULE

The payee identified in Section 3 of this Exhibit D below will be remunerated according to the following schedule:

	Percentage	Amount
		(US DOLLARS)
Initial Payment	25%	\$10,625.00
50% Subjects Completed	25%	\$10,625.00
All Subjects Completed	25%	\$10,625.00
100% Subjects Case Report Forms Completed and Submitted	15%	\$ 6,375.00
Final Report	10%	\$ 4,250.00

3. NAME AND ADDRESS OF PAYEE

Payment made to: Loyola University Medical Center
Dr. Patrick Stiff
Division of Hematology/Oncology
2160 South First Avenue
Cancer Center - Room 240
Maywood, IL 60153

4. TERMINATED STUDY - PAYMENT OBLIGATIONS

If either the Institution of Aastrom terminates the Study prior to its originally planned termination date, Aastrom shall compensate the Institution based upon the portion of the Study completed at the date of termination. This partial payment will be prorated according to the number of satisfactorily completed subject visits.

STOCK PURCHASE COMMITMENT AGREEMENT
(Series F Preferred Stock)

between

AASTROM BIOSCIENCES, INC.

and

COBE LABORATORIES, INC.

October 29, 1996

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EXHIBITS:

- A Amended and Restated Articles of Incorporation
- B Opinion of Legal Counsel to the Company

SCHEDULES:

- 5.5 Litigation
- 6.4 Stock Schedule

STOCK PURCHASE COMMITMENT AGREEMENT
(Series F Preferred Stock)

This Agreement is entered into as of October 29, 1996, by and between Aastrom Biosciences, Inc., a Michigan corporation (the "Company"), and Cobe Laboratories, Inc., a Colorado corporation (the "Purchaser"), with respect to the factual recitals set forth below.

Certain terms used in this Agreement are defined in Section 1 of this Agreement.

RECITALS

A. The Company and the Purchaser previously entered into that certain Stock Purchase Agreement dated as of October 22, 1993 (the "1993 Stock Purchase Agreement"), pursuant to which the Purchaser purchased 10,000 shares of the Company's Series C preferred stock. Pursuant to Section 5.05 of the 1993 Stock Purchase Agreement, the Company has a "put right" which obligates the Purchaser to purchase up to \$5 million of additional capital stock in the Company, under the terms and provisions set forth therein (the "Company's Put Right"). Pursuant to Section 5.04 of the 1993 Stock Purchase Agreement, the Company granted to the Purchaser certain preemptive rights to purchase additional shares of the Company's capital stock when the Company has its initial public offering ("IPO") of stock registered with the Securities and Exchange Commission or another equity financing (the "Purchaser's Preemptive Rights").

B. The Company has prepared Amended and Restated Articles of Incorporation, a copy of which is attached hereto as Exhibit A (the "Amended Articles"), which create 833,333 shares of Series F preferred stock (the "Shares") having rights, privileges and preferences as set forth in the Amended Articles.

WHEREFORE, the parties hereto mutually agree as follows:

1. Definitions.

"1993 Stock Purchase Agreement" is defined in Recital A hereof.

"Advisors" is defined in Section 4.4 hereof.

"Amended Articles" is defined in Recital B hereof.

"Closing" is defined in Sections 3.1 and 3.2 hereof.

"Common Stock" is defined in Section 4.1 hereof.

"Company's Put Right" is defined in Recital A hereof.

"Conversion Shares" is defined in Section 4.1 hereof.

"Disclosure Statement" is defined in Section 4.3 hereof.

"Financial Statements" is defined in Section 4.3 hereof.

"Investors' Rights Agreement" is defined in Section 7 hereof.

"IPO" is defined in Recital A hereof.

"Most Recent Financial Statements" is defined in Section 4.3 hereof.

"Notice to Purchase" is defined in Section 2.3 hereof.

"Prospectus" is defined in Section 4.3 hereof.

"Purchaser's Preemptive Right" is defined in Recital A hereof.

"Qualifying Financing" means any one of the following:

a. the Company entering into (or completing) a term sheet agreement (or other agreement) with investors or an underwriter by December 1, 1997, which provides for: (i) a scheduled closing by February 1, 1998, (ii) a public sale (i.e., an IPO) or private sale of equity securities of the Company, the gross proceeds from which equity sale is to aggregate to at least \$10 million, (iii) the proceeds of the sale are not designated by the investor for specified limited purposes, (iv) the price per share for the sale is set by mutual agreement between the Company and investors who invest at least \$1 million, and (v) the sale of equity securities actually is consummated by February 1, 1998; or

b. the Company entering into (or completing) a term sheet agreement (or other agreement) by December 1, 1997 for the merger or sale of the Company at a value of at least \$85 million, with (i) a scheduled closing for the merger or sale to be by February 1, 1998, and (ii) the merger or sale actually being consummated by February 1, 1998; or

c. the Company's Board of Directors adopting an Operational Plan for the Company to continue its operations in the ordinary course of business

through December 31, 1998, funded by the Company's own cash flow and other resources, without requiring outside equity or debt investment in the Company, and with said Operational Plan being consistent with the intent of the annual Product Development Plan ("PDP") that is part of the Distribution Agreement between the Company and the Purchaser.

"Securities Act" is defined in Section 4.1 hereof.

"Shares" is defined in Recital B hereof.

2. Commitment to Purchase Shares.

2.1. The Purchaser hereby commits to purchase from the Company up to 833,333 shares of Series F preferred stock, at \$6.00 per share, for an aggregate of up to \$5 million cash purchase price, in accordance with the Company's Notice to Purchase and the terms of this Agreement.

2.2. If the Company elects to sell any shares of Series F preferred stock to the Purchaser, in accordance with the terms of this Agreement, the Company shall give to the Purchaser a written notice (the "Notice to Purchase") which specifies the number of shares of Series F preferred stock which the Company is calling upon the Purchaser to purchase, and the scheduled date for the closing of said purchase. The Notice to Purchase may be given any time up through September 1, 1997, and shall specify a Closing date for consummating the purchase to be not less than 90 days after the Notice to Purchase is delivered to the Purchaser.

2.3. The Company may give to the Purchaser not more than two Notices to Purchase, such that the Purchaser is required to purchase the Shares in not more than two increments. Each increment shall be for not less than \$1 million worth of the Shares, and the first increment may be for as much as \$5 million worth of the Shares.

2.4. Upon the Company completing an IPO, the Purchaser's obligation to purchase additional shares of Series F preferred stock will terminate.

3. Closing.

3.1. At each closing (the "Closing") for the purchase and sale of an increment of the Shares pursuant to this Agreement, the parties shall execute and deliver all necessary documents to consummate the Closing as specified by this Agreement, and the Purchaser shall pay the full purchase price for the Shares specified in the Notice to Purchase, with payment by wire transfer to the Company's offices in Ann Arbor, Michigan.

3.2. At the Closing, to be held at the Company's offices in Ann Arbor, Michigan, the Company shall deliver to the Purchaser (a) a stock certificate representing the Shares purchased, (b) a copy of the Amended Articles, evidencing filing with the Corporations and Securities Bureau of the Department of Commerce of the State of Michigan, (c) a certificate signed by the Secretary of the Company evidencing that the necessary actions by the Company's Board of Directors and shareholders have been taken to approve the authorization, issuance and sale of the Shares pursuant to this Agreement, (d) an opinion of legal counsel to the Company substantially in the form attached hereto as Exhibit B, which opinion shall be addressed to the Purchaser and dated the date of the Closing, and (e) a certificate signed by the President of the Company confirming that the representations and warranties of the Company contained in this Agreement remain true and correct in all material respects at and as of the Closing, and that all of the covenants and agreements of the Company contained in this Agreement and required to be performed on or prior to the Closing shall have been performed in all material respects.

4. Representations and Warranties of the Purchaser. In order to induce the Company to sell the Shares to the Purchaser, the Purchaser hereby acknowledges, represents, warrants and agrees as follows:

4.1. None of the Shares of Series F Stock are (and the shares of common stock, no par value ("Common Stock") issuable upon conversion thereof ("Conversion Shares") will not be) registered under the Securities Act of 1933 (as amended, the "Securities Act") or any state securities laws. The Purchaser understands that the sale of the Shares is intended to be exempt from registration under Section 4(2) of the Securities Act and/or the provisions of Regulation D promulgated thereunder, based, in part, upon the representations, warranties and agreements contained in this Agreement.

4.2. Neither the Securities and Exchange Commission nor any state securities commission has approved any of the Shares or passed upon or endorsed the merits of this transaction.

4.3. Prior to its execution of this Agreement, the Purchaser has received from the Company (i) the draft Registration Statement on Form S-1 for the Company dated August, 1996, together with a supplemental update thereto dated October 3, 1996 (collectively called the "Disclosure Statement"), (ii) a copy of the Amended Articles, for the purpose of creating the Series F Stock, and (iii) the audited financial statements of the Company for the year ended June 30, 1996, and the unaudited financial statements of the Company for the month ended September 30, 1996 (the "Most Recent Financial Statements") (collectively, the "Financial Statements").

4.4. The Purchaser acknowledges that all documents, records and books pertaining to the investment in the Shares, including the Disclosure Statement, have been made available for inspection by the Purchaser, or by its attorney, accountant, purchaser representative and/or tax advisor (collectively, the "Advisors") and that the Purchaser and/or its Advisors have completed such review as they deem to be necessary to make the decision to purchase the Shares.

4.5. The Purchaser has reviewed the merits and risks of an investment in the Shares. The Purchaser and the Advisors have had a reasonable opportunity to ask questions of and receive answers from members of management of the Company concerning the offer and sale of the Shares and all such questions have been answered to the full satisfaction of the Purchaser.

4.6. In evaluating the suitability of an investment in the Shares, the Purchaser has not relied upon any representation or other information (oral or written) other than as contained in documents or answers to questions so furnished to the Purchaser or its Advisors by the Company.

4.7. No oral or written representations have been made or oral or written information furnished to the Purchaser or its Advisors in connection with this Agreement which were in any way inconsistent with the information provided to the Purchaser or its Advisors, including the Disclosure Statement.

4.8. The Purchaser, together with the Advisors, have such knowledge and experience in financial, tax and business matters so as to enable each of them to utilize the information made available to each of them in connection with the purchase of the Shares to evaluate the merits and risks of an investment in the Shares and to make an informed investment decision with respect thereto.

4.9. The Purchaser is not relying on the Company with respect to the tax and other economic considerations of an investment in the Shares, and the Purchaser has relied on the advice, or has consulted with, only its own Advisors concerning tax matters.

