

SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

AMENDMENT NO. 2  
TO

FORM S-3

REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933

AASTROM BIOSCIENCES, INC.  
(Exact Name of Registrant as Specified in Its Charter)

Michigan  
(State or Other Jurisdiction  
of Incorporation or Organization)

94-3096597  
(IRS Employer  
Identification Number)

24 FRANK LLOYD WRIGHT DRIVE  
P.O. BOX 376  
ANN ARBOR, MICHIGAN 48106  
(734) 930-5555  
(Address, Including Zip Code, and Telephone Number, Including  
Area Code, of Registrant's Principal Executive Offices)

R. DOUGLAS ARMSTRONG, PH.D.  
PRESIDENT AND CHIEF EXECUTIVE OFFICER  
AASTROM BIOSCIENCES, INC.  
24 FRANK LLOYD WRIGHT DRIVE  
P.O. BOX 376  
ANN ARBOR, MICHIGAN 48106  
(734) 930-5555  
(Name, Address, Including Zip Code, and Telephone Number, Including  
Area Code, of Agent for Service)

COPIES TO:

DOUGLAS J. REIN, ESQ.  
GRAY CARY WARE & FREIDENRICH LLP  
4365 EXECUTIVE DRIVE, SUITE 1600  
SAN DIEGO, CA 92121  
TELEPHONE: (619) 677-1400  
FACSIMILE: (619) 677-1477

APPROXIMATE DATE OF COMMENCEMENT OF PROPOSED SALE TO THE PUBLIC:  
From time to time as described in the Prospectus.

If the only securities being registered on this Form are being offered  
pursuant to dividend or interest reinvestment plans, please check the following  
box.

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, other than securities offered only in connection with dividend or interest  
reinvestment plans, 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, please 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

AMOUNT PROPOSED PROPOSED AMOUNT OF  
MAXIMUM MAXIMUM

TITLE OF SHARES  
TO BE REGISTERED

TO BE  
REGISTERED

AGGREGATE PRICE  
PER UNIT (2)

AGGREGATE  
OFFERING PRICE (2)

REGISTRATION  
FEE (2)

-----  
Common Stock, (\$0 par value) 4,163,855(1) \$2.125 \$8,848,192 \$2,610  
=====

- (1) Includes shares of Common Stock which may be offered pursuant to this Registration Statement consisting of an estimated 4,163,855 shares issuable upon conversion of 5,000 Series I Shares (as defined below). For purposes of estimating the number of shares of Common Stock to be included in this Registration Statement, the Company calculated 150% of the number of shares of Common Stock issuable in connection with the conversion of the Company's Series I Shares (as defined below) (based on a conversion price of \$1.827, which is the average of the closing bid prices of the Common Stock reported on the Nasdaq National Market for the lowest five consecutive trading days during the twenty trading days preceding October 6, 1998, multiplied by 94% pursuant to the terms of the Series I Shares). In accordance with Rule 416, this Registration Statement also covers such indeterminate number of additional shares as may become issuable upon conversion of or in respect of Series I Shares as a result of any future stock splits, stock dividends or similar transactions.
- (2) Estimated, pursuant to Rule 457(c), solely for the purpose of calculating the registration fee based on the average of the high and low prices for the Common Stock on October 5, 1998, as reported on the Nasdaq National Market of \$2.125. \$3,771.79 was previously paid at the time of original filing.

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.  
+++++

SUBJECT TO COMPLETION, DATED OCTOBER 7, 1998

PROSPECTUS  
- - - - -

4,163,855 SHARES OF COMMON STOCK  
AASTROM BIOSCIENCES, INC.

This Prospectus relates to the offer and sale of up to 5,537,765 shares (the "Shares") of Common Stock of Aastrom Biosciences, Inc., a Michigan corporation (the "Company"). The Shares are issuable upon conversion of shares of 1998 Series I Convertible Preferred Stock of the Company (the "Series I Shares"). The Shares may be offered for sale from time to time after such conversion by or on behalf of the holder of Series I Shares (the "Selling Shareholder"). See "Selling Shareholder." The Series I Shares were issued in connection with an equity financing pursuant to a Securities Purchase Agreement (the "Purchase Agreement"). The Company will not receive any proceeds from sales of the Shares by the Selling Shareholders or from conversions, if any, of the Series I Shares. The Company has agreed to register the Shares for resale under the Securities Act of 1933, as amended (the "Securities Act"). The Company is also obligated to list the Shares on the Nasdaq National Market. See "Plan of Distribution."

The Shares may be offered for sale in one or more transactions (which may include block transactions) effected on the Nasdaq National Market (or any national securities exchange or U.S. inter-dealer quotation system of a registered national securities association, on which the Shares are then listed), in sales occurring in the public market off such exchange, in private negotiated transactions, through the writing of options on the Shares, short sales or in a combination of such methods of sale, and on terms and at prices then obtainable. The Company has agreed to indemnify in certain circumstances the Selling Shareholder against certain liabilities, including liabilities under the Securities Act. The Selling Shareholder has agreed to indemnify the Company under certain circumstances against certain liabilities, including liabilities under the Securities Act. See "Plan of Distribution."

