Filed Pursuant to
Rule 424(b)(3)
Registration No. 333-108963

PROSPECTUS

AASTROM BIOSCIENCES, INC.
10,000,000 SHARES OF COMMON STOCK

We are offering to our shareholders up to an aggregate of 10,000,000 shares of our common stock for purchase from time to time under our Shareholder Direct Stock Purchase Plan. The prices at which shareholders may buy the shares will be determined by the prevailing market price for the shares.

Shareholders who enroll may purchase between $250 and $10,000 of stock each month. Purchases will be made on the first Wednesday after the 15th of each month. The purchase price of the shares will be 3% below the average of the closing sale prices for our common stock as reported by Nasdaq for the three trading days ending two days before the purchase date.

Our common stock is quoted on the Nasdaq SmallCap Market under the symbol “ASTM.” On January 26, 2004, the last reported sale price for our common stock was $1.65 per share.

INVESTING IN OUR COMMON STOCK INVOLVES A HIGH DEGREE OF RISK. YOU SHOULD CONSIDER CAREFULLY THE RISK FACTORS BEGINNING ON PAGE 6 OF THIS PROSPECTUS BEFORE MAKING A DECISION TO PURCHASE OUR STOCK.

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.

The date of this Prospectus is January 27, 2004.

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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. Information incorporated by reference in this prospectus is accurate only as of the date of the document incorporated by reference. In this prospectus, unless otherwise indicated, the words “we,” “us,” and “our” refer to Aastrom Biosciences, Inc. and its subsidiaries.

FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended and Section 21E of the Securities Exchange Act of 1934, as amended. Such forward-looking statements include statements regarding, among other things, (a) our expectations about product development activities, (b) our growth strategies, (c) anticipated trends in our industry, (d) our future financing plans, and (e) our anticipated needs for capital. Forward-looking statements, which involve assumptions and describe our future plans, strategies, and expectations, are generally identifiable by use of the words “may,” “will,” “should,” “expect,” “anticipate,” “estimate,” “believe,” “intend,” or “project” or the negative of these words or other variations on these words or comparable terminology. This information may involve known and unknown risks, uncertainties, and other factors that may cause our actual results, performance, or achievements to be materially different from the future results, performance, or achievements expressed or implied by any forward-looking statements. These statements may be found under “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Business,” in the Form 10-K and other reports that are incorporated by reference into this prospectus, as well as in this prospectus generally. Actual events or results may differ materially from those discussed in forward-looking statements as a result of various factors, including, without limitation, the risks outlined under “Risk Factors” and matters described in this prospectus (including the information incorporated by reference). In light of these risks and uncertainties, the events anticipated in the forward-looking statements may not occur.

SUMMARY

The following summary highlights selected information from this prospectus and in information incorporated by reference. Because this is a summary, it does not contain all the information about us that may be important to you. You should read this entire prospectus and the other documents and the financial statements and related notes which are incorporated by reference in this prospectus.

Our Business

Aastrom Biosciences, Inc. (Aastrom) was incorporated in March 1989 (Inception), began employee-based operations in 1991. We currently operate our business in one reportable segment - research and product development, conducted both on our own behalf and in connection with various collaborative research and development agreements with others, involving the development and sale of processes and products for the *ex vivo* production of human cells for use in cell therapy.

We are a late-stage development company that has strategically moved from a business model that was originally based on the Bone Marrow Transplantation market to a company focused on human cell-based therapies. We have identified a multiple path strategy to pursue revenue based on our proprietary *ex vivo* cell production technology, including the near-term Cell Production Products operation, and an active Prescription Cell Product pipeline for stem cell tissue repair and regeneration, and cancer and infectious disease treatments.

Our core technology is based on the Company's proprietary AastromReplicell™ System, an integrated system of instrumentation and single-use consumable kits that implements our patented Single-Pass Perfusion process in a fully automated closed-loop culturing system to optimize cell growth and viability. This system provides nutrients to cells by mimicking the natural cell-growth environment, and enabling cells to grow effectively while retaining high biological function, without various cloning approaches. Our programs currently use bone marrow, cord blood and blood cells as starting sources of cells. As such, federal support or other factors relating to embryonal stem cell research have no direct impact on our current product programs. In addition, this system enables GMP-compliant manufacturing and automated process control for the commercial-scale production of human cells. We do not believe that any other comparable system currently exists.