4.10. The Purchaser is acquiring the Shares solely for its own account, for investment, and not with a view to or for subdivision, resale or distribution, in whole or in part, and no other person has or will have a direct or indirect beneficial interest in the Shares, other than for any partner or shareholder owners of the Purchaser, if any.

4.11. The Purchaser must bear the economic risk of the investment indefinitely because none of the Shares of Series F Stock (or Conversion Shares) may be sold, hypothecated or otherwise disposed of unless (i) subsequently registered under the Securities Act and applicable state securities laws, or (ii) an exemption from registration is available at that time. Legends shall be placed on the Shares (and the Conversion Shares) to the effect that they have not been registered under the Securities Act or applicable state securities laws and appropriate notations thereon will be made in the Company's stock books.

4.12. The Purchaser has adequate means of providing for the Purchaser's current financial needs and foreseeable contingencies and the Purchaser accepts the fact that an investment in the Shares will not be liquid.

4.13. The Purchaser is aware that an investment in the Shares involves a number of very significant risks and, in particular, acknowledges that the Company is in the development stage. The Purchaser understands that the risks associated with an investment in the Shares could result in, and the Purchaser can sustain, a complete loss of its investment.

4.14. The Purchaser is an "accredited investor" as such term is defined in the regulations promulgated under the Securities Act.

4.15. The Purchaser represents that it has full power and authority to execute and deliver this Agreement and all other related agreements and certificates and to carry out the provisions hereof and thereof and to purchase and hold the Shares, and this Agreement is a legal, valid and binding obligation of the Purchaser. The execution and delivery of this Agreement will not violate or be in conflict with any order, judgment, injunction, agreement or controlling document to which the Purchaser is a party or by which it is bound.

4.16. The Purchaser represents to the Company that the information contained herein may be relied upon by the Company in determining the availability of an exemption from registration under federal and state securities laws. The Purchaser further represents and warrants that it will notify the Company immediately upon the occurrence of any material change to the information contained herein occurring prior to the Company's issuance of the Shares.

4.17. The Purchaser is unaware of, and in no way relying on, any form of general solicitation or general advertising in connection with the offer and sale of the Shares.

4.18. The Purchaser agrees that the Shares may not be sold, mortgaged, pledged, hypothecated or otherwise transferred unless the Shares are

registered under the Securities Act and applicable state securities laws or are exempt from registration thereunder; and that the certificate evidencing the Shares will contain a customary Securities Act legend with respect to the foregoing transfer restriction.

5. Representations and Warranties of the Company. The Company represents and warrants to the Purchaser that:

5.1. Organization, Qualifications and Corporate Power. The Company is a corporation duly incorporated, validly existing and in good standing under the laws of the State of Michigan and is duly licensed or qualified to transact business as a foreign corporation and is in good standing in each other jurisdiction in which the nature of the business transacted by it or the character of the properties owned or leased by it requires such licensing or qualification. The Company has the corporate power and authority to own and hold its properties and to carry on its business as now conducted and as proposed to be conducted, to execute, deliver and perform this Agreement, to issue, sell and deliver the Series F Stock, and to issue and deliver the Conversion Shares as provided in the Amended Articles.

5.2. Authorization of Agreement.

a. The execution and delivery by the Company of this Agreement, the performance by the Company of its obligations hereunder, the issuance, sale and delivery of the Series F Stock and the issuance and delivery of the Conversion Shares have been duly authorized by all requisite corporate action and will not violate any provision of law, any order of any court or other agency of government, the Amended Articles or the Bylaws of the Company (the "Bylaws"), or any provision of any indenture, agreement or other instrument to which the Company or any of its properties or assets is bound, or conflict with, result in a breach of or constitute (with due notice or lapse of time or both) a default under any such indenture, agreement or other instrument, or result in the creation or imposition of any lien, charge, restriction, claim or encumbrance of any nature whatsoever upon any of the properties or assets of the Company.

b. The Series F Stock has been duly authorized and, when issued in accordance with this Agreement, will be validly issued, fully paid and nonassessable shares of the Company with no personal liability attaching to the ownership thereof and will be free and clear of all liens, charges, restrictions, claims and encumbrances imposed by or through the Company except as set forth herein. The Conversion Shares have been duly reserved for issuance upon conversion of the Series F Stock and, when so issued, will be duly authorized, validly issued, fully paid and nonassessable shares of Common Stock with no personal liability attaching to the ownership thereof and, so long as the Series F

Stock tendered for conversion is free and clear of liens or encumbrances, will be free and clear of all liens, charges, restrictions, claims and encumbrances imposed by or through the Company except as set forth herein. Neither the issuance, sale or delivery of the Series F Stock nor the issuance or delivery of the Conversion Shares is subject to any preemptive right of stockholders of the Company or to any right of first refusal or other right in favor of any person which right has not been waived.

5.3. Validity. This Agreement has been duly executed and delivered by the Company and constitutes the legal, valid and binding obligation of the Company, enforceable in accordance with its terms.

5.4. Authorized Capital Stock. The authorized capital stock of the Company consists of 12,200,000 shares of Preferred Stock, and 21,500,000 shares of Common Stock. Immediately prior to the Closing, 2,829,735 shares of Common Stock and 9,451,766 shares of Preferred Stock will be validly issued and outstanding, fully paid and nonassessable with no personal liability attaching to the ownership thereof. The stockholders of record and holders of subscriptions, warrants, options, convertible securities, and other rights (contingent or other), if any, to purchase or otherwise acquire equity securities of the Company prior to the Closing Date and the number of shares of Common Stock and the number of such subscriptions, warrants, options, convertible securities, and other such rights, if any, held by each, are as set forth in the Disclosure Statement and/or in Schedule 6.4 attached hereto. The designations, powers, preferences, rights, qualifications, limitations and restrictions in respect of each class of authorized capital stock of the Company are as set forth in the Amended Articles, a copy of which has previously been delivered to the Purchaser, and all such designations, powers, preferences, rights, qualifications, limitations and restrictions are valid, binding and enforceable and in accordance with all applicable laws. Except as set forth in the attached Schedule 6.4 or in the Disclosure Statement, (a) no person owns of record or is known to the Company to own beneficially any share of Common Stock, (b) no subscription, warrant, option, convertible security, or other right (contingent or other) to purchase or otherwise acquire equity securities of the Company is authorized or outstanding and (c) there is no commitment by the Company to issue shares, subscriptions, warrants, options, convertible securities, or other such rights or to distribute to holders of any of its equity securities any evidence of indebtedness or asset. Except as provided for in the Amended Articles or as set forth herein, the Company has no obligation (contingent or other) to purchase, redeem or otherwise acquire any of its equity securities or any interest therein or to pay any dividend or make any other distribution in respect thereof. Except as set forth herein or in the Disclosure Statement, there are no voting trusts or agreements, stockholders agreements, pledge agreements, buy-sell agreements, rights of first refusal, preemptive rights or proxies relating to any securities of the Company (whether or

not the Company is a party thereto). All of the outstanding securities of the Company were issued in compliance with all applicable Federal and state securities laws.

5.5. Litigation.

Except as disclosed in Schedule 5.5 delivered to the Purchaser, there is no (a) action, suit, claim, proceeding or investigation pending or, to the best of the Company's knowledge, threatened against or affecting the Company or its directors, officers, or management, at law or in equity, or before or by any Federal, state, municipal or other governmental department, commission, board, bureau, agency or instrumentality, domestic or foreign, (b) arbitration proceeding relating to the Company pending under collective bargaining agreements or otherwise or (c) governmental inquiry pending or, to the best of the Company's knowledge, threatened against or affecting the Company (including without limitation any inquiry as to the qualification of the Company to hold or receive any license or permit), and, to the best knowledge of the Company, there is no basis for any of the foregoing. Without waiving any applicable attorney-client privilege, the Company has not received any opinion or memorandum or legal advice from legal counsel to the effect that it is exposed, from a legal standpoint, to any liability or disadvantage which may be material to its business, prospects, financial condition, operations, property or affairs. To the best knowledge of the Company, the Company is not in default with respect to any order, writ, injunction or decree known to or served upon the Company of any court or of any Federal, state, municipal or other governmental department, commission, board, bureau, agency or instrumentality, domestic or foreign.

5.6. Financial Statements. The Company has furnished to the Purchaser the Financial Statements. The Financial Statements are true and correct in all material respects and have been prepared in accordance with generally accepted accounting principles. The balance sheets included in the respective Financial Statements accurately reflect the financial condition and all assets and liabilities of the Company at the times referred to therein. The statements of income and cash flows accurately reflect the operations of the Company for the periods referred to therein. There are no undisclosed liabilities in the Financial Statements.

5.7. No Convictions. To the best of the knowledge of the Company, during the past ten (10) years, none of the directors, officers, or management of the Company have been arrested or convicted of any material crime, including any felony (whether material or not), have been indicted, have been bankrupt nor have any of them been restricted in any way from bidding on contracts with the government of the United States.

5.8. Brokers. The Company has no knowledge of any brokerage or finders fee due in conjunction with the transactions contemplated by this Agreement.

5.9. Subsidiaries. The Company has no subsidiaries. The Company does not (a) own of record or beneficially, directly or indirectly: (1) any shares of capital stock or securities convertible into capital stock of any corporation; or (2) any participating interest in any partnership, joint venture or other non-corporate business enterprise; or (b) control, directly or indirectly, any other entity.

5.10. Directors and Officers. The Disclosure Statement sets forth the names of the directors and officers of the Company, together with the title of each such person.

5.11. No Material Adverse Change. Since the date of the Most Recent Financial Statements, (a) there has been no material adverse change in the assets, liabilities or financial condition of the Company from that reflected in the Most Recent Financial Statements, except for changes in the ordinary course of business, and (b) none of the business, prospects, operations, property or affairs of the Company has been materially adversely affected by any occurrence or development, individually or in the aggregate, whether or not insured against.

5.12. Taxes. The Company has filed all tax returns, Federal, state, county and local, required to be filed by it, and the Company has paid all taxes shown to be due by such returns as well as all other taxes, assessments and governmental charges which have become due or payable, including without limitation all taxes which the Company is obligated to withhold from amounts owing to employees, creditors and third parties. All such taxes with respect to which the Company has become obligated pursuant to elections made by the Company in accordance with generally accepted practice have been paid and adequate reserves have been established for all taxes accrued but not yet payable. The Federal income tax returns of the Company have never been audited by the Internal Revenue Service. No deficiency assessment with respect to or proposed adjustment of the Company's Federal, state, county or local taxes is pending or, to the best of the Company's knowledge, threatened. There is no tax lien, whether imposed by any Federal, state, county or local taxing authority, outstanding against the assets, properties or business of the Company. Neither the Company nor, to the Company's knowledge, any of its stockholders, has ever filed consent pursuant to Section 341(f) of the Code, relating to collapsible corporations.

