

SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549

Amendment No. 1  
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  
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(Name, Address, Including Zip Code, and Telephone Number, Including  
Area Code, of Agent for Service)

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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

TITLE OF SHARES TO BE REGISTERED	AMOUNT TO BE REGISTERED	PROPOSED MAXIMUM AGGREGATE PRICE PER UNIT (1)	PROPOSED MAXIMUM AGGREGATE OFFERING PRICE (1)	AMOUNT OF REGISTRATION FEE (2)
Common Stock (\$0 par value)	7,700,000	\$0.96	\$7,392,000	\$1,848

(1) 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, as reported on the Nasdaq National Market on December 27, 2000.

(2) \$2,130 has paid with the initial 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.

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SUBJECT TO COMPLETION, DATED DECEMBER 29, 2000

The information in this prospectus is not complete and may be changed. The selling holder may not sell these securities under this prospectus until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell nor does it seek an offer to buy these securities in any state where the offer and sale would not be permitted.

PROSPECTUS

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AASTROM BIOSCIENCES, INC.

7,700,000 SHARES OF COMMON STOCK

We may from time to time issue up to 7,700,000 shares of our common stock. We will specify in the accompanying prospectus supplement or amendment the terms of any such offering. We may sell these common shares to or through underwriters and also to other purchasers or through agents. We will set forth the names of any underwriters or agents in the accompanying prospectus supplement or amendment.

You should read this document and any prospectus supplement or amendment carefully before you invest.

Our common stock is traded on the Nasdaq National Market under the symbol "ASTM." On December 27, 2000, the last reported sale price for our common stock was \$.90625 per share.

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INVESTING IN THE COMMON STOCK INVOLVES A HIGH DEGREE OF RISK. YOU SHOULD CONSIDER CAREFULLY THE RISK FACTORS BEGINNING ON PAGE 3 OF THIS PROSPECTUS BEFORE MAKING A DECISION TO PURCHASE OUR STOCK.

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NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

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THE DATE OF THIS PROSPECTUS IS DECEMBER \_\_, 2000.

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You should rely only on the information provided or incorporated by reference in this prospectus. We have not authorized anyone to provide you with additional or different information. This document may only be used where it is legal to sell these securities. You should not assume that any information in this prospectus is accurate as of any date other than the date of this prospectus.  
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## OUR BUSINESS

Because this is a summary, it does not contain all the information about us that may be important to you. You should read the more detailed information and the financial statements and related notes which are incorporated by reference in this prospectus.

Aastrom  
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Aastrom Biosciences, Inc. is developing proprietary process technologies and devices intended for a broad range of cell therapy applications. The AastromReplicell(TM) System is our lead product under development, and consists of a clinical cell culture system that operates single-use therapy kits tailored for patient therapy in the emerging cell therapy market. In April 1999, we began European commercialization and a lead U.S. pivotal clinical trial of the AastromReplicell(TM) System for use in stem cell therapy was in process. However, in October 1999, we suspended marketing efforts and our U.S. clinical development activities until we could obtain additional funding. With recently received funding, we have recommenced our U.S. clinical development program, and we are resuming pilot-scale marketing activities in Europe with targeted medical centers.

For the current applications in stem cell therapy, we believe that the AastromReplicell(TM) System method of producing cells will be a cost-effective, less invasive and less time-consuming alternative, or improvement to, currently available stem cell collection methods and may enhance the clinical utility of umbilical cord blood transplants in patients with certain forms of leukemia and other blood diseases by expanding the number of cells available for transplant. Further, the AastromReplicell(TM) System is designed as a platform product which implements our pioneering cell production technology. Accordingly, we believe that the AastromReplicell(TM) System can be modified to produce a wide variety of other cell types for selected emerging therapies currently in development, and we either have, or plan to initiate, development programs targeted towards some of these emerging therapies.

Our business model builds on two components: (i) proprietary procedures and devices to enable certain types of stem cells and other types of human cells to be produced with superior biological capabilities as compared with standard cell culture approaches, and (ii) the AastromReplicell(TM) System clinical platform that is designed to standardize and enable an effective commercialization pathway for bringing therapeutic cell production to medical practice. The product configuration of the AastromReplicell(TM) System consists of an instrumentation platform, to be integrated within the hospital or other centralized facility, that can operate a variety of single-use therapy kits that are specific to the desired medical application. This is intended to provide a product pathway for each cell therapy that is similar to a pharmaceutical product including regulatory approval, reimbursement, marketing and pricing. We believe that the product design of the AastromReplicell(TM) System will allow us to develop additional cell therapy kits to provide product standardization for a number of emerging cell therapies being developed by other researchers.