The Company will bear all reasonable expenses incurred in connection with the registration of the Shares for resale, including, without limitation, all registration and filing fees imposed by the Securities and Exchange Commission (the "Commission"), the National Association of Securities Dealers, Inc. (the "NASD") and blue sky laws, printing expenses, transfer agents' and registrars' fees, and the reasonable fees and disbursements of the Company's outside counsel and independent accountants, but excluding brokerage commissions, underwriting discounts or commissions, if any, and other expenses incurred by the Selling Shareholder in the offer and sale of the Shares.

The Company's Common Stock is quoted on The Nasdaq National Market under the symbol "ASTM." On October 5, 1998, the last sale price of the Company's Common Stock as reported on The Nasdaq National Market was \$2.00.

AN INVESTMENT IN THESE SECURITIES INVOLVES A HIGH DEGREE OF RISK.  
SEE "RISK FACTORS" BEGINNING ON PAGE 4.

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

THE DATE OF THIS PROSPECTUS IS \_\_\_\_\_, 1998.

#### AVAILABLE INFORMATION

The Company is subject to the informational requirements of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and in accordance therewith, files periodic reports, proxy statements and other information with the Commission. Such reports, proxy statements and other information may be inspected and copied at the public reference facilities maintained by the Commission at 450 Fifth Street, N.W., Washington, D.C. 20549 and at the Regional Offices of the Commission at 230 South Dearborn Street, Chicago, Illinois 60604; and at 75 Park Place, New York, New York 10007. In addition, copies of such material can also be obtained at prescribed rates from the Public Reference Section of the Commission at its principal office at 450 Fifth Street, N.W., Washington, D.C. 20549. The Company's Common Stock is traded on The Nasdaq National Market. Reports and other information concerning the Company can also be inspected at the offices of the National Association of Securities Dealers, Inc., Market Listing Section, 1735 K Street, N.W., Washington, D.C. 20006. Such reports and other information may also be inspected without charge at a Web site maintained by the Commission. The address of the site is <http://www.sec.gov>.

#### INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The following documents filed with the Commission by the Company (Commission File No. 0-22025), pursuant to the Exchange Act are incorporated herein by reference:

- (1) The Company's Annual Report on Form 10-K for the fiscal year ended June 30, 1998.
- (2) Form 8-K filed by the Company on July 15, 1997.
- (3) The portions of the registration statement on Form 8-A filed by the Company pursuant to the Exchange Act which contain a description of the Common Stock.

All documents and reports subsequently filed by the Company pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of the Registration Statement (the "Registration Statement") shall be deemed to be incorporated by reference herein and to be a part hereof from the date of filing of such documents or reports. Any statement contained in a document incorporated by reference or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for purposes of the Registration Statement to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of the Registration Statement.

The Company will provide without charge to each person to whom this Prospectus is delivered, upon oral or written request, a copy of any or all of the foregoing documents incorporated herein by reference (other than exhibits to such documents unless such exhibits are specifically incorporated by reference into the information that this Prospectus incorporates). Written or telephone requests should be directed to Mr. Todd E. Simpson, Chief Financial Officer, Aastrom Biosciences, Inc., 24 Frank Lloyd Wright Drive, P.O. Box 376, Ann Arbor, Michigan, 48106, telephone number (734) 930-5555.

## 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. 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 below.

### 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 AastromReplicell(TM) Cell Production System (the "AastromReplicell(TM) System"), 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 AastromReplicell(TM) System 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 AastromReplicell(TM) System 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 U.S. 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 in the U.S., 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. The Company is currently conducting pre-pivotal clinical trials to demonstrate the safety and biological activity of patient-derived or umbilical cord blood cells ("UCB cells") produced in the Company's prototype of the AastromReplicell(TM) System in a limited number of patients. If the results from these pre-pivotal trials are successful, the Company intends to seek clearance from the FDA to commence pivotal clinical trials. 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, reliability 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 trials. Further delays in patient accrual, in the Company's current pre-pivotal clinical trials, or in pivotal trials planned to be conducted, 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 AastromReplicell(/TM/) System 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; Extensive Government Regulation."

The Company's current pre-pivotal trials are designed to demonstrate specific biological safety and activity of cells produced in the AastromReplicell(/TM/) System, but are not designed to demonstrate long-term sustained engraftment of such cells. The patients enrolled in these pre-pivotal trials will have undergone extensive chemotherapy treatment prior to the infusion of cells produced in the AastromReplicell(/TM/) System. Such treatments will have substantially weakened these patients and may have irreparably damaged their hematopoietic systems. Due to these and other factors, it is possible that patients may die or suffer severe complications during the course of the current pre-pivotal trials or future trials. For example, in the trials to date, patients who were in the transplant recovery process have died from complications related to the patient's clinical condition that, according to the physicians involved, were unrelated to the AastromReplicell(/TM/) System procedure. 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 manufacture of its product candidates and their components, including certain cytokines, serum and media, with third parties, and expects to continue to do so in the foreseeable future. The Company has entered into collaborative product development and supply agreements with SeaMED Corporation ("SeaMED"), Ethox Corporation ("Ethox") and Anchor Advanced Products, Inc., Mid-State Plastics Division ("MSP"), for the collaborative development and manufacture of certain components of the AastromReplicell(/TM/) System and is dependent upon those suppliers to manufacture its products. The Company is also dependent upon Immunex Corporation ("Immunex"), Life Technologies, Inc. and Biowhittaker for the supply of certain cytokines, serum and media to be used in the AastromReplicell System. 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, MSP 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. Additionally, there can be no assurance that the Company will not require additional cytokines, components and other materials to manufacture, use or market its product candidates, or that necessary key components will be available for use on a sustained basis, if at all, by the Company in the markets in which it intends to sell its products. There can also be no assurance that the Company will be able to obtain alternative components and materials from other manufacturers of acceptable quality, or on terms or in quantities acceptable to the Company. 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 becomes limited or interrupted, the Company would not be able to conduct clinical trials or 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.