Our Cell Production Products operation has created a path to modest near-term revenue. The AastromReplicell™ System and DC-I (dendritic cells for fusion and transfection), DCV-I (complex antigen-loaded dendritic cells) and DCV-II (peptide-loaded dendritic cells) cell production kits are being sold to academic researchers and companies that are developing cancer vaccines. The recent commercialization of our automated cell production instruments and cell-specific production kits is expected to generate revenues, although we are not yet able to project the market size or potential revenues or revenue growth for these products. The European Union has recently issued new requirements regarding the manufacturing of cell products and clinical trials. These changes have delayed or in some cases temporarily halted dendritic cell clinical trials in Europe, which has reduced the number of customer opportunities and affected our progress in our Cell Production Products business.

In addition, we are leveraging our *ex vivo* cell production technology for a growing Prescription Cell Product pipeline focused on two areas: Tissue Repair Cells (TRCs) for stem cell-derived tissue repair and regeneration, and Therapeutic Cells (TCs) for immune system-directed attacks on certain cancers and other infectious diseases.

Using the AastromReplicell™ System with its patented single-pass perfusion, TRCs are grown from a small sample of a patient's bone marrow and, once administered back to the patient, are intended to generate normal tissue. The primary TRC application being evaluated is our OCG-I cells for bone grafting (fusions, fractures or dental defects). In August 2003, the FDA approved our IND application to begin a multi-center Phase I/II clinical trial for bone grafting, and we recently began OCG-I clinical trials in both the United States and Europe. We also have in development OC-I cells for osteoporosis, and SC-I cells for autologous bone marrow transplants in lymphoma patients. The SC-I kit has been CE-Marked in Europe and is currently being evaluated by a limited number of centers in Europe. In the United States, the SC-I therapy reached Phase III trials, although these trials have halted due to a shift in medical practice that reduced patient need and availability. We also believe that the stem cell components of our TRCs may be useful for other medical indications, including the regeneration of cardiac

and vascular tissues. Our CB-I clinical trials have been closed out. We have no plans to continue product development of the CB-I kit at this time, unless entirely funded by grants, due to the limited size of the potential market.

We are developing TC products using human cells to cause the patient's immune system to attack certain cancers and other infectious diseases. Blood-derived dendritic cells, which are the body's crucial mobilizers of the immune T-Cells response, are cultured in the AastromReplicell™ System to produce our proprietary Dendricell™. After being exposed to a particular biological signal, or antigen, the Dendricell™ may act to trigger a cell-mediated immune response in a patient against the cancer cells or viri. In December 2003, the first Dendricell™ clinical trial began at and at Duke University for a colorectal cancer vaccine, and additional trials are being planned, including a trial at Stanford University for a multiple myeloma cancer vaccine. In addition, we are in the pre-clinical stage for a T-cell therapeutic targeting the Epstein-Barr Virus.

In addition to our consumable DC-I, DCV-I and DCV-II cell product kits, we have begun marketing our automated cell production instruments in Europe and the United States for research use. Through Zellera AG, Aastrom's wholly owned subsidiary located in Berlin, Germany, we are actively coordinating country-specific sub-distributorships and service networks in Europe.

While we have initiated marketing activities in Europe for the CE Marked SC-I, DC-I, DCV-I and the DCV-II products, we do not expect to generate positive cash flows from our consolidated operations for at least the next two to three years and then only if we can successfully generate significant product sales. In the next two to three years, we expect that our revenue sources will consist of sales from our Cell Production Product operation to academic and commercial research centers, grant revenue and research funding and licensing fees from potential future corporate collaborators. To date, we have financed our operations primarily through public and private sales of our equity securities. As a development-stage company, we have never been profitable and do not anticipate having net income unless and until significant product sales commence. Achieving this objective will require significant additional funding. Through September 30, 2003, we have accumulated losses of approximately $105 million. We cannot provide any assurance that we will be able to achieve profitability on a sustained basis, if at all, obtain the required funding to achieve our operating objectives, or complete additional corporate partnering or acquisition transactions.

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.

The Offering

This offering relates to the sale of up to 10,000,000 shares of our common stock to our shareholders pursuant to our Shareholder Direct Stock Purchase Plan.

Enrollment: This Plan is available only to shareholders. If you currently own Aastrom common stock registered in your name, you may participate in the Plan by completing and returning an Authorization and Enrollment Form. If you own Aastrom stock, but your shares are currently held by a bank or broker in their name (i.e., "street name") you may participate by completing an Authorization and Enrollment Form and either: (1) having your bank or broker register at least one of the shares in your name or, (2) providing Aastrom with both a portion of your brokerage account statement that shows you owned Aastrom shares as of a date within the last 3 months and completing and returning a Share Ownership Certification Form.