We are currently developing our SC-I Therapy Kit, CB-I Therapy Kit and CB-II Therapy Kit for use in stem cell therapy in cancer patients. Stem cell therapy is a form of cell therapy used to restore blood and immune system function to cancer patients following chemotherapy or radiation therapy. Current stem cell collection methods, including bone marrow harvest and peripheral blood progenitor cell mobilization, can be costly, invasive and time-consuming for both medical personnel and patients. We believe that the AastromReplicell(TM) System may offer significant advantages over traditional stem cell collection methods in settings where it is difficult to obtain the desired quantity of cells for transplant using the current cell collection methods. The AastromReplicell(TM) System is intended to be used to produce cells for stem cell therapy from a small starting volume of bone marrow or umbilical cord blood cells. Although we may not market the AastromReplicell(TM) System in the United States for stem cell therapy unless and until approval is obtained from the U.S. Food and Drug Administration (FDA), production-level versions of the AastromReplicell(TM) System have been completed and we have obtained permission to affix the CE Mark to such versions. CE Mark approval allows for marketing of the product in Europe. We may also market the AastromReplicell(TM) System in the U.S. for research and investigational use.

We have also recently initiated development programs for AastromRepllicell(TM) System therapy kits for the production of bone-forming cells and for dendritic cells. The new OC-I Therapy Kit is intended for the production of bone-forming cells for the treatment of patients with degenerative bone diseases such as osteoporosis. We recently initiated our first Phase I/II-Pilot clinical study for the OC-I Therapy Kit in patients with severe osteoporosis. Our new DC-I Therapy Kit is being developed for the production of human dendritic cells to be used in cancer immunotherapy applications. Recent clinical studies conducted by others have indicated that modified dendritic cells may be an important new way to treat certain cancers.

Our principal executive offices are located at 24 Frank Lloyd Wright Drive, P. O. Box 376, Ann Arbor, MI 48106. Our telephone number is (734) 930-5555.

## RISK FACTORS

You should carefully consider the following risk factors before purchasing our common stock. The risks and uncertainties described below are not the only ones we face. There may be additional risks and uncertainties that are not known to us or that we do not consider to be material at this time. If the events described in these risks occur, our business, financial condition and results of operations would likely suffer. This prospectus contains forward-looking statements which involve risks and uncertainties. Our actual results may differ significantly from the results discussed in the forward-looking statements. This section discusses some of the factors that might cause those differences.

**If We Cannot Complete Our Product Development Activities Successfully, Our Ability to Operate or Finance Operations Will Be Severely Limited.**

Commercialization in the United States of our lead product candidate, the AastromReplicell(TM) Cell Production System, will require additional research and development as well as substantial clinical trials. While we have commenced initial marketing on a very limited basis of the AastromReplicell(TM) System in Europe, we believe that the United States will be the principal market for our products. We may not be able to successfully complete development of the AastromReplicell(TM) System or our other product candidates, or successfully market our technologies or product candidates. We and any of our potential collaborators may encounter problems and delays relating to research and development, regulatory approval and intellectual property rights of our technologies and product candidates. Our research and development programs may not be successful, and our cell culture technologies and product candidates may not facilitate the ex vivo production of cells with the expected biological activities in humans. Our technologies and product candidates may not prove to be safe and efficacious in clinical trials, and we may not obtain the intended regulatory approvals for our technologies or product candidates and the cells produced in such products. If any of these events occur, we may not have adequate resources to continue operations for the period required to resolve the issue delaying commercialization and we may not be able to raise capital to finance our continued operation during the period required for resolution of that issue.

**We Cannot Be Certain That We Will Be Able to Raise the Required Capital to Conduct Our Operations and Develop Our Products.**

We will require substantial capital resources in order to conduct our operations and develop our products. In October 1999, we were forced to reduce operations based on our declining level of capital resources and our limited financing alternatives available at that time. Although we have started to restore operating activities, the previous reduction in our operating activities has negatively affected our ability to develop our products and has delayed our product development programs. Based on current funding and anticipated operating activities, we expect that our available cash and expected interest income will be sufficient to finance our current activities through the end of our fiscal year ending June 30, 2001. This is a forward-looking statement and could be negatively affected by funding limitations, the implementation of additional research and development programs and other factors discussed under this heading. We are currently pursuing additional sources of financing. If we cannot obtain additional funding prior to that time, we will be forced to make substantial reductions in the scope and size of our operations, and may be forced to curtail activities that we currently plan to resume. In order to grow and expand our business, and to introduce our product candidates into the marketplace, we will need to raise additional funds. We will also need additional funds or a collaborative partner, or both, to finance the research and development activities of our new product candidates for the production of additional cell types.

Our future capital requirements will depend upon many factors, including:

- . 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;
- . the ability of Aastrom to establish additional collaborative relationships; and
- . effective commercialization activities and facility expansions if and as required.