Certain of the compounds used by the Company in its current stem cell expansion process involve the use of animal-derived products. The availability of these compounds for clinical and commercial use may become limited by suppliers or restricted by regulatory authorities, which may impose a potential competitive disadvantage for the Company's products compared to competing products and procedures. There can be no assurance that the Company will not experience delays or disadvantages related to the future availability of such materials. Any restriction on the use of such materials could have a material adverse effect on the Company's business, financial condition and results of operations, and there can be no assurance that the Company will be able to develop or obtain alternative compounds.

Like Seamed, Ethox, MSP and Immunex, 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 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 June 30, 1998, the Company has incurred net operating losses totaling approximately \$58.5 million. Such losses have resulted principally from costs incurred in the research and development of the Company's cell culture technologies and the AastromReplicell(TM) System, general and administrative expenses, and the prosecution of patent applications. The Company expects to incur significant and increasing operating losses until product sales commence, 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 will achieve 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 AastromReplicell(TM) System for stem cell therapy and related uses. Cobe has the right to terminate its Distribution Agreement with the Company upon twelve months notice upon a change of control of the Company, other than to Cobe, or if Cobe determines that commercialization of the AastromReplicell(TM) System 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 may 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, and if such relationships are established, that they will be successful or sustained on a long-term basis. 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 from the sale of the Series I Shares, together with the Company's available cash and expected interest income thereon, will be sufficient to finance the development and manufacture of the AastromReplicell(TM) System for use in clinical trials, expanded clinical trials, other research and development and working capital and other corporate requirements until mid 1999. 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 development of the Company's products for the expansion of additional cell types will require the Company to raise additional funds or to seek collaborative partners, or both, to finance related research and development activities.

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. The Company intends to seek additional collaborative partners to assist in the development of certain of its products. If the Company is not successful in finding, entering into and maintaining such arrangements, 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, if at all. Any of the foregoing capital constraints would have a material adverse effect on the Company's business, financial condition and results of operations.

#### 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 AastromReplicell(TM) System 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 AastromReplicell System(TM) 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 AastromReplicell System(TM). 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 guidelines or requirements for approval of such product candidates will continue to be subject to significant uncertainty.

Before marketing, the AastromReplicell System(TM) 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, changes in FDA classification of the Company's products, 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 governmental regulation may be established which could prevent or delay regulatory approval of the Company's products.

The Company believes that the AastromReplicell(TM) System's components will be regulated in Europe as Class I Sterile, Class IIb and Class III medical devices, under the authority of the new Medical Device Directives ("MDD") being implemented by European Union ("EU") member countries. In order for the Company to market its products in Europe, it must obtain a CE Mark from a Notified Body to certify that the Company and its operations comply with certain minimum quality standards and compliance procedures, or, alternatively, that its manufactured products meet a more limited set of requirements. There can be no assurance that the Company and its suppliers will be able to meet these minimum requirements, or, if met, that the Company and its suppliers will be able to maintain such compliance. The result of such non-compliance would have a material adverse effect on the Company's business, financial condition and results of operations. There can be no assurance, however, that the AastromReplicell(TM) System will ultimately be regulated in Europe as currently expected, and, if the

AstromReplicell(TM) System is not so regulated, the Company could be forced to obtain additional regulatory approvals and could be subject to additional regulatory requirements and uncertainty, which would have a material adverse effect on the Company's business, financial condition and results of operations.

#### CONSEQUENCES OF COBE RELATIONSHIP

Cobe is the largest single shareholder of the Company, beneficially owning approximately 20.2% of the outstanding Common Stock (prior to conversion of any Series I Shares into Common Stock, but including the shares of Common Stock issuable upon conversion of the outstanding 5 1/2% Convertible Preferred Stock as of August 31, 1998). In addition, Cobe has certain preemptive rights to maintain its relative percentage ownership and voting interest in the Company. Cobe also has an option, until February 2000, 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. Edward C. Wood, Jr., the President of Cobe BCT, is a director of the 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. 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.