5.13. Employee Benefit Plans. To the knowledge of the Company, each of the Company's employee benefit plans (and each related trust or insurance contract) complies in form and in operation in all respects with the

applicable requirements of the Employee Retirement Income Security Act of 1974 and the Internal Revenue Code of 1986, as amended. To the knowledge of the Company, all required reports and descriptions have been filed or distributed appropriately with respect to each employee benefit plan. There have been no prohibited transactions with respect to any employee benefit plan. No fiduciary has any liability for breach of fiduciary duty or any other failure to act or comply in connection with the administration or investment of the assets of any employee benefit plans. No charge, complaint, action, suit, proceeding, hearing, investigation, claim, or demand with respect to the administration or the investment of the assets of any employee benefit plan (other than routine claims for benefits) is pending or, to the Company's knowledge, threatened. The Company and its directors and officers (and employees with responsibility for employee benefits matters) have no knowledge of any basis for any such charge, complaint, action, suit, proceeding, hearing, investigation, claim, or demand.

5.14. Title to Properties. The Company has good and marketable title to its properties and assets reflected in the Financial Statements or acquired by it since the date of the Financial Statements (other than for equipment leased pursuant to financing leases, and other than properties and assets disposed of in the ordinary course of business since the date of the Financial Statements), and all such properties and assets are free and clear of mortgages, pledges, security interests, liens, charges, claims, restrictions and other encumbrances, except for equipment financing leases, and for liens to secure payment of obligations reflected in the Financial Statements and for current taxes not yet due and payable, and minor imperfections of title, if any, not material in nature or amount and not materially detracting from the value or impairing the use of the property subject thereto or impairing the operations or proposed operations of the Company.

5.15. Leasehold Interests. Each lease or agreement to which the Company is a party under which it is a lessee of any property, real or personal is a valid and enforceable agreement without any material default of the Company thereunder and, to the best of the Company's knowledge, without any default by the Company of any material term thereunder; the Company has not been notified of any default and has no reason to believe that it is in default of any term thereunder. To the best of the Company's knowledge, no other party to any such lease or agreement is in default of a material term thereunder. No event has occurred and is continuing which, with due notice or lapse of time or both, would constitute a default or event of default by the Company under any such lease or agreement or, to the best of the Company's knowledge, by any other party thereto. The Company's possession of such property has not been disturbed and, to the best of the Company's knowledge, no claim has been asserted against the Company adverse to its rights in such leasehold interests.

5.16. Insurance. The Company maintains as to its properties and business, with financially sound and reputable insurers, insurance against such casualties and contingencies and of such types and in such amounts as is customary for companies similarly situated.

5.17. Other Agreements. With respect to each material contract to which the Company is a party, the Company and, to the best of the Company's knowledge, each other party thereto, have in all material respects performed all the obligations required to be performed by them to date, have received no notice of default and are not in default (with due notice or lapse of time or both) under any material lease, agreement or contract now in effect to which the Company is a party or by which it or its property may be bound. The Company has no present expectation or intention of not fully performing all its obligations under each such material lease, contract or other agreement and the Company has no knowledge of any breach or anticipated breach by the other party to any contract or commitment to which the Company is a party.

5.18. Patents, Trademarks, Etc.

a. The Disclosure Statement describes all material patents, patent rights, patent applications, trademarks, trademark applications, service marks, service mark applications, trade names and copyrights, and all material applications for such which are in the process of being prepared, owned by or registered in the name of the Company, or of which the Company is a licensor or licensee or in which the Company has any right, and in each case a brief description of the nature of such right. The Disclosure Statement contains an accurate and complete description of all material licenses. The Company is in compliance in all material respects with each of such licenses. The Company owns or possesses adequate licenses or other rights to use all patents, patent applications, trademarks, trademark applications, service marks, service mark applications, trade names, copyrights, manufacturing processes, formulae, trade secrets and know how (collectively, "Intellectual Property") necessary to the conduct of its business as conducted, and no claim is pending or, to the best of the Company's knowledge, threatened to the effect that the operations of the Company infringe upon or conflict with the asserted rights of any other person under any Intellectual Property, and, to the best knowledge of the Company, there is no basis for any such claim (whether or not pending or threatened). No claim is pending or threatened to the effect that any such Intellectual Property owned or licensed by the Company, or which the Company otherwise has the right to use, is invalid or unenforceable by the Company, or that the Company is not in compliance with any term or condition of a license, and there is no basis for any such claim (whether or not pending or threatened). The Company has not granted or assigned to any other person or entity any right to manufacture, have manufactured, assemble or sell the products or proposed products or to provide

the services or proposed services of the Company except as set forth in the Disclosure Statement.

b. The Company has taken reasonable security measures to protect the secrecy, confidentiality, and value of the Company's trade secrets; any of their employees and any other persons who, either alone or in concert with others, developed, invented, discovered, derived, programmed, or designed these secrets, or who have knowledge of or access to information relating to them, have entered into agreements protecting the confidentiality thereof.

5.19. Proprietary Information of Third Parties. To the best of the Company's knowledge, no third party has claimed or has reason to claim that any person employed by or affiliated with the Company has (a) violated or may be violating any of the terms or conditions of his employment, non-competition or nondisclosure agreement with such third party, (b) disclosed or may be disclosing or utilized or may be utilizing any trade secret or proprietary information or documentation of such third party or (c) interfered or may be interfering in the employment relationship between such third party and any of its present or former employees. No third party has requested information from the Company which suggests that such a claim might be contemplated. To the best of the Company's knowledge, no person employed by or affiliated with the Company has employed or proposes to employ any trade secret or any information or documentation proprietary to any former employer, and to the best of the Company's knowledge, no person employed by or affiliated with the Company has violated any confidential relationship which such person may have had with any third party, in connection with the development, manufacture or sale of any product or proposed product or the development or sale of any service or proposed service of the Company, and the Company has no reason to believe there will be any such employment or violation. To the best of the Company's knowledge, none of the execution or delivery of this Agreement, or the carrying on of the business of the Company as officers, employees or agents by any officer, director or key employee of the Company, or the conduct or proposed conduct of the business of the Company, will conflict with or result in a breach of the terms, conditions or provisions of or constitute a default under any contract, covenant or instrument under which any such person is obligated.

5.20. Compliance With Law. To the best of the Company's knowledge, the Company has complied with all laws, rules, regulations and orders applicable to its business, operations, properties, assets, products and services, the violation of which would have a material adverse effect upon the Company, and the Company has all necessary permits, licenses and other authorizations required to conduct its business as it is now conducted. To the best of the Company's knowledge, there is no existing law, rule, regulation or order, and the

Company after due inquiry is not aware of any proposed law, rule, regulation or order, whether Federal or state, which would prohibit or restrict the Company from, or otherwise materially adversely affect the Company in, conducting its business, in which it is now conducting business or in which it proposes to conduct business, other than the customary governmental approvals required for medical products. Without limiting the foregoing in any manner, to the best of the Company's knowledge, the Company has complied in all material respects with all applicable laws relating to the employment of labor, including provisions relating to wages, hours, equal opportunity, collective bargaining and the payment of Social Security and other taxes, with the Employee Retirement Income Security Act of 1974, as amended, with the Occupational Health and Safety Act, and with the Americans With Disabilities Act. To the best of the Company's knowledge, the Company is in full compliance with the Immigration Reform and Control Act of 1986, as amended, and all key employees who are not United States citizens are currently authorized under United States immigration laws to hold United States employment and will continue to have such employment authorization throughout the term of the Series F Stock investment, and are otherwise in compliance with United States immigration laws.

5.21. Loans and Advances. The Company does not have any outstanding loans or advances to any person and is not obligated to make any such loans or advances, except as reflected on the Financial Statements, and except, in each case, for advances to employees of the Company in respect of reimbursable business expenses anticipated to be incurred by them in connection with their performance of services for the Company. In the near future, the Company expects to borrow funds from the State Treasurer of the State of Michigan pursuant to a pending convertible loan commitment, as described in Section 12 hereof.

5.22. Assumptions, Guaranties, Etc. of Indebtedness of Other Persons. Except as disclosed in the Financial Statements, the Company has not assumed, guaranteed, endorsed or otherwise become directly or contingently liable on any indebtedness of any other person (including, without limitation, liability by way of agreement, contingent or otherwise, to purchase, to provide funds for payment, to supply funds to or otherwise invest in the debtor, or otherwise to assure the creditor against loss), except for guaranties by endorsement of negotiable instruments for deposit or collection in the ordinary course of business.

5.23. Governmental Approvals. Subject to the accuracy of the representations and warranties of the Purchaser set forth in Section 4, no registration or filing with, or consent or approval of or other action by, any Federal, state or other governmental agency or instrumentality is or will be necessary for the valid execution, delivery and performance by the Company of this Agreement, the issuance, sale and delivery of the Series F Stock or, upon conversion of the Series F Stock, the issuance and delivery of the Conversion Shares, other than (a) filings pursuant to state securities laws (all of which filings have been or will be made by the Company) in connection with the sale of the Series F Stock and (b) with respect to the Registration Rights as set forth in Section 7 hereof, the registration of the shares covered thereby with the Commission and filings pursuant to state securities laws.

5.24. Disclosure. The Company's Disclosure Statement, contains only true and accurate facts and representations, and does not contain any untrue information and does not omit any material fact necessary to make the statements contained therein not misleading. Neither this Agreement, nor any Schedule or Exhibit to this Agreement, contains an untrue statement of a material fact or omits a material fact necessary to make the statements contained herein or therein not misleading. None of the statements, documents, certificates or other items prepared or supplied by the Company with respect to the transactions contemplated hereby contains an untrue statement of a material fact or omits a material fact necessary to make the statements contained therein not misleading. As of the date hereof, no facts have come to the attention of the Company which would, in its opinion, require the Company to revise or amplify the Disclosure Statement.

5.25. Offering of Shares. This Agreement is being made by the Company pursuant to an exemption from the registration requirements of the Securities Act.

5.26. Transactions With Affiliates. Except as set forth in the Disclosure Statement, no director, officer, employee or stockholder of the Company, or member of the family of any such person, or any corporation, partnership, trust or other entity in which any such person, or any member of the family of any such person, has a substantial interest in or is an officer, director, trustee, partner or holder of more than 5% of the outstanding capital stock thereof, is a party to any transaction with the Company, including any contract, agreement or other arrangement providing for the employment of, furnishing of services by, rental of real or personal property from or otherwise requiring payments to any such person or firm.

6. Covenants of the Company.

6.1. Ordinary Course of Business. From the date hereof through the last Closing under this Agreement, the Company shall continue to operate the Company's business in the ordinary course, expecting only for any extraordinary activity as may be approved by the Company's Board of Directors.