Purchases: Once you have enrolled, you may make purchases in any amount from $250 to $10,000 per month by check or through automatic monthly deductions from a qualified bank account. Purchases will be made monthly on the first Wednesday after the 15th of each month. The purchase price will be 3% below the average of the closing sale prices for our common stock as reported by Nasdaq for the three trading days ending two days before the purchase date.

Payment: Payments must be received at least five business days before the purchase date. Payments may be made by wire transfer, check or direct deductions from a bank account.

Safekeeping of Shares: All shares of Aastrom common stock purchased through the Plan will be held by the Plan Administrator in book-entry form in your account. If you hold Aastrom common stock certificates outside of the Plan, you may deposit those certificates for safekeeping with the Plan Administrator and those shares will be reflected in your Plan account.

Sale of Shares: The Plan provides you with the ability to sell all or any portion of Aastrom common stock held in the Plan in book-entry form. You may also request to receive a certificate for these shares and sell the shares outside the Plan.

Fees: There is a $10.00 enrollment fee associated with the Plan, as well as fees in the event of insufficient funds for checks or automatic deductions

More Information: For more information about the Plan, call the Plan's toll free number, (800) 509-5586 or see our website at www.aastrom.com.

Risk Factors

You should consider carefully all of the information contained in and incorporated by reference in this prospectus, including the information set forth under the caption "Risk Factors," before making an investment in the shares.

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 that involve risks and uncertainties. Our actual results may differ significantly from the results discussed in the forward-looking statements. This section discusses the risk factors that might cause those differences. You should also consider the additional information set forth in our SEC reports on Forms 10-K, 10-Q and 8-K and in the other documents considered a part of this prospectus. See "Where You Can Find More Information."

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, 2003, we have incurred cumulative net losses totaling approximately $105 million. These losses have resulted principally from costs incurred in the research and development of our cell culture technologies and the AastromReplicell™ 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 pre-clinical 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.

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 cell product candidates may commence in the United States, which we believe will be the largest market for our products. We may also be required to obtain additional approvals from foreign regulatory authorities to continue or increase our sales activities of cells and equipment 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. 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 hematopoietic 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 and regulatory agencies in other countries continue to review and inspect marketed products, manufacturers and manufacturing facilities, which may create additional regulatory burdens. 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, regulatory agencies may establish additional regulations that could prevent or delay regulatory approval of our products.

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. The AastromReplicell™ System may be regulated as a Class III medical device, or the FDA may ultimately choose to regulate the AastromReplicell™ System under another category. Because our product development programs are designed to satisfy the standards applicable to Class III medical devices and biological licensure for our cellular products, any change in the regulatory classification or designation would affect our ability to obtain FDA approval of our products. The AastromReplicell™ System is used to produce different cell mixtures, and each of these cell mixtures will, under current regulations be regulated as biologic products, which require a BLA.

The European Union has recently issued new requirements regarding the manufacturing of cell products and clinical trials. These changes have delayed or in some cases temporarily halted dendritic cell clinical trials in Europe, which has reduced the number of customer opportunities and affected our progress in our Cell Production Products business. Additionally, recent changes to the European Union Medical Products Prime Directive shifted patient-derived cells to the medicinal products category. These new regulations may delay some of our current planned clinical trials in Europe.

Our inability to complete our product development activities successfully would severely limit our ability to operate or finance operations.

Commercialization in the United States of our cell product candidates will require substantial clinical trials. While we have commenced initial marketing on a limited basis of the AastromReplicell™ System in Europe, we believe that the United States will be the largest market for our products. We may not be able to successfully complete development of our 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 production of cells outside the human body with the expected result. Our technologies and product candidates may not prove to be safe and efficacious in clinical trials, and we may not obtain the requisite 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 may not 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. The previous reduction in our operating activities has delayed our product development programs. We expect that our available cash and financing will be sufficient to fund currently planned activities through our 2004 fiscal year (ending June 30, 2004). However, in order to grow and expand our business, and to introduce our new 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 product candidates for the expansion of additional cell types. Accordingly, we are continuing to pursue additional sources of financing.

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

- continued scientific progress in our research and development programs;
- costs and timing of conducting clinical trials and seeking regulatory approvals;
- competing technological and market developments;
- our ability to establish additional collaborative relationships; and
- the effect of commercialization activities and facility expansions if and as required.

Because of our long-term funding requirements, we are likely 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 in the future, we may be required to further delay or terminate research and development programs, curtail capital expenditures, and reduce business development and other operating activities.

The issuance of additional common stock for funding has the potential for substantial dilution.