#### 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 AstromReplicell(TM) System 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, suggests that cells expanded in the AstromReplicell(TM) System using its current process will enable hematopoietic recovery within the time frames currently achieved by bone marrow harvest, however, neutrophil and platelet recovery times may be slower than with PBPC collection methods. The Company is evaluating techniques and methods to optimize the cells produced in the AstromReplicell(TM) System to reduce the recovery time of neutrophils and platelets in patients. There can be no assurance that if such procedure optimization does not lead to recovery times equal to or faster than those of PBPC collection methods, such outcome would not have a material adverse effect on the Company's business, financial condition and results of operations. 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 AstromReplicell(TM) System 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, Novartis, A.G., VimRx Pharmaceuticals, Inc. 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 or operations.

#### 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 for certain 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, which would have a material adverse effect on the Company's business, financial condition and results of operations. 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 the 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.

## 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 depends 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 of the use of each of the Company's products to each payor separately. Significant uncertainty exists as to the payments 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.

## 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.

## PRODUCT LIABILITY AND LIMITED INSURANCE

The Company faces an inherent business risk of exposure to product liability claims in the event that the use of the AastromReplicell System during research and development efforts, including clinical trials, or after commercialization results in adverse effects. As a result, the Company may incur significant product liability exposure. There can be no assurance that existing insurance coverage will be adequate or that adequate insurance coverage for future clinical trials or commercial activities will be available at an acceptable cost, if at all, or that a product liability claim would not materially adversely affect the business, financial condition or results of operations of the Company.

#### 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.

#### SHARES ELIGIBLE FOR FUTURE SALE; POTENTIAL FOR DILUTION

Future sales of shares by existing shareholders could adversely affect the market price of the Company's Common Stock. Substantially all of the outstanding shares of Common Stock and the shares issuable upon the conversion of the various series of preferred stock of the Company are freely tradeable, subject to restrictions imposed by Rule 144 under the Securities Act of 1933, as amended, with respect to sales by affiliates.

As of October 5, 1998, 5,000 of the Series I Shares were issued and outstanding. The Series I Shares are each convertible into such number of shares of Common Stock as is determined by dividing the stated value (\$1,000) of each Series I Share (as such value is increased by a premium based on the number of days the Series I Shares are held) by the then current conversion price (which is determined by reference to the then current market price). If circumstances were such that the Selling Shareholder was able to and did convert all of its Series I Shares as of October 6, 1998, the Selling Shareholder would have received 2,484,848 shares of Common Stock, but this number of shares could prove to be significantly greater in the event of a decrease in the trading price of the Common Stock. Purchasers of Common Stock could therefore experience substantial dilution of their investment upon conversion of the Series I Shares. The Series I Shares are not registered and may be sold only if registered under the Securities Act or sold in accordance with an applicable exemption from registration, such as Rule 144. The shares of Common Stock into which the Series I Shares may be converted are being registered pursuant to this Registration Statement.

#### CONTROL BY EXISTING MANAGEMENT AND SHAREHOLDERS

As of August 31, 1998, the Company's directors, executive officers, and certain principal shareholders, including Cobe, affiliated with members of the Board of Directors and their affiliates beneficially own approximately 29.0% of the outstanding shares of Common Stock (prior to conversion of any Series I Shares into Common Stock, but including the shares of Common Stock issuable upon conversion of the outstanding 5 1/2% Convertible Preferred Stock). 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.

#### POSSIBLE STOCK PRICE AND VOLUME VOLATILITY

The trading price and volume of the Company's Common Stock has experienced significant volatility. The trading price and volume 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 technology companies for reasons frequently unrelated to or disproportionate to the

operating performance of the specific companies. These market fluctuations, as well as shortfalls in revenue or earnings as compared with public market analysts' expectations, changes in such analysts' recommendations or projections and fluctuations in the stock markets generally, as well as sales or offers of the large amounts of Shares, may adversely affect the market price of the Common Stock. In addition, since the Company's initial public offering in February 1997, the average daily trading volume of the Common Stock on the Nasdaq National Market has generally been relatively low. There can be no assurance that a more active trading market will develop in the future.

#### ANTI-TAKEOVER EFFECT OF CHARTER AND BYLAW PROVISIONS AND MICHIGAN LAW

The Company's Restated Articles of Incorporation authorize the Board of Directors to issue, without shareholder approval, an additional 2,792,000 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 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. The Company's Restated Articles of Incorporation eliminate the right of shareholders to act without a meeting, do not provide for cumulative voting in the election of directors and provide that the holders of at least two-thirds of the outstanding shares of Common Stock must approve certain transactions resulting in a change of control of the Company. In addition, certain provisions of Michigan laws applicable to the Company, including, but not limited to, provisions requiring class or series votes in certain circumstances with respect to proposed business combinations, could also delay or make more difficult a merger, tender offer or proxy contest involving the Company.

#### ABSENCE OF DIVIDENDS

The Company has never paid cash dividends on its Common Stock and does not anticipate paying any cash dividends on its Common Stock in the foreseeable future. The Company's 5 1/2% Convertible Preferred Stock accrues a dividend at 5 1/2% per annum, payable, at the Company's option, in cash or through the issuance of shares of Common Stock of the Company. As of June 30, 1998, 72,940 shares have been issued as payment of this dividend.