Because of our long-term funding requirements, we may attempt to access the public or private equity markets if and whenever conditions are favorable, even if we do not have an immediate need for additional capital at that time. Further, we may enter into financing transactions at rates which are at a substantial discount to market. This additional funding may not be available to us on reasonable terms, or at all. If adequate funds are not available, we may be required to further delay or terminate research and development programs, curtail capital expenditures, and reduce business development and other operating activities.

**We Must Successfully Complete Our Clinical Trials to be Able to Market Our Products.**

To be able to market products in the United States, we must demonstrate, through extensive preclinical studies and clinical trials, the safety and efficacy of our processes and product candidates, together with the cells produced by such processes in such products, for application in the treatment of humans. We are currently conducting clinical trial to demonstrate the safety and biological activity of patient-derived cells produced in the AastromReplicell System(TM). Depending on the availability of resources, we intend to commence at least one additional clinical trial to demonstrate the safety and biological activity of umbilical cord blood cells produced in the AastromReplicell(TM) System. If our clinical trials are not successful, our products may not be marketable.

Our ability to complete our clinical trials in a timely manner depends on many factors, including the rate of patient enrollment. Patient enrollment can vary with the size of the patient population, the proximity of suitable patients to clinical sites, perceptions of the utility of stem cell therapy for the treatment of certain diseases and the eligibility criteria for the study. We have experienced delays in patient accrual in our previous and current clinical trials. If we experience future delays in patient accrual, we could experience increased costs and delays associated with clinical trials which would impair our product development programs and our ability to market our products. Furthermore, the U.S. Food and Drug Administration ("FDA") monitors the progress of clinical trials and it may suspend or terminate clinical trials at any time due to patient safety or other considerations.

**Failure to Obtain and Maintain Required Regulatory Approvals Would Severely Limit Our Ability to Sell Our Products.**

We must obtain the approval of the FDA before commercial sales of our product candidates may commence in the United States, which we believe will be the principal market for our products. We may also be required to obtain additional approvals from foreign regulatory authorities to continue or increase our sales activities in those jurisdictions. If we cannot demonstrate the safety, reliability and efficacy of our product candidates, or of the cells produced in such products, we may not be able to obtain required regulatory approvals. Many of the patients enrolled in the clinical trials will have previously undergone extensive treatment which will have substantially weakened the patients and may have irreparably damaged the ability of their blood and immune system to recover. Some patients undergoing the transplant recovery process have died, from causes that were, according to the physicians involved, unrelated to the AastromReplicell(TM) System procedure, and it is possible that other patients may die or suffer severe complications during the course of either the current or future clinical trials. In addition, patients receiving cells produced with our technologies and product candidates may not demonstrate long-term engraftment in a manner comparable to cells obtained from current stem cell therapy procedures. If we cannot demonstrate the safety or efficacy of our technologies and product candidates, including long-term sustained engraftment, or if one or more patients die or suffer severe complications, the FDA or other regulatory authorities could delay or withhold regulatory approval of our product candidates.

Finally, even if we obtain regulatory approval of a product, that approval may be subject to limitations on the indicated uses for which it may be marketed. Even after granting regulatory approval, the FDA, other regulatory agencies, and governments in other countries continue to review and inspect marketed products, manufacturers and manufacturing facilities. Later discovery of previously unknown problems with a product, manufacturer or facility may result in restrictions on the product or manufacturer, including a withdrawal of the product from the market. Further, governmental regulatory agencies may establish additional regulations which could prevent or delay regulatory approval of our products.



Even If We Obtain Regulatory Approvals to Sell Our Products, Lack of Commercial Acceptance Would Impair Our Business.

Our product development efforts are primarily directed toward obtaining regulatory approval to market the AastromReplicell(TM) System as an alternative to, or as an improvement for, the bone marrow harvest and peripheral blood progenitor cell stem cell collection methods. These stem cell collection methods have been widely practiced for a number of years, and our technologies or product candidates may not be accepted by the marketplace as readily as these or other competing processes and methodologies. Additionally, our technologies or product candidates may not be employed in all potential applications being investigated, and any limited applications would limit the market acceptance of our technologies and product candidates and our potential revenues. As a result, even if we obtain all required regulatory approvals, we cannot be certain that our products and processes will be adopted at a level that would allow us to operate profitably.

Failure of Third Parties to Manufacture Component Parts or Provide Limited Source Supplies Would Impair Our New Product Development and Our Sales Activities.