6.2. Updated Information. From the date hereof through the last Closing under this Agreement, the Company shall promptly inform the Purchaser of any new facts or circumstances which come to the attention of the Company and which are likely to have any material adverse effect on the Company or which constitute any material adverse variation from the representations made by the Company herein.

6.3. Board of Directors Seat. From the date hereof and continuing so long as the Purchaser owns at least 15% of the issued and outstanding common stock of the Company (calculated on the basis of all preferred stock being converted into common stock pursuant to the conversion formula set forth in the Company's Restated Articles of Incorporation), the Company will use reasonable and good faith efforts to cause to be elected as a member of the Company's Board of Directors one person nominated by the Purchaser; provided that the Board of Directors determines in the exercise of its fiduciary duties that the Purchaser's nominee is qualified to serve on the Board. If the Board so determines that the nominee is not qualified, then the Purchaser may make further nominations until the Board determines that the nominee is qualified.

7. Stock Registration Rights. The Shares shall be entitled to the benefits and subject to the terms of the stock registration rights provisions as set forth in Sections 2.4 through 2.14, inclusive, of the Company's Amended and Restated Investors' Rights Agreement dated as of April 7, 1992, as amended (the "Investors' Rights Agreement"), a copy of which has been furnished to the Purchaser.

8. Market Stand-off Restriction. The Purchaser (and any other holders of the Shares) shall abide by the 180-day "market stand-off" restriction on the sale of the Shares following the Company's public stock offering, as applicable to all other holders of the Company's preferred stock, and/or as required by the Investors' Rights Agreement.

9. Information Rights. The holder(s) of the Shares shall be entitled to receive the Company's information and financial statements as specified in Sections 3.1 through 3.7, inclusive, of the Investors' Rights Agreement.

10. Company's Put Right. To the extent that the Purchaser purchases shares of Series F preferred stock pursuant to this Agreement, the Purchaser's obligations under the Company's Put Right (as specified in Section 5.05 of the 1993 Stock Purchase Agreement) shall be reduced on a dollar for dollar basis. For example, if the Purchaser purchases \$1 million of Series F preferred stock pursuant to the terms of this Agreement, then the Purchaser's obligation under the Company's Put Right shall be reduced from \$5 million to \$4 million.

11. Purchaser's Preemptive Rights. To the extent that the Purchaser purchases shares of Series F preferred stock pursuant to this Agreement, the shares of Series F Preferred Stock purchased by the Purchaser will be excluded from the determination of the Purchaser's percentage ownership of the Company for purposes of calculating the Purchaser's Preemptive Rights (as granted pursuant to Section 5.04 of the 1993 Stock Purchase Agreement).

12. Condition. The Purchaser's obligations under this Agreement are conditional upon the Company also entering into a Convertible Loan Commitment Agreement with the State Treasurer of the State of Michigan for \$5,000,000, in substantially the same form and substance as was approved by the Company's Board of Directors in September 1996.

13. General Provisions.

13.1. Irrevocability; Binding Effect. The Purchaser hereby acknowledges and agrees that the commitment hereunder is irrevocable by the Purchaser, except as required by applicable law, and that this Agreement shall be binding upon and inure to the benefit of the parties and their respective successors, legal representatives, and permitted assigns.

13.2. Modification. This Agreement shall not be modified or waived except by an instrument in writing signed by the party against whom any such modification or waiver is sought.

13.3. Notices. A notice or other communication required or permitted to be given hereunder shall be in writing and shall be given by any means, including without limitation, mail, express delivery service, or facsimile. Any notice or other communication shall be deemed given at the time it is received at the party's address set forth on the signature page of this Agreement, or at such other address as the party shall have furnished in writing in accordance with the provisions of this Section 13.3.

13.4. Assignability. This Agreement and the rights, interests and obligations hereunder are not transferable or assignable by the Purchaser,

except to an affiliate of the Purchaser who qualifies as an "accredited investor," and the Purchaser further agrees that the transfer or assignment of the Shares shall be made only in accordance with all applicable laws.

13.5. Applicable Law. This Agreement shall be governed by and construed in accordance with the internal laws of the state of Michigan without regard to its conflicts of laws principles.

13.6. Confidentiality. The Purchaser acknowledges and agrees that any information or data it has acquired from or about the Company, including the information contained in the Disclosure Statement and the Financial Statements, but excluding any information which was in the public domain, was received in confidence. The Purchaser agrees not to divulge, communicate or disclose, except as may be required by law or for the performance of this Agreement, or use to the detriment of the Company or for the benefit of any other person or persons, or misuse in any way, any confidential information of the Company, including any scientific, technical, trade or business secrets of the Company and any scientific, technical, trade or business materials that are treated by the Company as confidential or proprietary, including, but not limited to, ideas, discoveries, inventions, developments and improvements belonging to the Company and confidential information obtained by or given to the Company about or belonging to third parties.

13.7. Entirety. This Agreement, together with the Exhibits, Schedules and other documents referenced herein, constitutes the entire agreement between the Purchaser and the Company with respect to the purchase and sale of the Series F Shares, and supersedes all prior oral or written agreements and understandings, if any, relating thereto. The terms and provisions of this Agreement may be waived, or consent for the departure therefrom granted, only by a written document executed by the party entitled to the benefits of such terms or provisions.

13.8. Survival. The Purchaser's representations and warranties made in this Agreement shall survive the execution and delivery hereof and of the Shares.

13.9. Expenses. Each of the parties hereto shall pay its own fees and expenses (including the fees of any attorneys, accountants, appraisers or others engaged by such party) in connection with this Agreement and the transactions contemplated hereby whether or not the transactions contemplated hereby are consummated.

13.10. Construction. All pronouns and any variations thereof used herein shall be deemed to be to the masculine, feminine, neuter, singular or

plural as the identity of the person or persons referred to may require. Paragraph titles are for descriptive purposes only and shall not control or alter the meaning of this Agreement as set forth in the text.

13.11. Severability. Each provision of this Agreement shall be considered separable and if for any reason any provision or provisions hereof are determined to be invalid or contrary to applicable law, such invalidity shall not impair the operation of or affect the remaining portions of this Agreement, so long as the material economic benefits remain enforceable.

13.12. Counterparts. This Agreement may be executed in one or more counterparts each of which shall be deemed an original, but all of which shall together constitute one and the same instrument. Signatures may be transmitted by facsimile.

IN WITNESS WHEREOF, the parties have executed and delivered this Agreement as of the date set forth on the first page of this Agreement.

COMPANY:

Aastrom Biosciences, Inc.,
a Michigan corporation
Domino's Farms, Lobby L
24 Frank Lloyd Wright Drive
Ann Arbor, MI 48105
Fax: 313/930-5546

By: /s/ R. Douglas Armstrong

R. Douglas Armstrong, Ph.D.,
President

PURCHASER:

Cobe Laboratories, Inc.,
a Colorado corporation
1185 Oak Street
Lakewood, CO 80215
Fax: 303/230-4195

By: /s/ Edward C. Wood

Litigation

1. R. M. Schwartz. The Company has written letters to a former employee, Richard M. Schwartz, Ph.D. and Dr. Schwartz's new employer, SyStemix, (i) reminding them of Dr. Schwartz's duty to maintain strict confidentiality as to the Company's trade secrets; and (ii) asking if there has been any breach of this confidentiality obligation; and (iii) commenting that a new invention by Systemix's appears to be derived from the Company's trade secrets. Systemix and Dr. Schwartz have denied any use of the Company's trade secrets. The Company has reserved its rights in this matter, but does not presently contemplate pursuing this potential claim in the near future.

2. Sundberg-Ferar. The Company has commenced an arbitration proceeding against Sundberg-Ferar ("S-F") for what the Company asserts to be a breach by S-F of the contractual obligations of S-F to not solicit away from the Company's employment its employees. This arbitration is for the Company to seek damages recovery from S-F, although if the Company is not successful in this arbitration, then S-F may seek to recover its attorney's fees incurred in defending the arbitration proceedings.

SCHEDULE 6.4

Stock Schedule

	Shares Issued and Outstanding	Shares Authorized
Preferred Stock		
Series A	2,500,000	2,500,000
Series B	3,030,000	3,030,000
Series C	10,000	10,000
Series D	2,500,001	3,000,000
Series E	1,617,647	1,617,647
Series F	*833,333	833,333
Undesignated	---	1,209,020
Subtotals:	10,490,981	12,200,000
Common Stock	2,829,735	21,500,000

* Shares to be sold to Cobe Laboratories, Inc., pursuant to this Agreement.

CONVERTIBLE LOAN COMMITMENT AGREEMENT

This Agreement is entered into as of October 15, 1996, by and between Aastrom Biosciences, Inc., a Michigan corporation (the "Company"), and The State Treasurer of the State of Michigan, Custodian of the Michigan Public School Employees' Retirement System, State Employees' Retirement System, Michigan State Police Retirement System, and Michigan Judges Retirement System (the "State"), as follows:

1. Definitions.

"Funding Request" is defined in Section 2.3 hereof.

"IPO" shall mean an initial public offering of stock by the Company which is registered with the United States Securities and Exchange Commission, resulting in the sale of securities aggregating to at least \$10 million.

"Loan" or "Loans" are described in Section 2 hereof.

"Maturity Date" is defined in Section 2.5 hereof.

"Qualifying Financing" shall mean any one of the following:

i. the Company entering into (or completing) a term sheet agreement (or other agreement) with investors or an underwriter by the Maturity Date, which provides for: (a) a scheduled closing by February 1, 1998, (b) a public sale (i.e., an IPO) or private sale of equity securities of the Company, the gross proceeds from which equity sale is to aggregate to at least \$10 million, (c) the proceeds of the sale are not designated by the investor for specified limited purposes, (d) the price per share for the sale is set by mutual agreement between the Company and new investors who invest at least \$1 million, and (e) the sale of equity securities actually is consummated by February 1, 1998; or

ii. the Company entering into (or completing) a term sheet agreement (or other agreement) by the Maturity Date for the merger or sale of the Company at a value of at least \$85 million, with (a) a scheduled closing for the merger or sale to be by February 1, 1998, and (b) the merger or sale actually is consummated by February 1, 1998; or

iii. the Company's Board of Directors adopting an Operational Plan for the Company to continue its operations in the ordinary course of business through December 31, 1998, funded by the Company's own cash flow and other resources, without requiring outside equity or debt investment in the Company.

2. Loan Commitment.

2.1. In accordance with and subject to the terms of this Agreement, the State agrees to make Loans to the Company, in accordance with Funding Requests, up to an aggregate principal balance owing on the Loans not to exceed \$5 million.