#### FORWARD-LOOKING STATEMENTS

This Prospectus contains certain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, including, but not limited to, statements regarding: uncertainties related to product development and marketability; uncertainties related to clinical trials; manufacturing and supply uncertainties and dependence on third parties; history of operating losses and anticipation of future losses; limited sales and marketing capabilities and dependence on collaborative relationships; future capital needs and uncertainty of additional funding; uncertainty of regulatory approval and extensive government regulation; consequences of Cobe relationship; competition and technological change; uncertainty regarding patents and proprietary rights; no assurance of third party reimbursement; hazardous materials; and potential product liability and availability of insurance. These statements are subject to risks and uncertainties, including those set forth under this caption, and actual results could differ materially from those expressed or implied in these statements. All forward-looking statements included in this Prospectus are made as of the date hereof, and the Company assumes no obligation to update any such forward-looking statement or reason why actual results might differ.

## THE COMPANY

Aastrom Biosciences, Inc. is developing proprietary process technologies and devices for a range of cell therapy applications, including stem cell therapies and selected emerging therapies such as immunotherapy, solid tissue repair and ex vivo gene therapy. The AastromReplicell(TM) System is the Company's lead product under development, and consists of a clinical cell culture system that operates single-use therapy kits tailored for each patient therapy for use in the rapidly growing cell therapy market. The Company is currently conducting pre-pivotal trials at multiple sites in the United States and Europe of the AastromReplicell(TM) System for use in stem cell therapy in preparation for pivotal trials in the United States and potential marketing in Europe. The Company believes that the AastromReplicell(TM) System method will be cost-effective, less invasive and a less time consuming alternative to currently available stem cell collection methods and may enhance the clinical utility of umbilical cord blood ("UCB") transplants by expanding the number of cells available for transplant. For stem cell therapy, the Company has entered into a strategic collaboration for the marketing, distribution and customer service of the AastromReplicell(TM) System with Cobe BCT, Inc., a subsidiary of Gambro AB and a leading provider of blood cell processing products.

The AastromReplicell(TM) System is designed as a platform product which implements the Company's pioneering stem cell replication technology. The Company also believes that the AastromReplicell(TM) System can be modified to produce a wide variety of other cell types for selected emerging therapies being developed by other companies and institutions. The Company intends to develop additional strategic collaborations for the development of the AastromReplicell(TM) System in certain of these other cell therapy market segments. In ex vivo gene therapy, the Company is also developing the Aastrom Gene Loader, which is being designed to address the production of gene-modified 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. Other novel applications of stem cell therapy are under development by third parties, which include the treatment of autoimmune diseases and augmenting recipient acceptance of organ transplants. Current stem cell collection 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. 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, which the Company believes may ultimately be addressed by the AastromReplicell(TM) System.

The Company believes that the AastromReplicell(TM) System will offer significant advantages over traditional stem cell collection methods. The AastromReplicell(TM) System is intended to be used to produce cells used for stem cell therapy from a small starting volume of bone marrow or UCB cells. The AastromReplicell(TM) System may also permit higher and more frequent doses of chemotherapy to be administered to cancer patients by enabling the production of multiple doses of cells from patient samples taken at the initial collection. Further, in an evaluation of seven tumor-contaminated bone marrow samples that were expanded with the AastromReplicell(TM) System process, the presence of breast cancer cells in each sample was either substantially reduced or was no longer detectable. The Company believes that the 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.

Aastrom is currently conducting pre-pivotal stem cell therapy clinical trials in patients with cancer and other genetic diseases at multiple sites in the U.S. and Europe. These clinical trials are designed to demonstrate that cells produced using the AastromReplicell(TM) System can provide hematopoietic recovery in accordance with trial endpoints in such patients who have received myeloablative chemotherapy. Pending a positive outcome of these and other related trials, the Company intends to seek FDA approval to begin a multi-center pivotal trial for use of the AastromReplicell(TM) System 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. The Company has also initiated two clinical sites in Europe. The Company may not market the AastromReplicell(TM) System in the United States for stem cell therapy unless and until FDA and other necessary regulatory approvals are received and in Europe until CE Mark certification is obtained. The Company is currently attempting to complete product development versions of the AastromReplicell(TM) System and obtain permission to affix the CE Mark to such versions to allow for their limited marketing 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) establish multiple strategic collaborations.

For stem cell therapy, Aastrom has entered into a strategic collaboration with Cobe BCT to be the Company's exclusive worldwide marketing, distribution and service provider for the AastromReplicell(TM) System. In 1993, the Company entered into a series of agreements, pursuant to which Code BCT purchased an aggregate of \$20,000,000 of the Company's equity securities, and acquired the worldwide distribution rights to the AastromReplicell(TM) System for stem cell therapy. Under the terms of the collaboration, Aastrom retains manufacturing rights and 58% to 62% of all revenue generated by Cobe BCT's sale of the AastromReplicell(TM) System, subject to the Company's obligation to make certain royalty payments. Aastrom also retains all marketing and distribution rights to the AastromReplicell(TM) System for other cell types and ex vivo gene therapy applications, including stem cells.