As noted above, we will need additional equity funding to provide us with the capital to reach our objectives. At current market prices, such an equity issuance would cause a substantially larger number of shares to be outstanding and would dilute the ownership interest of existing stockholders.

Our stock price has been volatile and future sales of substantial numbers of our shares could have an adverse affect on the market price of our shares.

The market price of shares of our common stock has been volatile, ranging in closing price between $0.23 and $1.77 during the twelve month period ended September 30, 2003. 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;
- entering into or terminating strategic relationships;
- 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;
- reports by securities analysts; and
- status of the investment markets.

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 stock, regardless of our operating performance or prospects.

We must successfully complete our clinical trials to be able to market certain of our products.

To be able to market Prescription Cell 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, for application in the treatment of humans. 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 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 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.

Even if we obtain regulatory approvals to sell our products, lack of commercial acceptance could impair our business.

We are seeking to obtain regulatory approval to market stem cell tissue repair and regeneration treatments, and cancer and infectious disease treatments. 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. Our tissue repair products will face competition from existing, and/or potential other new treatments in the future which could limit revenue potential. It may be necessary to increase the yield and/or cell type purity, for certain of our AastromReplicell™ System cell processes to gain commercial acceptance. Our technologies or product candidates may not be employed in all potential applications being investigated, and any reduction in applications would limit the market acceptance of our technologies and product candidates and our potential revenues.

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 such as Astro, Moll, Cambrex and Amgen to manufacture our product candidates, component parts and 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. 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 bone marrow or cord blood 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. Our inability to develop or obtain alternative compounds would harm our product development and commercialization efforts.

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 stock may be delisted from Nasdaq, which could affect its market price and liquidity.

We are required to meet certain financial tests (including a minimum bid price for our common stock of $1.00) to maintain the listing of our common stock on the Nasdaq Stock Market. Our common stock may be recommended for delisting (subject to any appeal we would file) if we do not maintain compliance with the Nasdaq requirements within specified periods and subject to permitted extensions. If our common stock were delisted, it could be more difficult to buy or sell our common stock and to obtain accurate quotations, and the price of our stock could suffer a material decline. Delisting would also impair our ability to raise capital.

Given our limited internal sales and marketing capabilities, we need to develop increased internal capability or collaborative relationships to sell, market and distribute our products.

While we have commenced initial marketing on a limited basis of the AastromReplicell™ System and SC-I, DC-I, DCV-I and DCV-II cell production kits in Europe and domestically for research use, we have only limited internal sales, marketing and distribution capabilities. We intend to get assistance to market our products through collaborative relationships with companies with established sales, marketing and distribution capabilities. While we have entered into such arrangements with respect to Switzerland, Turkey and Italy, we will need to establish additional relationships to be able to achieve the market coverage we desire. Our inability to develop and maintain those relationships would limit our ability to market, sell and distribute our products. Our inability to enter into successful, long-term relationships could require us to develop alternate arrangements at a time when we need sales, marketing or distribution capabilities to meet existing demand.

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 products is very competitive, is subject to rapid technological changes and varies for different individual products. For each of our potential products, we believe that there are potentially many competitive approaches being pursued, including some by private companies for which information is difficult to obtain.

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. As an example, in the past, published studies have suggested that hematopoietic stem cell therapy may have limited clinical benefit in the treatment of breast cancer, which was a significant portion of the overall hematopoietic stem cell transplant market. This resulted in a substantial decline in the market for the AastromReplicell™ System with our SC-I kit.

Our products are designed to improve and automate the processes for producing cells used in therapeutic procedures. Even if we are able to demonstrate improved or equivalent results, researchers and practitioners may not use our products and we will suffer a competitive disadvantage. As a result, we may be unable to recover the net book value of our inventory. Finally, to the extent that others develop new technologies that address the targeted application for our products, our business will suffer.

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. Further, in an effort to conserve financial resources, we have implemented 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. The Company has a key man life insurance policy for R. Douglas Armstrong, the Chairman, Chief Executive Officer and President of Aastrom. Our inability to replace any other lost key employee could harm our operations.

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, patents may not be granted on any of our pending or future patent applications. Also, the scope of any of our issued patents may not 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 three exclusive, world-wide licenses relating to the production of human cells granted to us by the University of Michigan for certain of our patent rights. If we materially breach such agreements or otherwise fail to materially comply with such agreements, or if such agreements expire or are otherwise terminated by us, we may lose our rights under the patents held by the University of Michigan. At the latest, these licenses will terminate when the patent underlying the license expires. The first of these underlying patents will expire on March 21, 2012. We also rely on trade secrets and unpatentable know-how that 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 government maintains certain rights in technology that we develop using government grant money and we may lose the revenues from such technology if we do not commercialize and utilize the technology pursuant to established government guidelines.