2.2. Each Loan shall be for an amount not less than \$1 million principal.

2.3. Each Funding Request shall be in writing and shall be submitted by the Company to the State requesting a Loan to be made from the State to the Company in 45 days from the date of the Funding Request (or such longer period as may be specified by the Company). The Company may not submit a Funding Request prior to October 15, 1996, nor after September 1, 1997. The Company may not submit more than three (3) Funding Requests.

2.4. As a precondition to the Company's first Funding Request, the Company must first have requested and obtained (or be in the process of obtaining) all of the \$5 million equity investment from Cobe Laboratories, Inc. ("Cobe") for purchasing Series F preferred stock.

2.5. Each Loan shall be evidenced by a promissory note signed and delivered by the Company to the State, specifying the principal amount of the Loan as specified in the Funding Request, in the form of the promissory note attached hereto as Exhibit A. As specified in more detail in said promissory note, (a) simple interest shall accrue at 10% per annum and be payable with principal at maturity, (b) the Company shall have an option to prepay any or all of the principal and/or accrued interest at any time, without penalty, (c) in lieu of the Company repaying the promissory note in cash, the Company shall have the option to satisfy the promissory note by converting any unpaid principal and accrued interest owing on the promissory note into equity stock of the Company, in accordance with the provisions set forth in the promissory note, (d) if the Company does not elect to convert the promissory note into equity, then all principal and accrued interest owing on the promissory note shall mature and be fully due and payable on the Maturity Date, which shall be the earlier of (i) 60 days following consummation of the Company's IPO or Qualifying Financing or (ii) 12 months following the date when the State makes the first Loan to the Company, and all promissory notes shall have this same Maturity Date, (e) the Company's obligations on the promissory notes shall be senior to or in parity with all other unsecured debt owed by the Company, and (f) within 15 days following completion of an IPO or Qualifying Financing, the Company shall give written notice to the State specifying whether the Company will (i) repay the promissory note at the Maturity Date, or (ii) convert the promissory note into equity stock of the Company.

2.6. The parties acknowledge that the Company is obligated, pursuant to previously existing agreements, to offer to many of the Company's existing shareholders the right to participate and invest in the same convertible debt commitment as is set forth in this Agreement. In the event any of the Company's other shareholders elect to so participate, then the \$5 million level of the State's commitment shall be reduced on a dollar for dollar basis by each dollar committed by another shareholder for this convertible debt investment. The number of Commitment Stock Warrants (hereinafter described) grant to the State shall also be reduced on a prorata basis to the extent the Company's other shareholders elect to so participate. For example, if the other shareholders commit in the aggregate to \$1 million convertible debt on the same terms as set forth in this Agreement, then the State's commitment level pursuant to this Agreement shall be reduced from \$5 million to \$4 million, and the Commitment Stock Warrant shall be reduced from 104,167 warrant shares to 83,334 warrant shares (i.e., a one-fifth reduction).

2.7. Once the Company has submitted a Funding Request to the State in accordance with the foregoing, and met the conditions as specified in Section 3 hereof, the State shall make the requested loan to the Company by wiring funds to the Company's bank account, pursuant to wire transfer instructions furnished to the State by the Company.

2.8. Upon the Company completing an IPO, the State's obligation to make further loan advances will terminate.

3. Conditions for Each Loan. As a condition to the State's

obligation to make each Loan in accordance with the Company's Funding Request, the Company shall submit to the State the following:

a. the promissory note for said Loan, duly signed by the Company, with authority for the State to insert the date on said promissory note when the State advances the Loan proceeds to the Company;

b. a certificate signed by the President and the Chief Financial Officer of the Company certifying that, (i) the Company is not in material default under any of the Company's material obligations, and (ii) to the best of their knowledge and belief, all items of the information furnished to the State (via Joseph Taylor or such other representative as may be designed by the State), including without limitation, financial statements, minutes of Board meetings, draft Registration Statement on Form S-1 for the Company, dated August 1996, as supplemented by an update dated as of October 3, 1996 (collectively called the "Disclosure Statement"), and all other written materials and oral information, remain true and correct, and, when read together, do not contain any untrue statement of a material fact or omit to state a material fact necessary in order to make the statements contained therein not misleading, and (iii) the Company's

Board of Directors has authorized the officers of the Company to execute and deliver the promissory note, and (iv) the Company has previously requested and obtained (or is in the process of obtaining) \$5 million of equity funding from Cobe pursuant to that certain Stock Purchase Commitment Agreement between Cobe and the Company.

4. Equity Conversion. In lieu of the Company repaying the promissory

notes in cash, the Company shall have the option to convert any unpaid principal and interest owing on the promissory notes into equity stock of the Company, in accordance with the following provisions:

a. if, by the Maturity Date, the Company has an IPO or another Qualifying Financing, then the Company has the option to convert the principal and interest owing on the promissory notes into the Company's capital stock, consisting of common stock issued pursuant to the IPO or the preferred stock or other equity issued by the Company pursuant to the Qualifying Financing, at a conversion price equal to 90% of the price paid by the other investors in the IPO or Qualifying Financing (without deduction for underwriter's commissions and discounts).

b. if, by the Maturity Date, the Company has not yet had an IPO or another Qualifying Financing, and if the Company does not repay the promissory notes in cash by the Maturity Date, then the principal and accrued interest owing on the promissory notes shall be converted into a new series of the Company's preferred stock (to be designated as Series G preferred stock), at \$4.65 per share, which preferred stock shall have a liquidation preference and conversion price of \$4.65 per share, with a liquidation preference senior to all other preferred stock existing at the time of issuance of the Series G preferred stock, and with other rights, preferences and privileges comparable to the Company's Series E preferred stock. Said Series G preferred stock will include a customary weighted average anti-dilution protection provision applicable to the Company's next following sale of preferred stock of at least \$1 million to new investors.

c. In the event the "Qualifying Financing" is an "Operational Plan" as described in subparagraph (iii) of the definition of a Qualifying Financing, , then the equity securities into which the principal and interest owing on the promissory notes shall be converted pursuant to Section 4 hereof shall be a new series of the Company's preferred stock (Series G) having rights, preferences and privileges comparable to those of the Company's Series E preferred stock, but with a conversion price and liquidation preference being equal to 90% of the then current fair market value of the Company's then most recently issued preferred stock sold to cash investors (excluding stock sold to RPR), and with a liquidation preference senior to all other preferred stock existing at the time of issuance of the Series G preferred stock. Said fair market value of said preferred stock shall be determined by mutual agreement between the Company and the State, but if no

mutual agreement can be reached, then said fair market value shall be determined by a nationally recognized investment banking firm which is mutually selected by the Company and the State, with the fees for obtaining said valuation determination to be borne equally by the Company and the State. Said Series G preferred stock will include a customary weighted average anti-dilution protection provision applicable to the Company's next following sale of preferred stock of at least \$1 million to new investors.

5. Stock Warrants.

5.1. As consideration for the State entering into this Agreement for a \$5 million commitment, the Company shall issue to the State a stock warrant (the "Commitment Stock Warrant") entitling the State to purchase up to 104,167 shares of the Company's common stock (subject to reduction as specified in Section 2.6 hereof), on the following terms:

i. the exercise price shall be the lesser of:

(a) \$6.00 share, increasing by \$2.00 per share on each anniversary of the date the Company completes its IPO; or

(b) 85% of the fair market value of the Company's stock at the time the stock warrant is exercised, which value shall be determined as follows:

(1) if the Company's common stock is traded in the public stock market at the time the stock warrant is exercised, then said fair market value shall be the public trading price, calculated using the average of the last trading price of the day for the 20 trading days preceding the date of exercise.

(2) if the exercise of the stock warrant is made prior to the Company completing an IPO, then said fair market value shall be the fair market value of the Company's then most recently issued preferred stock sold to cash investors (excluding stock sold to RPR), determined by mutual agreement between the Company and the State. If no such mutual agreement is reached, then the fair market value of said preferred stock shall be determined by a nationally recognized investment banking firm which is mutually selected by the Company and the State, with the fees for such determination to be borne equally between the Company and the State.

ii. The warrant shall become exercisable any time after the earlier of (a) 90 days after the Company completes its IPO or a Qualifying Financing, or (b) October 15, 1999 (provided that this date is not within 90 days

after the IPO is completed, in which event the warrant shall be exercisable at the end of said 90 days).

iii. The warrant shall expire on October 15, 2000, to the extent it has not been exercised prior thereto.

5.2. In addition to the Commitment Stock Warrant, the Company shall also issue to the State a "Funding Stock Warrant" applicable to each increment of Loan funding advanced by the State to the Company pursuant to Section 2 above, based upon a 7.5% coverage formula, namely: 12,500 warrant shares for each \$1 million of principal Loan funds advanced, or an aggregate of 62,500 warrant shares if all \$5 million of Loan funds are advanced. The terms of said Funding Stock Warrants shall be the same as the terms of the above-described Commitment Stock Warrant.

5.3. The form of the Commitment Stock Warrant and the Funding Stock Warrant shall be as set forth on Exhibit B attached hereto.

6. Piggyback Stock Registration Rights. The shares to be issued by

the Company to the State pursuant to the conversion of the Loan into equity (Section 4 above), and upon exercise of the stock warrants (Section 5 above), shall have piggyback stock registration rights comparable to those given by the Company to the holders of the Company's Series E preferred stock.

7. General Provisions.

7.1. Irrevocability; Binding Effect. The State hereby acknowledges

and agrees that the commitment hereunder is irrevocable by the State, except as required by applicable law, and that this Agreement shall be binding upon and inure to the benefit of the parties and their respective successors, legal representatives, and permitted assigns.

7.2. Modification. This Agreement shall not be modified or waived

except by an instrument in writing signed by the party against whom any such modification or waiver is sought.

7.3. Notices. A notice or other communication required or permitted

to be given hereunder shall be in writing and shall be given by any means, including without limitation, mail, express delivery service, or facsimile. Any notice or other communication shall be deemed given at the time it is received at the party's address set forth on the signature page of this Agreement, or at such other address as the party shall have furnished in writing in accordance with the provisions of this Section 7.3.

7.4. Assignability. This Agreement and the rights, interests and

obligations hereunder are not transferable or assignable by the State, except to an affiliate of the State who qualifies as an "accredited investor". However, the promissory notes, stock warrants and stock issued by the Company to the State may be assigned by the State in accordance with their terms and in accordance with all applicable laws.

7.5. Applicable Law. This Agreement shall be governed by and

construed in accordance with the internal laws of the State of Michigan, without regard to its conflicts of laws principles.