The Company has exclusive rights to 14 issued U.S. patents, including patents relating to production methods and composition of matter for stem and progenitor cells and the genetic modification of stem and other cell types, as well as patents for cell culture devices for human cells.

The Company's principal executive offices are located at 24 Frank Lloyd Wright Drive, P. O. Box 376, Ann Arbor, MI 48106.

#### SELLING SHAREHOLDER

This Prospectus relates to the offering by the Selling Shareholder for resale of up to 4,163,855 shares of Common Stock. After giving effect to the Offering, the Selling Shareholder will beneficially own no shares of Common Stock of the Company. RGC International Investors, LDC ("RGC") will acquire the Shares upon conversion, from time to time, of the Series I Shares that it acquired pursuant to the Purchase Agreement in July 1998. If circumstances were such that RGC was able to and did convert all of its Series I Shares as of October 6, 1998, RGC would have received 2,484,848 shares of Common Stock. The following table sets forth certain information with respect to the Selling Shareholder as of October 6, 1998, as follows: (i) the name and position or other relationship with the Company within the past three years, if any, of the Selling Shareholder; (ii) the number of such shares of Common Stock beneficially owned by the Selling Shareholder (including shares obtainable under options exercisable within sixty (60) days of such date) prior to the offering hereby; (iii) the number of shares of Common Stock being offered hereby; and (iv) the number and percentage of the Company's outstanding shares of Common Stock to be beneficially owned by the Selling Shareholder after completion of the sale of Common Stock being offered hereby. There is no assurance that the Selling Shareholder will sell any or all of the shares offered hereby.



SELLING SHAREHOLDER -----	NUMBER OF SHARES BENEFICIALLY OWNED PRIOR TO THE OFFERING -----	NUMBER OF SUCH SHARES BEING OFFERED -----	NUMBER OF SHARES BENEFICIALLY OWNED AFTER THE OFFERING -----
RGC International Investors, LDC (1) (2) -----	2,484,848	2,484,848	0

- (1) The number of shares set forth in the table represents an estimate of the number of shares of Common stock to be offered by the Selling Shareholder. The actual number of shares of Common Stock issuable upon conversion of Series I Shares is indeterminate, is subject to adjustment and could be materially less or more than such estimated number depending on factors which cannot be predicted by the Company at this time, including, among other factors, the future market price of the Common Stock. The actual number of shares of Common Stock offered hereby, and included in the Registration Statement of which this Prospectus is a part, includes such additional number of shares of Common Stock as may be issued or issuable upon conversion of the Series I Shares by reason of any stock split, stock dividend or similar transaction involving the Common Stock, in order to prevent dilution, in accordance with Rule 416 under the Securities Act.
- (2) The number of shares of Common Stock beneficially owned by the Selling Shareholder with respect to Series I Shares is based on a conversion price of \$2.041. If circumstances were such that the Selling Shareholder was able to and did convert the Series I Shares on October 6, 1998, the conversion price would have been \$2.041 (the average of the closing bid prices of the Common Stock for the lowest five consecutive trading days during the twenty trading days preceding such date, multiplied by 105% pursuant to the terms of the Series I Shares). The Series I Shares are convertible by any holder only to the extent that the number of shares of Common Stock owned by such holder and its affiliates (but not including shares of Common Stock underlying unconverted Series I Shares) after such conversion would not exceed 4.9% of the then outstanding Common Stock as determined in accordance with Section 13(d) of the Exchange Act. Accordingly, the number of shares of Common Stock set forth in the table for the Selling Shareholder exceeds the number of shares of Common Stock that the Selling Shareholder could own beneficially at any given time through its ownership of Series I Shares. In that regard, beneficial ownership of the Selling Shareholder set forth in the table is not determined in accordance with Rule 13d-3 under the Exchange Act.

PLAN OF DISTRIBUTION

The Shares being offered by the Selling Shareholder or its permitted donees, pledgees, transferees, or other successors in interest, will be sold in one or more transactions (which may involve block transactions) on the Nasdaq National Market or on such other market on which the Common Stock may from time to time be trading (the Purchase Agreement requires the Company to obtain and maintain listing of the Shares on the Nasdaq National Market), in privately-negotiated transactions, through the writing of options on the Shares, short sales or any combination thereof. The sale price to the public may be the market price prevailing at the time of sale, a price related to such prevailing market price or such other price as the Selling Shareholder determines from time to time. The Shares may also be sold pursuant to Rule 144. The Selling Shareholder shall have the sole and absolute discretion not to accept any purchase offer or make any sale of Shares if they deem the purchase price to be unsatisfactory at any particular time.

The Selling Shareholder or its permitted donees, pledgees, transferees, or other successors in interest, may also sell the Shares directly to market makers acting as principals and/or broker-dealers acting as agents for themselves or their customers. Brokers acting as agents for the Selling Shareholder will receive usual and customary commissions for brokerage transactions, and market makers and block purchasers purchasing the Shares will do so

for their own account and at their own risk. It is possible that the Selling Shareholder will attempt to sell shares of Common Stock in block transactions to market makers or other purchasers at a price per share which may be below the then market price. There can be no assurance that all or any of the Shares offered hereby will be issued to, or sold by, the Selling Shareholder.