We rely solely on third parties to manufacture our product candidates and their component parts. We also rely solely on third party suppliers to provide necessary key mechanical components, as well as growth factors and other materials used in the cell expansion process. We would not be able to obtain alternate sources of supply for many of these items on a short-term basis. In October 1999, we suspended manufacturing of our products. While we are in the process of re-establishing our product manufacturing capabilities, we have not yet completed those activities and resumed production of certain components of our product line. If any of our key manufacturers or suppliers fail to perform their respective obligations or if our supply of growth factors, components or other materials is limited or interrupted, we would not be able to conduct clinical trials or market our product candidates on a timely and cost-competitive basis, if at all.

Furthermore, some of the compounds used by us in our current stem cell expansion processes involve the use of animal-derived products. Suppliers or regulatory authorities may limit or restrict the availability of such compounds for clinical and commercial use. Any restrictions on these compounds would impose a potential competitive disadvantage for our products. If we were not able to develop or obtain alternative compounds, our product development and commercialization efforts would be harmed.

Finally, we may not be able to continue our present arrangements with our suppliers, supplement existing relationships, establish new relationships or be able to identify and obtain the ancillary materials that are necessary to develop our product candidates in the future. Our dependence upon third parties for the supply and manufacture of these items could adversely affect our ability to develop and deliver commercially feasible products on a timely and competitive basis.

Our Past Losses and Expected Future Losses Cast Doubt on Our Ability to Operate Profitably.

We were incorporated in 1989 and have experienced substantial operating losses since inception. As of September 30, 2000, we have incurred net operating losses totaling approximately \$80.4 million. These losses have resulted principally from costs incurred in the research and development of our cell culture technologies and the AastromReplicell(TM) System, general and administrative expenses, and the prosecution of patent applications. We expect to incur significant operating losses until product sales increase, primarily owing to our research and development programs, including preclinical studies and clinical trials, and the establishment of marketing and distribution capabilities necessary to support commercialization efforts for our products. We cannot predict with any certainty the amount of future losses. Our ability to achieve profitability will depend, among other things, on successfully completing the development of our product candidates, obtaining regulatory approvals, establishing manufacturing, sales and marketing arrangements with third parties, and raising sufficient funds to finance our activities. We may not be able to achieve or sustain profitability.

Our Stock Price Has Been Volatile and Future Sales of Substantial Numbers of Our Shares Could Have an Adverse Effect on the Market Price of Our Shares.

The Market price of shares of our common stock has been volatile. The price of our common stock may continue to fluctuate in response to a number of events and factors, such as:

- . clinical trial results;
- . the amount of our cash resources and our ability to obtain additional funding;
- . announcements of research activities, business developments, technological innovations or new products by us or our competitors;
- . changes in government regulation;

- . disputes concerning patents or proprietary rights;
- . changes in our revenues or expense levels;
- . public concern regarding the safety, efficacy or other aspects of the products or methodologies we are developing; and
- . changes in potential recommendations by securities analysts.

Any of these events may cause the price of our shares to fall, which may adversely affect our business and financing opportunities. In addition, the stock market in general and the market prices for biotechnology companies in particular have experienced significant volatility that often has been unrelated to the operating performance or financial conditions of such companies. These broad market and industry fluctuations may adversely affect the trading price of our shares, regardless of our operating performance or prospectus. For example, since November, 1999 our stock price has experienced a day where it closed at approximately twice the previous day's closing price and another day when it dropped by over 20% from the previous day's closing price. Additionally, since December 1999 the closing market price of our common stock has ranged from \$0.60 to \$7.75 per share. Based upon market fluctuations in our stock and depending upon the timing and amount of shares sold by us, if any, pursuant to this prospectus, investors who purchase our common stock may experience a significant decrease in the market price of their shares over a short period of time.

In addition, sales, or the possibility of sales, of substantial numbers of shares of common stock in the public market, including sales pursuant to this prospectus, could adversely affect prevailing market prices of shares of common stock. Our employees hold a significant number of options to purchase shares, many of which are presently exercisable. Employees may exercise their options and sell shares shortly after such options become exercisable, particularly if they need to raise funds to pay for the exercise of such options or to satisfy tax liabilities that they may incur in connection with exercising their options. Additionally, beginning January 1, 2001, COBE BCT will be able to sell all of its approximately 2.4 million shares of our common stock without restriction.

Given Our Limited Internal Sales and Marketing Capabilities, We Need to Develop Collaborative Relationships to Sell, Market and Distribute Our Products.

While we have commenced initial marketing on a limited basis of the AastromReplicell(TM) System in Europe, we have only limited internal sales, marketing and distribution capabilities. We intend to market our products through collaborative relationships with companies for sales, marketing and distribution capabilities. If we cannot develop and maintain those relationships, we would have only a limited ability to market, sell and distribute our products. Even if we are able to enter into such relationships, they may not succeed or be sustained on a long-term basis, and termination would require us to develop alternate arrangements at a time when we need sales, marketing or distribution capabilities to meet existing demand. For example, in November 1998 Aastrom and COBE BCT terminated a strategic alliance for the worldwide distribution of the AastromReplicell(TM) System for stem cell therapy and related uses. We are now seeking to enter into other arrangements relating to the development and marketing of our product candidates.