7.6. Confidentiality. The State acknowledges and agrees that any

information or data it has acquired from or about the Company, not otherwise properly in the public domain, was received in confidence. The State agrees not to divulge, communicate or disclose, except as may be required by law or for the performance of this Agreement, or use to the detriment of the Company or for the benefit of any other person or persons, or misuse in any way, any confidential information of the Company, including any scientific, technical, trade or business secrets of the Company and any scientific, technical, trade or business materials that are treated by the Company as confidential or proprietary, including, but not limited to, ideas, discoveries, inventions, developments and improvements belonging to the Company and confidential information obtained by or given to the Company about or belonging to third parties.

7.7. Entirety. This Agreement, together with the Exhibits and other

documents referenced herein, constitutes the entire agreement between the State and the Company with respect to the transactions described herein, and supersedes all prior oral or written agreements and understandings, if any, relating thereto. The terms and provisions of this Agreement may be waived, or consent for the departure therefrom granted, only by a written document executed by the party entitled to the benefits of such terms or provisions.

7.8. Construction. All pronouns and any variations thereof used

herein shall be deemed to be to the masculine, feminine, neuter, singular or plural as the identity of the person or persons referred to may require. Paragraph titles are for descriptive purposes only and shall not control or alter the meaning of this Agreement as set forth in the text.

7.9. Severability. Each provision of this Agreement shall be

considered separable and if for any reason any provision or provisions hereof are determined to be invalid or contrary to applicable law, such invalidity shall not impair the operation of or affect the remaining portions of this Agreement, so long as the material economic benefits remain enforceable.

7.10. Counterparts. This Agreement may be executed in one or more

counterparts each of which shall be deemed an original, but all of which shall together constitute one and the same instrument. Signatures may be transmitted by facsimile.

IN WITNESS WHEREOF, the parties have executed and delivered this Agreement as of the date set forth above.

COMPANY:

AASTROM BIOSCIENCES, INC.,
a Michigan corporation
Domino's Farms, Lobby L
24 Frank Lloyd Wright Drive
Ann Arbor, MI 48105
Fax: 313/930-5546

STATE:

THE STATE TREASURER OF THE STATE OF MICHIGAN,
Custodian of the Michigan Public School
Employees' Retirement System, State Employees'
Retirement System, Michigan State Police
Retirement System, and Michigan Judges
Retirement System
430 W. Allegan St.
Lansing, MI 48922
Fax: 517/335-3668

By: /s/ R. Douglas Armstrong

By: /s/ Paul E. Rice

EXHIBIT A

Promissory Note

PROMISSORY NOTE

\$ _____

Ann Arbor, Michigan
_____, 199__

1. Obligation. Aastrom Biosciences, Inc., a Michigan corporation

("Maker"), for value received, hereby promises to pay to the order of The State Treasurer of the State of Michigan, Custodian of the Michigan Public School Employees' Retirement System, State Employees' Retirement System, Michigan State Police Retirement System, and Michigan Judges Retirement System ("Lender"), at Ann Arbor, Michigan, or at such other place as the holder hereof may in writing direct, the loan advances made from Lender to Maker, in the principal sum of _____ (\$ _____), together with interest thereon, at the rate, and due and payable, as set forth below. Maker's obligations on this Promissory Note shall be senior to or in parity with all other unsecured debt owed by Maker.

2. Series of Promissory Notes. This Promissory Note is one of a series

of promissory notes of Maker being issued to Lender in pursuant to the Convertible Loan Commitment Agreement dated _____, 1996, by and between Lender and Maker (the "Loan Agreement"). Capitalized terms not otherwise defined in this Promissory Note shall have the meanings given to such terms in the Loan Agreement.

3. Interest. The outstanding principal balance shall bear interest from

the date of disbursement to Maker at the rate of ten (10%) per annum, simple interest, until repaid in full. Accrued interest under this Promissory Note shall be payable at the Maturity Date, as specified herein. If interest is not be paid when due, it shall thereafter bear interest at the same rate as principal bears interest.

4. Maturity Date. The entire unpaid principal balance and all unpaid

accrued interest shall be due and payable on the "Maturity Date", which shall be the earlier to occur of (i) sixty (60) days following consummation of Maker's IPO or Qualifying Financing; or (ii) _____, 199__.

5. Prepayment. Maker shall have the option to prepay any or all of the

principal and/or accrued interest owing on this Promissory Note at any time, without penalty or premium.

6. Conversion to Equity.

a. Within 15 days following completion of an IPO or a Qualifying Financing, Maker shall give written notice to Lender specifying whether Maker will (1) repay this Promissory Note at the Maturity Date, or (2) convert this Promissory Note into equity stock pursuant to Section 6b hereof.

b. In lieu of Maker repaying this Promissory Note in cash, Maker shall have the option to convert any unpaid principal and interest owing on this Promissory Note into equity stock of Maker, in accordance with the following provisions:

(i) if, by the Maturity Date, Maker has an IPO or a Qualifying Financing (as defined below), then Maker has the option to convert the principal and interest owing on this Promissory Note into Maker's capital stock, consisting of common stock issued pursuant to the IPO or the preferred stock or other equity issued by Maker pursuant to the Qualifying Financing, at a conversion price equal to 90% of the price paid by the other investors in the IPO or Qualifying Financing (without deduction for underwriter's commissions and discounts).

(ii) if, by the Maturity Date, Maker has not yet had an IPO or a Qualifying Financing, and if Maker does not repay this Promissory Note in cash by the Maturity Date, then the principal and accrued interest owing on this Promissory Note shall be converted into a new series of Maker's preferred stock (to be designated as Series G preferred stock), at \$4.65 per share, which preferred stock shall have a liquidation preference and conversion price of \$4.65 per share, with a liquidation preference senior to all other preferred stock of Maker, and with other rights, preferences and privileges comparable to Maker's Series E preferred stock. Said Series G preferred stock will include a customary weighted average anti-dilution protection provision applicable to Maker's next following sale of preferred stock of at least \$1 million to new investors.

c. As used in this Promissory Note, the term "Qualifying Financing" means any one of the following:

(i) Maker entering into (or completing) a term sheet agreement (or other agreement) with investors or an underwriter by the Maturity Date, which provides for: (1) a scheduled closing by February 1, 1998, (2) a public or private sale of equity securities of Maker, the gross proceeds from which equity sale is to aggregate to at least \$10 million, (3) the proceeds of the sale are not designated by the investor for specified limited purposes, (4) the price per share for the sale is set by mutual agreement between Maker and new investors who invest at least \$1 million, and (5) the sale of equity securities actually is consummated by February 1, 1998; or

(ii) Maker entering into (or completing) a term sheet agreement (or other agreement) by the Maturity Date for the merger or sale of Maker at a value of at least \$85 million, with (a) a scheduled closing for the merger or sale to be by February 1, 1998, and (b) the merger or sale actually is consummated by February 1, 1998; or

(iii) Maker's Board of Directors adopting an Operational Plan for Maker to continue its operations in the ordinary course of business through December 31, 1998, funded by Maker's own cash flow and other resources, without requiring outside equity or debt investment in Maker. In the event the "Qualifying Financing" is such "Operational Plan", then the equity securities into which the principal and interest owing on this Promissory Note shall be converted pursuant to Section 6bi above shall be a new series of Maker's preferred stock

(Series G) having rights, preferences and privileges comparable to those of Maker's Series E preferred stock, but with a conversion price and liquidation preference being equal to 90% of the then current fair market value of Maker's then most recently issued preferred stock sold to cash investors (excluding stock sold to RPR), and with a liquidation preference senior to all other preferred stock. Said fair market value of said preferred stock shall be determined by mutual agreement between Maker and Lender, but if no mutual agreement is reached, then said fair market value shall be determined by a nationally recognized investment banking firm which is mutually selected by Maker and Lender, with the fees for obtaining said valuation determination to be borne equally by Maker and Lender. Said Series G preferred stock will include a customary weighted average anti-dilution protection provision applicable to Maker's next following sale of preferred stock of at least \$1 million to new investors.

7. Default. Upon a default by Maker, as specified below, Lender may

declare the entire unpaid balance of principal and accrued interest immediately due and owing. Each of the following events shall constitute a default:

a. Default in the payment of principal or interest due hereunder, and such default continues for a period of thirty (30) days after the due date thereof.

b. The making of an assignment for the benefit of creditors by Maker, or the appointment of a receiver for all or substantially all of Maker's property, or the filing by Maker of a petition in bankruptcy or other similar proceeding under law for the relief of debtors; or

c. The filing against Maker of a petition in bankruptcy or other similar proceeding under law for relief of debtors, and such petition is not vacated or discharged within sixty (60) days after the filing thereof

8. Costs of Collection. If this Promissory Note is not paid when due,

whether at maturity or by acceleration, Maker promises to pay all costs incurred by Lender in collecting the amounts due hereunder, including reasonable attorneys' fees and expenses incurred by Lender in connection with any insolvency, bankruptcy, reorganization, arrangement or other similar proceedings involving Maker which in any way affects the exercise by Lender of its rights and remedies under this Promissory Note.

9. Waiver. Presentment, demand, protest, notices of protest, dishonor

and non-payment of this Promissory Note and all notices of every kind are hereby waived. No single or partial exercise of, or forbearance from exercising, any power hereunder or under any other agreement or instrument pertaining to this Promissory Note shall preclude other or further exercises thereof or the exercise of any other power. No delay or omission on the part of Lender in exercising any right hereunder shall operate as a waiver of such right or of any other right under this Promissory Note.

10. Governing Law. Principal and interest are payable in lawful money of

the United States. This Promissory Note has been executed and delivered by Maker in the State of Michigan and shall be governed by and construed in accordance with the laws of the State of

Michigan. In any action brought under or arising out of this Promissory Note, Maker hereby consents to the jurisdiction of any competent court within the State of Michigan and consents to service of process by any means authorized by Michigan law.

11. Authority. The undersigned individual signing this Promissory Note

represents and warrants that the undersigned individual is duly authorized and empowered to execute and deliver this Promissory Note on behalf of Maker.

MAKER:

AASTROM Biosciences, Inc.

By: -----

EXHIBIT B

Stock Warrant

STOCK WARRANT

THIS WARRANT AND THE SECURITIES ISSUABLE UPON EXERCISE OF THIS WARRANT HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), AND MAY NOT BE OFFERED FOR SALE, SOLD OR OTHERWISE TRANSFERRED UNLESS SO REGISTERED, UNLESS AN EXEMPTION FROM THE REQUIREMENT OF SUCH REGISTRATION IS AVAILABLE UNDER THE CIRCUMSTANCES AT THE TIME OBTAINING AND DEMONSTRATED BY AN OPINION OF COUNSEL SATISFACTORY TO THE COMPANY.