The Selling Shareholder, alternatively, may sell all or any part of the Shares through an underwriter. The Selling Shareholder has not entered into any agreement with a prospective underwriter and there is no assurance that any such agreement will be entered into. If a Selling Shareholder enters into such an agreement or agreements, the relevant details will be set forth in a supplement or revisions to this Prospectus.

The Selling Shareholder and any other persons participating in a distribution of the Shares will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including without limitation, Regulation M, which may restrict certain activities of, and limit the timing of purchases and sales of the Shares by the Selling Shareholder and other persons participating in a distribution of the Shares. Furthermore, under Regulation M, persons engaged in distributions of securities are prohibited from simultaneously engaging in market making and certain other activities with respect to the Shares for a specified period of time prior to the commencement of such distribution subject to specified exceptions or exemptions. All of the foregoing may affect the marketability of the Shares offered hereby.

The Company has agreed to indemnify the Selling Shareholder, or certain transferees or assignees, against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the Selling Shareholder, or certain transferees or assignees, may be required to make in respect thereof. The Selling Shareholder has agreed to indemnify the Company against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the Company may be required to make in respect thereof.

The Selling Shareholder, RGC International Investors, LDC is a party to an investment management agreement with Rose Glen Capital Management, L.P., a limited partnership of which the general partner is RGC General Partner Corp. Messrs. Wayne Bloch, Gary Kaminsky and Steve Katznelson own all of the outstanding capital stock of RGC General Partner Corp., are the sole officers and directors of RGC General Partner Corp. and are parties to a shareholders' agreement pursuant to which they collectively control RGC General Partner Corp. Through RGC General Partner Corp., such individuals control Rose Glen Capital Management, L.P. Such individuals disclaim beneficial ownership of the Company's Common Stock owned by the Selling Stockholder.

#### USE OF PROCEEDS

The Company will not receive any proceeds from sales of the Shares or from conversions of the 1998 Series Shares, if any.

#### LEGAL MATTERS

The validity of the Common Stock offered hereby will be passed upon for the Company by Pepper Hamilton LLP, Detroit, Michigan. Gray Cary Ware & Freidenrich LLP, San Diego, California, has acted as special counsel to the Company in connection with this offering.

#### EXPERTS

The financial statements incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended June 30, 1998, have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, independent accountants, given on the authority of said firm as experts in auditing and accounting.

No dealer, salesman or other person has been authorized to give any information or to make any representations other than those contained or incorporated by reference in this prospectus in connection with the offering described herein, and, if given or made, such information or representation must not be relied upon as having been authorized by the Company. This prospectus does not constitute an offer to sell, or a solicitation of an offer to buy, any securities other than the registered securities to which it relates, or an offer to sell, or a solicitation of an offer to buy, in any jurisdiction in which it is unlawful to make such offer or solicitation. Neither the delivery of this prospectus nor any sale made hereunder shall, under any circumstances, create an implication that there has been no change in the affairs of the Company since the date hereof or that the information contained herein is correct as of any time subsequent to the date hereof.

4,163,855 SHARES

COMMON STOCK

-----  
 PROSPECTUS  
 -----

SUMMARY TABLE OF CONTENTS

	Page
	----
Available Information.....	3
Incorporation of Certain Documents by Reference.....	3
Risk Factors.....	4
The Company.....	14
Selling Shareholder.....	15
Plan of Distribution.....	16
Use of Proceeds.....	17
Legal Matters.....	17
Experts.....	17

\_\_\_\_\_, 1998

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION.

Other expenses in connection with the registration of the Common Stock hereunder will be substantially as follows:

Item -----	Company Expense -----
SEC Registration Fee.....	\$ 3,770.00
Printing and engraving expenses.....	\$ 2,000.00
Legal fees and expenses.....	\$30,000.00
Accounting Fees and expenses.....	\$ 5,000.00
Miscellaneous.....	\$19,230.00
Total.....	\$60,000.00 -----

- - - - -  
\* Estimated for purposes of this filing.

ITEM 15. 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 Registrant, provide that the Registrant 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 Registrant 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 Registrant, 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 Registrant or its shareholders. This section also authorizes the Registrant to advance expenses incurred by any agent of the Registrant 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 Registrant to purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the Registrant 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 Registrant would have the power to indemnify such person against such liability under the provisions of the MBCA.

The Registrant 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 Registrant, 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 Registrant, 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 Registrant'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 Registrant'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.

ITEM 16. EXHIBITS.

EXHIBIT NUMBER - - - - -	DESCRIPTION OF DOCUMENT - - - - -
3.1*	Certificate of Designations, Preferences and Rights of Series I Shares
5.1*	Consent and Opinion of Pepper Hamilton LLP
10.1*	Securities Purchase Agreement for Series I Shares
10.2*	Registration Rights Agreement for Series I Shares
23.1	Consent of PricewaterhouseCoopers LLP, independent accountants
23.2*	Consent of Gray Cary Ware & Freidenrich LLP
23.3*	Consent of Pepper Hamilton LLP (included in Exhibit 5.1)
24.1*	Power of Attorney
24.2**	Power of Attorney

\* Filed as an exhibit to the Company's Registration Statement on Form S-3 (No. 333-60125) on July 28, 1998.