Any Changes in the Governmental Regulatory Classifications of Our Products Could Prevent, Limit or Delay Our Ability to Market or Develop Our Products.

The FDA establishes regulatory requirements based on the classification of a product. Although the FDA has indicated it intends to regulate the AastromReplicell(TM) System for stem cell therapy as a Class III medical device, the FDA may ultimately choose to regulate the AastromReplicell(TM) System under another category. Because our product development programs are designed to satisfy the standards applicable to Class III medical devices, a change in the regulatory classification would affect our ability to obtain FDA approval of our products. Also, the FDA is in the process of developing its requirements with respect to somatic cell therapy and gene cell therapy products. Until the FDA issues definitive regulations covering our product candidates, the regulatory guidelines or requirements for approval of such product candidates and/or the cells produced by them will continue to be uncertain.

If We Do Not Keep Pace With Our Competitors and With Technological and Market Changes, Our Products May Become Obsolete and Our Business May Suffer.

The market for our product is very competitive and is subject to rapid technological changes. Many of our competitors have significantly greater resources, more product candidates and have developed product candidates and processes that directly compete with our products. Our competitors may have developed, or could in the future develop, new technologies that compete with our products or even render our products obsolete. In addition, some recently published studies have suggested that stem cell therapy, which is the current principal market for our SC-I Therapy Kit, may have limited clinical benefit in the treatment of breast cancer, which is a significant portion of the current overall stem cell transplant market. Our products are designed to improve upon traditional stem cell collection methods, but even if we are able to demonstrate improved or equivalent results, practitioners may not switch to our new processes. Given the experience and expertise associated with traditional methods, if we cannot develop our cell production procedure to lead to a less expensive and quicker recovery time than seen with the traditional methods, then we will suffer a competitive disadvantage. Finally, to the extent that others develop new technologies that address the diseases and health conditions we have targeted, our business will suffer.

If Our Patents and Proprietary Rights Do Not Provide Substantial Protection, Then Our Business and Competitive Position Will Suffer.

Our success depends in large part on our ability to develop or license and protect proprietary products and technologies. However, we cannot be assured that patents will be granted on any of our pending or future patent applications. We also cannot be assured that the scope of any of our issued patents will be sufficiently broad to offer meaningful protection. In addition, our issued patents or patents licensed to us could be successfully challenged, invalidated or circumvented so that our patent rights would not create an effective competitive barrier. Furthermore, we rely on licenses granted by the University of Michigan for certain of our patent rights. If we breach such agreements or otherwise fail to comply with such agreements, or if such agreements expire or are otherwise terminated, we may lose our rights under the patents held by the University of Michigan. We also rely on trade

secrets and unpatentable know-how which we seek to protect, in part, by confidentiality agreements with our employees, consultants, suppliers and licensees. These agreements may be breached, and we might not have adequate remedies for any breach. If this were to occur, our business and competitive position would suffer.

#### Intellectual Property Litigation Could Harm Our Business.

Our success will also depend in part on our ability to develop commercially viable products without infringing the proprietary rights of others. Although we have not been subject to any filed infringement claims, other patents could exist or could be filed which would prohibit or limit our ability to market our products or maintain our competitive position. In the event of an intellectual property dispute, we may be forced to litigate. Intellectual property litigation would divert management's attention from developing our products and would force us to incur substantial costs regardless of whether we are successful. An adverse outcome could subject us to significant liabilities to third parties, and force us to curtail or cease the development and sale of our products and processes.

#### The Market for Our Products Will Be Heavily Dependent on Third Party Reimbursement Policies.

Our ability to successfully commercialize our product candidates will depend on the extent to which government healthcare programs, such as Medicare and Medicaid, as well as private health insurers, health maintenance organizations and other third party payors will pay for our products and related treatments. 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. Reimbursement in the United States or foreign countries may not be available or maintained for any of our product candidates. If we do not obtain approvals for adequate third-party reimbursements, we may not be able to establish or maintain price levels sufficient to realize an appropriate return on our investment in product development. Any limits on reimbursement available from third-party payors may reduce the demand for, or negatively affect the price of, our products. For example, recently published studies have suggested that stem cell transplantation in breast cancer, which constitutes a significant portion of the overall stem cell therapy market, may have limited clinical benefit. The market for our products would be negatively affected by lack of reimbursement for these procedures by insurance payors.