Void after 5:00 p.m., Michigan Time, on October 15, 2000

Warrant to Purchase
up to _____ Shares of
Common Stock

AASTROM BIOSCIENCES, INC.

Common Stock Purchase Warrant

1. Grant of Warrant to Purchase Shares. This is to certify that, for

value received,

The State Treasurer of the State of Michigan,
Custodian of the Michigan Public School Employees' Retirement System,
State Employees' Retirement System, Michigan State Police Retirement System,
and Michigan Judges Retirement System

or assigns (the "Holder"), is entitled, subject to the provisions of this Warrant, to purchase from Aastrom Biosciences, Inc., a Michigan corporation (the "Company"), at any time within the Exercise Period (hereinafter defined), up to _____ fully paid and non-assessable shares (the "Shares") of Common Stock of the Company ("Stock"), at a purchase price per share (the "Exercise Price") as defined below. The Shares deliverable upon exercise of this Warrant, as adjusted from time to time, are hereinafter sometimes referred to as "Warrant Stock" and the exercise price to purchase a share of Warrant Stock is hereinafter sometimes referred to as the "Exercise Price."

2. Definitions.

The "Exercise Period" shall commence on the earlier of (a) 90 days after the Company completing its IPO (as defined below), (b) the Company completing a Qualifying Financing, or (c) October 15, 1999 (provided that this date is not within 90 days after the IPO is completed, in which event the option shall be exercisable at the end of said 90 days); and the Exercise Period shall end on October 15, 2000.

The "Exercise Price" shall be the lesser of:

(1) \$6.00 share, increasing by \$2.00 per share on each anniversary of the date the Company completes its IPO; or

(2) 85% of the fair market value of the Company's stock, which value shall be determined as follows:

(a) if the Company's common stock is traded in the public stock market at the time the stock warrant is exercised, then said fair market value shall be the public trading price, calculated using the average of the last trading price of the day for the 20 trading days preceding the date of exercise.

(b) if the exercise of the stock warrant is made prior to the Company completing an IPO, then said fair market value shall be the fair market value of the Company's then most recently issued preferred stock sold to cash investors (excluding stock sold to RPR), determined by mutual agreement between the Company and the State. If no such mutual agreement is reached, then the fair market value of said preferred stock shall be determined by a nationally recognized investment banking firm which is mutually selected by the Company and the State, with the fees for such determination to be borne equally between the Company and the State.

The term "IPO" means an initial public offering of the Company's Common Stock which is registered with the United States Securities and Exchange Commission.

The term "Qualifying Financing" means any one of the following:

a. the Company entering into (or completing) a term sheet agreement (or other agreement) with investors or an underwriter by the Maturity Date, which provides for: (1) a scheduled closing by February 1, 1998, (2) a public or private sale of equity securities of the Company, the gross proceeds from which equity sale is to aggregate to at least \$10 million, (3) the proceeds of the sale are not designated by the investor for specified limited purposes, (4) the price per share for the sale is set by mutual agreement between the Company and new investors who invest at least \$1 million, and (5) the sale of equity securities actually is consummated by February 1, 1998; or

b. the Company entering into (or completing) a term sheet agreement (or other agreement) by the Maturity Date for the merger or sale of the Company at a value of at least \$85 million, with (1) a scheduled closing for the merger or sale to be by February 1, 1998, and (2) the merger or sale actually is consummated by February 1, 1998; or

c. the Company's Board of Directors adopting an Operational Plan for the Company to continue its operations in the ordinary course of business through December 31, 1998, funded by the Company's own cash flow and other resources, without requiring outside equity or debt investment in the Company.

3. Number of Shares Issuable Upon Exercise. This Warrant may be exercised from time to time to purchase up to an aggregate maximum of _____ Shares.

4. Method of Exercise. During the Exercise Period, this Warrant may be exercised by the Holder, in whole or in part, by surrender of this Warrant, together with an Exercise Agreement in the form attached hereto as Exhibit A, duly executed by the Holder, to

the Company or at the office of its stock transfer agent, if any, accompanied by the cash payment of the Exercise Price for the number of Shares specified in such Exercise Agreement. Upon payment of the Exercise Price as provided in this Section 4, the Holder shall thereupon be entitled to receive the number of Shares of Warrant Stock determined as provided hereunder. If this Warrant should be exercised in part only, the Company shall, upon surrender of this Warrant for cancellation, execute and deliver a new Warrant evidencing the right of the Holder to purchase the balance of the Shares purchasable hereunder. Upon receipt by the Company of this Warrant in proper form for exercise and accompanied by payment, the Holder shall be deemed to be the holder of record of the Shares of Warrant Stock issuable upon such exercise, notwithstanding that the stock transfer books of the Company shall then be closed or that certificates representing such shares of Warrant Stock shall not then be actually delivered to the Holder.

5. Expiration Date. This Warrant shall expire October 15, 2000, or

such earlier date as the Company may complete a merger or sale of the Company, so long as the Holder is given at least 60 days' prior written notice of the proposed merger or sale, and an opportunity to exercise this Warrant, as contemplated by Section 12 hereof.

6. Reservation of Shares. The Company hereby agrees that it will at

all times reserve and keep available for issuance and delivery upon exercise of this Warrant such number of shares of Stock as shall be issuable from time to time upon exercise of this Warrant.

7. Fractional Shares. No fractional Shares or scrip representing

fractional Shares shall be issued upon the exercise of this Warrant. With respect to any fraction of a Share called for upon any exercise hereof, the Company will pay to the Holder cash in an amount equal to such fraction multiplied by the then current market value of such fractional Share, determined in such reasonable manner as may be determined by the Board of Directors of the Company, such determination to be final and binding on the Holder.

8. Exchange, Assignment or Loss of Warrant. This Warrant is

exchangeable, without expense, at the option of the Holder, upon presentation and surrender to the Company or at the office of its stock transfer agent, if any, for other Warrants of different denominations entitling the Holder to purchase in the aggregate the same number of Shares of Warrant Stock purchasable hereunder. This Warrant may be divided or combined with other Warrants which carry the same rights upon presentation hereof at the office of the Company or at the office of its stock transfer agent, if any, together with a written notice signed by the Holder specifying the denominations in which new Warrants are to be issued. The term "Warrant" as used herein includes any Warrants issued in substitution for or replacement of this Warrant, or into which this Warrant may be divided or exchanged. Upon receipt by the Company of evidence satisfactory to it of the loss, theft, destruction or mutilation of this Warrant, and (in the case of loss, theft or destruction) of reasonably satisfactory indemnification, or (in the case of mutilation) upon surrender and cancellation of this Warrant, as the case may be, the Company shall issue to the Holder a new Warrant of like tenor and date.

9. Rights of Holder. The Holder shall not, by virtue hereof, be

entitled to any rights of a shareholder of the Company, either at law or equity, and the rights of the Holder are

limited to those expressed in this Warrant and are not enforceable against the Company except to the extent set forth herein.

10. Adjustment Provisions.

10.1 Adjustment of Exercise Price for Stock Splits, Stock

Dividends Etc. In case the Company shall at any time or from time to time

issue stock by way of dividend or other distribution on any capital stock of the Company, or subdivide or combine the outstanding shares of Stock, the Exercise Price shall be proportionately decreased in the case of such issuance (on the day following the date fixed for determining shareholders entitled to receive such dividend or other distribution) or decreased in the case of such subdivision or increased in the case of such combination (in either case, on the date that such subdivision or combination shall become effective).

10.2 No Adjustment for Small Amounts. Anything in this Section

10 to the contrary notwithstanding, the Company shall not be required to give effect to any adjustment in the Exercise Price unless and until the net effect of one or more adjustments pursuant to this Section 10 shall cause a change of the Exercise Price by at least one cent, but when the cumulative net effect of more than one adjustment so determined shall be to change the Exercise Price by at least one cent, such change in the Exercise Price shall then be given effect.

10.3 Number of Shares Adjusted. Upon any adjustment of the

Exercise Price pursuant to this Section 10, the Holder shall thereafter (until another such adjustment) be entitled to purchase, at the adjusted Exercise Price, the number of Shares of Warrant Stock, calculated to the nearest full share, obtained by multiplying the number of Shares of Warrant Stock issuable upon exercise of this Warrant prior to such adjustment by the Exercise Price in effect prior to such adjustment and dividing the product so obtained by the new Exercise Price.

11. Officer's Certificate. Whenever the Exercise Price shall be

adjusted pursuant to Section 10, the Company shall promptly create and file in the custody of its Secretary or an Assistant Secretary at its principal office, and with its stock transfer agent, if any, and mail to the Holder at his or her address as listed on the books and records of the Company, an officer's certificate showing the adjusted Exercise Price determined as herein provided and setting forth in reasonable detail the facts requiring such adjustment. The original of each such officer's certificate shall be available for inspection during office hours at the Company's principal place of business. Such certificate shall be conclusive as to the correctness of such adjustment.

12. Reclassification, Reorganization or Merger. In case of any

reclassification, capital reorganization or other change of outstanding shares of Stock of the Company (other than a change in par value, or as a result of an issuance of Stock by way of dividend or other distribution or of a subdivision or combination), or in case of any sale or conveyance to another corporation of the property of the Company as an entirety or substantially as an entirety, the Company shall cause effective provision to be made so that the Holder shall have the right thereafter, by exercising this Warrant, to purchase the kind and amount of shares of stock and other securities and property receivable upon such reclassification, capital reorganization or other change, consolidation, sale or conveyance as the Holder would have received had this

Warrant been exercised immediately prior to such event. Any such provision shall include provision for adjustments which shall be as nearly equivalent as may be practicable to the adjustments provided for in this Warrant. The foregoing provisions of this Section 12 shall similarly apply to successive reclassifications, capital reorganizations and changes of shares of Stock. In the event of a merger (where the Company is not the surviving entity), consolidation or other sale or conveyance (in all such cases where the consideration to be received by the holders of the Stock of the Company consists solely of cash or securities registered under the Securities Act of 1933, as amended, the "Act") and if requested by the Company, the Holder shall agree to exercise this Warrant immediately prior to such event, or otherwise the expiration date shall be accelerated to the day preceding the effective date of the merger, consolidation or other sale or conveyance.