\*\* Filed as an exhibit to the Company's Amendment No. 1 to Registration Statement on Form S-3 (No. 333-60125) on September 9, 1998.

A. The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by section 10(a)(3) of the Securities Act of 1933 (the "Securities Act");

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement;

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement; provided, however, that paragraphs (a)(1)(i) and (a)(1)(ii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed by the Registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment 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.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

B. The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the Registrant's annual report pursuant to section 13(a) or section 15(d) of the Securities Exchange Act of 1934 that is incorporated by reference in the registration statement 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.

C. The undersigned Registrant hereby undertakes to deliver or cause to be delivered with the prospectus, to each person to whom the prospectus is sent or given, the latest annual report to security holders that is incorporated by reference in the prospectus and furnished pursuant to and meeting the requirements of Rule 14a-3 or Rule 14c-3 under the Securities Exchange Act of 1934; and, where interim financial information required to be presented by Article 3 of Regulation S-X are not set forth in the prospectus, to deliver, or cause to be delivered to each person to whom the prospectus is sent or given, the latest quarterly report that is specifically incorporated by reference in the prospectus to provide such interim financial information.

D. Insofar as indemnification for liabilities arising under the Securities Act 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 Securities 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 Securities Act and will be governed by the final adjudication of such issue.

E. The undersigned Registrant hereby undertakes that:

(1) For the purposes of determining any liability under the Securities Act, 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 shall be deemed to be part of the registration statement as of the time it was declared effective.

(2) For the purposes of determining any liability under the Securities Act, 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, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements of filing on Form S-3 and has duly caused this Amendment No. 2 to Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized in the City of Ann Arbor, State of Michigan, on October 7, 1998.

AASTROM BIOSCIENCES, INC.

By: /s/ R. Douglas Armstrong, Ph.D.

-----  
 R. Douglas Armstrong, Ph.D.  
 President and Chief Executive Officer  
 (Principal Executive Officer)

Pursuant to the requirements of the Securities Act of 1933, this Amendment No. 2 to Registration Statement has been signed below by the following persons in the capacities and on the dates indicated.

Signature -----	Title -----	Date ----
/s/ R. Douglas Armstrong, Ph.D. ----- R. Douglas Armstrong, Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	October 7, 1998
/s/ Todd E. Simpson ----- Todd E. Simpson	Vice President, Finance and Administration, Chief Financial Officer, Secretary and Treasurer (Principal -Financial and Accounting Officer)	October 7, 1998
Mary L. Campbell* ----- Mary L. Campbell	Director	October 7, 1998
Robert J. Kunze* ----- Robert J. Kunze	Chairman of the Board and Director	October 7, 1998
Stephen G. Emerson, M.D., Ph.D.* ----- Stephen G. Emerson, M.D., Ph.D.	Director	October 7, 1998
Horst R. Witzel, Dr.-Ing.* ----- Horst R. Witzel, Dr.-Ing.	Director	October 7, 1998
Edward C. Wood, Jr.* ----- Edward C. Wood, Jr.	Director	October 7, 1998
*By: /s/ R. Douglas Armstrong, Ph.D. ----- R. Douglas Armstrong, Ph.D. Attorney-in-fact		

INDEX TO EXHIBITS

EXHIBIT NUMBER -----	DESCRIPTION OF DOCUMENT -----
3.1*	Certificate of Designations, Preferences and Rights of Series I Shares
5.1*	Consent and Opinion of Pepper Hamilton LLP
10.1*	Securities Purchase Agreement for Series I Shares
10.2*	Registration Rights Agreement for Series I Shares
23.1	Consent of PricewaterhouseCoopers LLP, independent accountants
23.2*	Consent of Gray Cary Ware & Freidenrich LLP
23.3*	Consent of Pepper Hamilton LLP (included in Exhibit 5.1)
24.1*	Power of Attorney
24.2**	Power of Attorney

-----  
\* Filed as an exhibit to the Company's Registration Statement on Form S-3 (No. 333-60125) on July 28, 1998.

\*\* Filed as an exhibit to the Company's Amendment No. 1 to Registration Statement on Form S-3 (No. 333-60125) on September 9, 1998.



Consent of Independent Accountants

We hereby consent to the incorporation by reference in the Prospectus constituting part of this Amendment No. 2 to Registration Statement on Form S-3 of our report dated August 7, 1998, which appears on page 9 of the 1998 Annual Report to Shareholders of Aastrom Biosciences, Inc. which is incorporated by reference in Aastrom Biosciences, Inc.'s Report on Form 10-K for the year ended June 30, 1998. We also consent to the reference to us under the heading "Experts" in such Prospectus.

/s/ PRICEWATERHOUSECOOPERS LLP  
-----  
PRICEWATERHOUSECOOPERS LLP

Bloomfield Hills, Michigan

October 6, 1998