#### Potential Product Liability Claims Could Effect Our Earnings and Financial Condition.

We face an inherent business risk of exposure to product liability claims in the event that the use of the AastronReplicell(TM) System during research and development efforts, including clinical trials, or after commercialization results in adverse effects. As a result, we may incur significant product liability exposure, which could exceed existing insurance coverage. We may not be able to maintain adequate levels of insurance at reasonable cost and/or reasonable terms. Excessive insurance costs or uninsured claims would increase our operating loss and affect our financial condition.

#### If We Cannot Attract and Retain Key Personnel, Then Our Business Will Suffer.

Our success depends in large part upon our ability to attract and retain highly qualified scientific and management personnel. We face competition for such personnel from other companies, research and academic institutions and other entities. In an effort to conserve financial resources, we have been forced to implement reductions in our work force on two separate occasions. As a result of these and other factors, we may not be successful in hiring or retaining key personnel.

#### Our Outstanding Warrants Have the Potential for Substantial Dilution of Stockholders.

In June 2000, we issued warrants to purchase up to 3,348,915 shares of our common stock at \$0.01 per share. If all 3,348,915 shares of common stock are issued under the warrants, then holders of common stock could experience significant dilution of their investment.

The exercise price of the warrants that we issued in February 2000 is subject to reduction in the event the price of our common stock goes down at specified times in the future or if we issue additional securities at less than the warrant exercise price. If the exercise price of these warrants is reduced, there would also be an increase in the number of shares that could be issued upon exercise of the warrants. The warrants are currently exercisable for 1,382,816 shares of common stock. This number of shares could increase to 2,614,386 shares of common stock and the exercise price could be reduced to as low as \$1.60 per share. Holders of common stock could therefore experience dilution of their investment upon exercise of these warrants.

Our Corporate Documents and Michigan Law Contain Provisions That May Make It More Difficult For Us to Be Acquired.

Our board of directors has the authority, without shareholder approval, to issue additional shares of preferred stock and to fix the rights, preferences, privileges and restrictions of these shares without any further vote or action by our shareholders. This authority, together with certain provisions of our charter documents, may have the effect of making it more difficult for a third party to acquire, or of discouraging a third party from attempting to acquire, control of our company. This effect could occur even if our shareholders consider the change in control to be in their best interest.

We May Be Required to Redeem a Portion of Our Shares, Which Would Significantly Reduce Our Limited Cash Resources.

The original purchasers of the shares and warrants issued in February 2000 and June 2000 may require us to redeem some or all of those shares in the event that we fail to perform certain administrative activities that are within our control. These administrative activities include: issuing the shares of common stock upon the exercise of the warrants, transferring or instructing the transfer agent to transfer shares of common stock issued upon exercise of the warrants when required and removing any restrictive legends from such shares of common stock when required. Such a redemption could significantly reduce our limited capital resources.

If We Do Not Continue to Meet the Nasdaq Listing Requirements Then Our Stock May Be Delisted From Nasdaq, Which Could Affect the Market Price and Liquidity of Our Stock.

We are required to meet certain financial tests (including, but not limited to, a minimum bid price of our common stock of \$1.00 and \$4 million in tangible net worth) to maintain the listing of our common stock on the Nasdaq National Market. Within the last year, our common stock price has fallen below the minimum level for some periods and during other periods our tangible net worth has been below the amount required. During late December 2000, our stock price has again fallen below \$1.00. In the future, our stock price or tangible net worth may fall below the Nasdaq requirements, or we may not comply with other listing requirements, with the result being that our common stock might be delisted. If that happened the market price and liquidity of our common stock would be impaired.

Absence of Dividends Could Reduce Our Attractiveness to Investors.

Some investors favor companies that pay dividends, particularly in market downturns. We have never paid cash dividends on our common stock and do not anticipate paying any cash dividends on our common stock in the foreseeable future. Therefore, your return on this investment will depend on your ability to sell our stock at a profit.

#### 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. These forward-looking statements include statements regarding:

- . uncertainties related to potential strategic collaborations with others;
- . future capital needs and uncertainty of additional funding;
- . uncertainties related to product development and marketability;
- . uncertainties related to clinical trials;
- . manufacturing and supply uncertainties and dependence on third parties;
- . anticipation of future losses;
- . limited sales and marketing capabilities;
- . uncertainty of regulatory approval and extensive government regulation;
- . 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 in this Risk Factors section, 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. We assume no obligation to update any such forward-looking statement or reason why actual results might differ.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document we file at the SEC's public reference rooms located at Room 1024, 450 Fifth Street, N.W., Washington, D.C. 20549, at The Citicorp Center, 500 West Madison Street, Suite 1400, Chicago, Illinois 60661, and at Seven World Trade Center, Suite 1300, New York, New York 10048. Please call the SEC at 1-800-SEC-0330 for further information on the public reference rooms. Our filings with the SEC are also available to the public on the SEC's Internet web site at <http://www.sec.gov>.