13. Stock Registration. Upon exercise of this Warrant, and with

respect to the Warrant Stock acquired by said exercise, the Holder shall become a "Purchaser" under, and be entitled to all of the rights set forth in, the Stock Registration Rights Agreement, dated as of April 2, 1992, as amended (the "Registration Agreement"), a copy of which has been given previously to the Holder, and the Holder agrees to be bound by the terms and conditions of the Registration Agreement, as applicable. Except as set forth in the Registration Agreement, the Company has no obligation to register any of the Shares of Warrant Stock issuable upon the exercise of this Warrant. Unless and until the shares of Warrant Stock are registered under the Act, the resale of the Warrant Stock by the Holder is restricted, and the Shares will be subject to the limitations and restrictions of Rule 144 after the Company has a public stock offering, and the Shares may be sold by the Holder only pursuant to exemptions from the registration requirements of the Act, if any are then available. In connection with an underwritten initial public offering by the Company of its equity securities pursuant to a registration statement filed under the Act, the Holder shall not sell, pledge, dispose or transfer any interest in (or otherwise agree to engage in any of the foregoing transactions with respect to) any of the Warrant Stock or any interest herein without the prior written consent of the Company or its underwriters for a period of up to 180 days following the effectiveness of the registration statement, and the Holder agrees to enter into a "lockup letter" so restricting such transfers; provided, that the Holder's obligations to refrain from transferring Warrant Stock and to enter into a lockup letter shall be effective only if the executive officers and directors of the Company also enter into similar lockup letters. In order to enforce the limitations of this Section 13, the Company may impose stop-transfer instructions with respect to the Warrant Stock until the end of the applicable lockup period.

14. Transfers. Subject to the terms and conditions contained in

Section 13 hereof, this Warrant and all rights hereunder are transferable in whole or in part by the Holder and any successor transferee; provided, however, that in no event shall the total number of transfers of any of the rights and interests in all of the Warrant exceed five (5) transferees. The transfer shall be recorded on the books of the Company upon receipt by the Company of a notice of transfer in the form attached hereto as Exhibit B (the "Transfer Notice"), at its principal offices, and the payment to the Company of all transfer taxes and other governmental charges imposed on such transfer. The Transfer Notice shall also be accompanied with an opinion of counsel reasonably satisfactory in substance to the Company that the transfer will not (i) violate any provision of the Act and any applicable state securities laws or (ii) cause the Company to

lose the exemption from registration under applicable federal and state securities laws used for the original issuance of this Warrant.

15. Legend. Each certificate representing Warrant Stock or any other

security issued or issuable upon exercise of this Warrant shall bear the following legend, unless counsel for the Company is of the opinion as to any such certificate that such legend is unnecessary:

The securities represented by this certificate may not be offered for sale, sold or otherwise transferred except pursuant to an effective registration statement made under the Securities Act of 1933 (the "Act"), or pursuant to an exemption from registration under the Act.

16. Applicable Law. This Warrant shall be governed by, and construed

in accordance with, the laws of the State of Michigan.

Date: _____, 199__ AASTROM Biosciences, Inc.

By:_____

ACCEPTANCE OF WARRANT AGREEMENT

The undersigned hereby accepts this Warrant and agrees to abide by all the terms and conditions hereof. The undersigned further represents and agrees that it is an "accredited investor" as defined by Rule 501 promulgated by the Securities and Exchange Commission and that it is accepting this Warrant for its own account for investment purposes and not with a view to or for sale in connection with a distribution of the Warrant or the Warrant Stock.

Dated: _____, 199__

WARRANT HOLDER:

The State Treasurer of the State of Michigan,
Custodian of the Michigan Public School
Employees' Retirement System, State Employees'
Retirement System, Michigan State Police
Retirement System, and Michigan Judges
Retirement System

By: _____

EXHIBIT A

EXERCISE AGREEMENT

To: _____

Dated: _____

The undersigned, pursuant to the provisions set forth in the within Warrant, hereby agrees to subscribe for and purchase _____ shares of the Warrant Stock covered by such Warrant and makes payment herewith in the sum of \$_____ as full payment for such Warrant Stock, at the price per share of \$_____, as provided by such Warrant.

Signature:

Print Name:

Address:

Federal Tax
Identification
Number:

EXHIBIT B

TRANSFER NOTICE

(To transfer or assign the foregoing Warrant, execute this form and supply the information and materials required by Section 14 of the Warrant. Do not use this form to purchase shares.)

FOR VALUE RECEIVED, the foregoing Warrant and all rights evidenced thereby are hereby transferred and assigned to

(Please Print)

whose address is

Dated

Holder's Signature

Print Holder's Name

Holder's Address

Signature Guaranteed:

NOTE: The signature to this Transfer Notice must correspond with the name as it appears on the face of the Warrant, without alteration or enlargement or any change whatever. Officers of corporations and those acting in a fiduciary or other representative capacity should file proper evidence of authority to assign the foregoing Warrant.

EXHIBIT 11.1

AASTROM BIOSCIENCES, INC.
STATEMENT RE COMPUTATION OF PRO FORMA NET LOSS PER SHARE

	Year ended June 30.			Three months ended September 30,	
	1994	1995	1996	1995	1996
Weighted average number of common shares outstanding	1,294,000	1,724,000	1,749,000	1,740,000	1,752,000
Issuance of Common Stock(1)	135,000	135,000	135,000	135,000	136,000
Assumed exercise of stock options to purchase Common Stock(1)	121,000	121,000	121,000	121,000	121,000
Series E Preferred Stock issued in January 1996	1,078,000	1,078,000	1,078,000	1,078,000	1,078,000
Weighted average number of common shares representing assumed conversion of Series A, Series B, Series C and Series D					
Convertible Preferred Stock from the date of issuance	4,833,000	5,586,000	7,020,000	7,020,000	7,020,000
Pro forma weighted average number of common and common equivalent shares outstanding	7,461,000	8,644,000	10,103,000	10,094,000	10,107,000
Net loss	\$ (6,140,000)	\$ (5,717,000)	\$ (9,917,000)	\$ (1,299,000)	\$ (3,273,000)
Pro forma net loss per share	\$ (.82)	\$ (.66)	\$ (.98)	\$ (.13)	\$ (.32)

- - - - -

- (1) Represents shares of common stock or common stock equivalents issued subsequent to October 1995 at a price per share less than the offering price of \$8.00. Such shares are considered to be cheap stock and, accordingly, reflected as outstanding since inception.

CONSENT OF INDEPENDENT ACCOUNTANTS

We consent to the inclusion in this registration statement on Form S-1 of our report dated October 31, 1996, on our audits of the financial statements of Aastrom Biosciences, Inc. We also consent to the reference to our firm under the caption "Experts."

/s/ COOPERS & LYBRAND L.L.P.

Detroit, Michigan
October 31, 1996

THIS SCHEDULE CONTAINS SUMMARY FINANCIAL INFORMATION EXTRACTED FROM THE
COMPANY'S REGISTRATION STATEMENT ON FORM S-1 AND IS QUALIFIED IN ITS ENTIRETY BY
REFERENCE TO SUCH FINANCIAL STATEMENTS.

YEAR		
	JUN-30-1996	
	JUL-01-1995	
	JUN-30-1996	
		10,967,000
		0
		0
		0
		0
	11,485,000	
		2,339,000
	1,151,000	
	12,673,000	
1,634,000		
		0
	0	
	34,218,000	
		324,000
	(23,692,000)	
12,673,000		
		0
	1,609,000	
		0
	12,142,000	
	0	
	0	
	62,000	
	(9,917,000)	
		0
(9,917,000)		
	0	
	0	
		0
	(9,917,000)	
	(.98)	
	0	

THIS SCHEDULE CONTAINS SUMMARY FINANCIAL INFORMATION EXTRACTED FROM THE
COMPANY'S REGISTRATION STATEMENT ON FORM S-1 AND IS QUALIFIED IN ITS ENTIRETY BY
REFERENCE TO SUCH FINANCIAL STATEMENTS.

YEAR		
	JUN-30-1995	
	JUL-01-1994	
	JUN-30-1995	
		2,680,000
		8,388,000
		0
		0
		0
	11,272,000	
		1,925,000
		646,000
	12,551,000	
	953,000	
		0
	0	
	28,253,000	
		241,000
	(17,308,000)	
12,551,000		
		0
	517,000	
		0
	6,447,000	
	0	
	0	
	66,000	
	(5,717,000)	
		0
(5,717,000)		
	0	
	0	
		0
	(5,717,000)	
	(.66)	
	0	

JUN-30-1994
JUL-01-1993
JUN-30-1994

THIS SCHEDULE CONTAINS SUMMARY FINANCIAL INFORMATION EXTRACTED FROM THE
COMPANY'S REGISTRATION STATEMENT ON FORM S-1 AND IS QUALIFIED IN ITS ENTIRETY BY
REFERENCE TO SUCH FINANCIAL STATEMENTS.

3-MOS		
	SEP-30-1996	
	JUL-01-1996	
	SEP-30-1996	
		5,908,000
	1,200,000	0
		0
		0
	7,706,000	
		2,512,000
	1,287,000	
	8,931,000	
1,166,000		0
	0	
	37,718,000	
		365,000
	(30,465,000)	
8,931,000		0
	224,000	
		0
	3,612,000	
	0	
	0	
	11,000	
	(3,273,000)	
		0
(3,273,000)		
	0	
	0	
		0
	(3,273,000)	
	(.32)	
	0	

SEP-30-1995

JUL-01-1995

SEP-30-1995

0

0

0

0

0

0

0

0

0

0

0

0

0

0

0

0

0

211,000

0

1,641,000

0

0

18,000

(1,299,000)

0

(1,299,000)

0

0

0

(1,299,000)

(.13)

0

THIS SCHEDULE CONTAINS SUMMARY FINANCIAL INFORMATION EXTRACTED FROM THE COMPANY'S REGISTRATION STATEMENT ON FORM S-1 AND IS QUALIFIED IN ITS ENTIRETY BY REFERENCE TO SUCH FINANCIAL STATEMENTS.

OTHER

JUN-30-1996		
JUN-30-1996		
	0	0
	0	
	0	
	0	
0		0
	0	
	0	
0		
		0
0		
	0	
	0	
0		
		0
		0
		0
0		
		0
		0
3,782,000		
		0
32,164,000		
0		
0		
219,000		
(27,025,000)		
	0	
(27,025,000)		
	0	
	0	
		0
(27,025,000)		
	0	
	0	

INCEPTION-TO-DATE

THIS SCHEDULE CONTAINS SUMMARY FINANCIAL INFORMATION EXTRACTED FROM THE COMPANY'S REGISTRATION STATEMENT ON FORM S-1 AND IS QUALIFIED IN ITS ENTIRETY BY REFERENCE TO SUCH FINANCIAL STATEMENTS.

OTHER	JUN-30-1997	SEP-30-1996
		0
		0
		0
		0
	0	0
		0
	0	0
	0	0
		0
	0	0
		0
0		0
	4,006,000	0
	35,776,000	
	0	
	0	
	230,000	
	(30,298,000)	
	0	
(30,298,000)		
	0	
	0	
		0
	(30,298,000)	
	0	
	0	

INCEPTION-TO-DATE