Filed Pursuant To Rule 424 (b)(2)

File Number: 333-51350

PROSPECTUS SUPPLEMENT
(TO PROSPECTUS DATED JANUARY 5, 2001)

773,994 shares

AASTROM BIOSCIENCES, INC.

Common Stock

You should read this prospectus supplement and the related prospectus carefully before you invest. Both documents contain information you should consider when making your investment decision.

INVESTING IN OUR COMMON STOCK INVOLVES A HIGH DEGREE OF RISK. SEE "RISK FACTORS" BEGINNING ON PAGE 5 OF OUR PROSPECTUS DATED JANUARY 5, 2001 TO READ ABOUT FACTORS YOU SHOULD CONSIDER BEFORE BUYING SHARES OF OUR COMMON STOCK.

We are offering 773,994 shares of our common stock to Radyr Group Investments. Under the terms of the subscription agreement between Radyr and us, we negotiated the purchase price for these shares of common stock at an aggregate price of $1,250,000, or approximately $1.615 per share. We expect this transaction to close shortly following this filing. On June 14, 2001, the last reported sales price of our common stock on the Nasdaq National Market was $1.67 per share.

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

The date of this prospectus supplement is June 14, 2001.

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GENERAL

This prospectus supplement is part of a registration statement that we filed with the SEC using a "shelf" registration process. Under this shelf process, we may offer up to 7,700,000 shares of our common stock from time to time in one or more offerings. This prospectus supplement provides specific information about the offering of 773,994 shares of our common stock under the shelf registration statement. You should read carefully this prospectus supplement, the prospectus, and the information that we incorporate by reference into those documents. In case there are any differences or inconsistencies between this prospectus supplement the prospectus, and the information incorporated by reference, you should only rely on the information contained in the document with the latest date. Please refer to the information and documents listed under the heading "Where You Can Find More Information" in the prospectus. Since we filed the last amendment to the registration statement, we have filed with the SEC the following documents which are incorporated by reference into the prospectus and this prospectus supplement:

- Report on Form 10-Q for the quarter ended December 31, 2000.
- Report on Form 10-Q for the quarter ended March 31, 2001.

You should rely only on the information provided or incorporated by reference in this prospectus supplement and the related prospectus. We have not authorized anyone else to provide you with different information. You should not assume that the information in this prospectus supplement is accurate as of any date other than the date on the front of these documents.

MARKET FOR OUR COMMON STOCK

On June 14, 2001, the last reported sales price of our common stock on the Nasdaq National Market was $1.67 per share. Our common stock is traded on the Nasdaq National Market under the symbol "ASTM."

As of June 14, 2001 and before the issuance of the 773,994 shares pursuant to this prospectus supplement, we had 36,259,734 shares of common stock outstanding.

USE OF PROCEEDS

The net proceeds to us from this offering will be approximately $1,245,000. We plan to use the net proceeds for general corporate purposes, including activities described in the prospectus. We expect to evaluate from time to time the acquisition or license of businesses, technologies or products for which a portion of the net proceeds may be used; however, we have no present plan or commitments for any acquisition or license. Pending those uses, to the extent the proceeds exceed the amount of cash we estimate we will need for current expenditures, we will invest the net proceeds in interest-bearing United States Government securities.

PLAN OF DISTRIBUTION

The sale of common stock to Radyr is being made on terms negotiated between Radyr and us. The subscription agreement between Radyr and us includes the following representations:

- Radyr is buying these shares as a principal for its own account for investment and has no present plans, arrangements or obligations to sell any of these shares to any other person.

- Radyr is not a broker, dealer or member of the NASD or any affiliate of the foregoing.

DISCLOSURE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the information incorporated by reference into this prospectus supplement contains a number of forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act. Statements in this document that are not historical facts are forward-looking statements. Such forward-looking statements include those relating to:

- potential strategic collaborations with others
- future capital needs and plans for additional funding
- product development plans and marketing strategies
- clinical trial expectations
- projected capital needs and financial performance
- timing and results of regulatory approvals and the effect of government regulation
- expectations as to competitive conditions

Statements containing terms such as "believes," "plans," "expects," "intends," "estimates," "anticipates" and other phrases of similar meaning imply uncertainty and are also forward-looking statements.

These forward-looking statements involve known or unknown risks and uncertainties which may cause our actual results in future periods to differ materially from our current expectations. We make cautionary statements in certain sections of the prospectus, including under the caption "Risk Factors." These cautionary statements apply to all forward-looking statements wherever they appear in this prospectus supplement or the prospectus, or in the materials incorporated by reference into this prospectus supplement or the prospectus. In light of these risks, uncertainties and assumptions, the forward-looking statement discussed in this prospectus supplement, the prospectus or other documents incorporated by reference might not occur. You should not place undue reliance on any forward-looking statement.

Filed Pursuant To Rule 424(b)(2)
File Number: 333-51350

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 $0.90625 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 5 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 JANUARY 5, 2001.

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

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 AastromReplicell(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 shortly. 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 Aastrom Replicell(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 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 clinicals trial to demonstrate the safety and biological activity of patient-derived cells produced in the AastromReplicell(TM) System. 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 prospects. 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 AastromReplicell(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.

Our Stock May Be Delisted From Nasdaq, Which Could Affect its Market Price and Liquidity.

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.

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.