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The SEC allows us to "incorporate by reference" the information we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus, and information that we file with the SEC later will automatically update and supersede the information in this prospectus or incorporated by reference. The following documents filed by us and any future filings made by us with the SEC under Sections 13(a), 13(c) 14 or 15(d) of the Securities Exchange Act of 1934, until we sell all of the common stock offered hereby, are incorporated by reference in this prospectus:

1. Our Annual Report on Form 10-K for the year ended June 30, 2000 (Commission File No.: 000-22025);
2. Our Quarterly Report on Form 10-Q for the quarter ended September 30, 2000 (Commission File No. 000-22025); and
3. Our Registration Statement on Form 8-A filed with the Commission on April 11, 1997 (Commission File No.: 000-22025).

YOU MAY REQUEST A COPY OF THESE FILINGS, AT NO COST, BY WRITING OR TELEPHONING US AT AASTROM BIOSCIENCES, INC., 24 FRANK LLOYD WRIGHT DRIVE, P.O. BOX 376, ANN ARBOR, MICHIGAN 48106, TELEPHONE NUMBER (734) 930-5555, ATTENTION: CHIEF FINANCIAL OFFICER.

## PLAN OF DISTRIBUTION

We may offer our common stock:

- directly to purchasers;
- to or through underwriters;
- through dealers, agents or institutional investors; or
- through a combination of such methods.

Regardless of the method used to sell the securities, we will provide a prospectus supplement or amendment that will disclose:

- the identity of any underwriters, dealers, agents or investors who purchase the securities;
- the material terms of the distribution, including the amount sold and the consideration paid;
- the amount of any compensation, discounts or commissions to be received by the underwriters, dealers or agents;
- the terms of any indemnification provisions, including indemnification from liabilities under the federal securities laws; and
- the nature of any transaction by an underwriter, dealer or agent during the offering that is intended to stabilize or maintain the market price of the securities.

We may sell our common stock at fixed prices, which may change, at market prices prevailing at the time of sale, at prices related to prevailing market prices or at negotiated prices.

In connection with the sale of our common stock, underwriters may receive compensation from us or from purchasers of our common stock in the form of discounts, concessions or commissions. Underwriters, dealers and agents that participate in the distribution of our common stock may be deemed to be underwriters. Discounts or commissions they receive and any profit on their resale of our common stock may be considered underwriting discounts and commissions under the Securities Act of 1933.

We may agree to indemnify underwriters, dealers and agents who participate in the distribution of our common stock against various liabilities, including liabilities under the Securities Act of 1933. We may also agree to contribute to payments which the underwriters, dealers or agents may be required to make in respect of these liabilities. We may authorize dealers or other persons who act as our agents to solicit offers by various institutions to purchase our common stock from us under contracts which provide for payment and delivery on a future date. We may enter into these contracts with commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and others. If we enter into these agreements concerning any series of our common stock, we will indicate that in the prospectus supplement or amendment.

In connection with an offering of our common stock, underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of our common stock. Specifically, underwriters may over-allot in connection with the offering, creating a syndicate short position in our common stock for their own account. In addition, underwriters may bid for, and purchase, our common stock in the open market to cover short positions or to stabilize the price of our common stock. Finally, underwriters may reclaim selling concessions allowed for distributing our common stock in the offering if the underwriters repurchase previously distributed common stock in transactions to cover short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of our common stock above independent market levels. Underwriters are not required to engage in any of these activities and may end any of these activities at any time. Agents and underwriters may engage in transactions with, or perform services for, us and our affiliates in the ordinary course of business.



## USE OF PROCEEDS

We cannot guarantee that we will receive any proceeds in connection with this offering because we may choose not to issue any shares of common stock.

Unless otherwise provided in a supplement or amendment to this prospectus, we intend to use any net proceeds from this offering, together with other available funds, for operating costs, capital expenditures and working capital needs and for other general corporate purposes.

We have not specifically identified the precise amounts we will spend on each of these areas or the timing of these expenditures. The amounts actually expended for each purpose may vary significantly depending upon numerous factors, including the amount and timing of the proceeds from this offering, progress with clinical product development and other cell therapy application programs. In addition, expenditures may also depend on the establishment of new collaborative arrangements with other companies, the availability of other financing, and other factors.

We anticipate that we will be required to raise substantial additional capital to continue to fund the clinical development of our cell therapy applications. Additional capital may be raised through additional public or private financing, as well as collaborative relationships, incurring debt and other available sources.

## LEGAL MATTERS

The validity of the common stock offered hereby will be passed upon for Aastrom by Pepper Hamilton LLP, Detroit, Michigan acting as special counsel to Aastrom. Gray Cary Ware & Freidenrich LLP, San Diego, California, has acted as counsel to Aastrom 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, 2000, 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.

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 (all expenses other than the SEC Registration Fee are estimates):

Item -----	Company Expense -----
SEC Registration Fee.....	\$ 2,130
Printing and engraving expenses	\$ 5,000
Legal fees and expenses.....	\$ 50,000
Accounting fees and expenses....	\$ 10,000
Nasdaq Filing Fees.....	\$ 17,500
Miscellaneous.....	\$ 15,370
-----	-----
 Total.....	 \$100,000
=====	=====

ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS.

Sections 1561 through 1571 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 -----
4.1*	Restated Articles of Incorporation
4.2*	Bylaws, as amended
5.1	Consent and Opinion of Pepper Hamilton LLP
23.1	Consent of PricewaterhouseCoopers LLP
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
*	Filed previously.

5. ITEM 17. UNDERTAKING.

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;
- (2) To include any prospectus required by section 10(a)(3) of the Securities Act of 1933 (the "Securities Act");
- (3) 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;
- (4) 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.
- (5) 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.
- (6) 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.

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.

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.

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.

The undersigned Registrant hereby undertakes that:  
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.

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 amended Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized in the City of Ann Arbor, State of Michigan, on December 29, 2000.

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 amended Registration Statement has been signed below by the following persons in the capacities and on the dates indicated.

Signature ----- Date -----	Title -----	
/s/ R. Douglas Armstrong, Ph.D. ----- R. Douglas Armstrong, Ph.D.	President, Chief Executive Officer and Chairman of the Board of Directors (Principal Executive Officer)	December 29, 2000
/s/ Todd E. Simpson ----- Todd E. Simpson	Vice President, Finance and Administration, Chief Financial Officer, Secretary and Treasurer (Principal Financial and Accounting Officer)	December 29, 2000
* ----- Fabrizio Bonanni	Director	December 29, 2000
* ----- Mary L. Campbell	Director	December 29, 2000
* ----- Arthur F. Staubitz	Director	December 29, 2000
* ----- Joseph A. Taylor	Director	December 29, 2000
* ----- Alan M. Wright	Director	December 29, 2000
* By: R. Douglas Armstrong ----- Attorney in Fact		

INDEX TO EXHIBITS

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24.1*	Power of Attorney

\* Filed previously

Exhibit 5.1

December 29, 2000

Securities and Exchange Commission  
Judiciary Plaza  
450 Fifth Street, N.W.  
Washington, D.C. 20549

Re: Aastrom Biosciences, Inc. amended Registration  
Statement on Form S-3

File No.: 333-51350

Gentlemen:

We have acted as special counsel to Aastrom Biosciences, Inc., a Michigan corporation (the "Company"), in connection with the preparation and filing with the Securities and Exchange Commission (the "Commission") of an amended registration statement filed with the SEC on December 29, 2000 (the "Registration Statement") of the Company on Form S-3 under the Securities Act of 1933, as amended (the "Act"). The Registration Statement relates to the proposed issuance by the Company of shares of the Company's Common Stock (the "Shares") covered by the Registration Statement.

In this connection, we have examined the Registration Statement, including the exhibits thereto, the originals or copies, certified or otherwise identified to our satisfaction, of the Articles of Incorporation and the By-Laws of the Company amended to date, resolutions of the Company's Board of Directors and such other documents and corporate records relating to the Company, and the issuance and sale of the Company's common stock as we have deemed appropriate. The opinion expressed herein is based exclusively on the applicable provisions of the Michigan Business Corporation Act as in effect on the date hereof.

On the basis of the foregoing, we are of the opinion that the Shares, assuming payment made in accordance with a duly authorized prospectus supplement or amendment, will be, duly authorized, validly issued, fully paid, and non-assessable.

We hereby consent to the reference to our firm under the caption "Legal Matters" in the Registration Statement and to the filing of this opinion as an exhibit to the Registration Statement. Such consent does not constitute a consent under Section 7 of the Act, since we have not certified any part of such Registration Statement and do not otherwise come within the categories of persons whose consent is required under Section 7 of the Act or the rules and regulations of the Commission promulgated thereunder.

Very truly yours,

PEPPER HAMILTON LLP

By: /s/ Michael B. Staebler

\_\_\_\_\_  
Michael B. Staebler

Exhibit 23.1

CONSENT OF INDEPENDENT ACCOUNTANTS

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of our report dated August 4, 2000 relating to the financial statements, which appears in Aastrom Biosciences, Inc.'s Annual Report on Form 10-K for the year ended June 30, 2000. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/ PriceWaterhouseCoopers LLP

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PRICewaterhouseCOOPERS LLP

Minneapolis, Minnesota

December 28, 2000