Certain of our and our licensors' research have been or are being funded in part by government grants. As a result of such funding, the U.S. Government has certain rights in the technology developed with the grant. These rights include a non-exclusive, paid-up, world-wide license to use the technology for any governmental purpose. In addition, the government has the right to require us to grant an exclusive license to use the developed technology to a third party if the government determines that:

- we have not taken adequate steps to commercialize such technology;
- such action is necessary to meet public health or safety needs; or
- such action is necessary to meet requirements for public use under federal regulations.

In these instances, we would not receive revenues on the products we developed. Additionally, technology that was partially funded by a federal research grant is subject to the following government rights:

- products using the technology which are sold in the United States are to be manufactured substantially in the United States, unless a waiver is obtained;
- the government may force the granting of a license to a third party who will make and sell the needed product if we do not pursue reasonable commercialization of a needed product using the technology; and
- the U.S. Government may use the technology for its own needs.

If we fail to meet these guidelines, we would lose our exclusive rights to these products and we would lose potential revenue derived from the sale of these products.

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, in the past, published studies have suggested that stem cell transplantation for breast cancer, that constituted a significant portion of the overall stem cell therapy market, at the time, may have limited clinical benefit. The lack of reimbursement for these procedures by insurance payors would negatively affect the marketability of our products.

Potential product liability claims could affect 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™ System during research and development efforts, including clinical trials, or after commercialization results in adverse affects. 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.

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 affect 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 affect could occur even if our shareholders consider the change in control to be in their best interest.

Forward-looking statements

This prospectus and the information incorporated by reference in it 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:

- potential strategic collaborations with others;
- future capital needs;
- product development and marketing plan;
- clinical trial plans and anticipated results;
- anticipation of future losses;
- replacement of manufacturing sources;
- commercialization plans; and
- revenue expectations and operating results.

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. In some cases, you can identify these statements by our use of forward-looking words such as “may,” “will,” “should,” “anticipate,” “expect,” “estimate,” “plan,” “believe,” “potential,” or “intend.” All forward-looking statements included in this registration statement 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 450 Fifth Street, N.W., Washington, D.C. 20549. 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. We also provide information on our website: http//www.aastrom.com/.

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 Section 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, 2003;

2. Our Quarterly Report on Form 10-K for the quarter ended September 30, 2003;

3. Our Current Reports on Form 8-K filed with SEC on July 10, 2003; September 2, 2003; December 11, 2003; and January 14, 2004; and

4. The description of our common stock set forth in our Registration Statement on Form 8-A filed with the SEC on April 11, 1997, as amended (Commission File No.: 000-22025).

In addition, we will deliver without charge a copy of any of the information incorporated by reference into this prospectus to each person (including a beneficial owner) receiving a copy of this prospectus. If you need a copy of these documents, you may request copies, at no cost, by writing or telephoning us at the following address:

Aastrom Biosciences, Inc,.
Attention: Chief Financial Officer
24 Frank Lloyd Wright Drive
Ann Arbor, MI 48105

Telephone Number: (734) 930-5555

USE OF PROCEEDS

We cannot guarantee that we will receive any proceeds in connection with this offering, as the amount of shares sold will depend on the interest our shareholders have in purchasing shares under this Plan. Any proceeds we receive will be used for operating costs, capital expenditures, working capital and 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. We may raise additional capital through additional public or private financing, as well as collaborative relationships, incurring debt and other available sources.

INFORMATION ABOUT THE PLAN

Purpose

1. Why did Aastrom establish the Shareholder Direct Stock Purchase Plan?

We established the Plan to promote long term ownership in our stock and to give our shareholders a simple, convenient and economical way to purchase additional shares. This Plan is also designed to enable us to raise additional capital through the direct sale of newly issued shares.

Benefits and Risks

2. What are the benefits of participation in the Plan?

By participating in the Plan, you may purchase shares in relatively small amounts, which would allow you to conveniently add to your investment over time without incurring brokerage costs and to buy shares at a slight discount to a recent average market price. The Plan permits you to monitor your investment and make new purchases efficiently by using the forms included with your Plan Statement. Additionally, by having the Plan Administrator hold your shares in book-entry form, you eliminate concerns over lost and stolen stock certificates.

3. Are there potential disadvantages or risks to participating the Plan?

There are potential disadvantages to participating in the Plan compared to purchases of Common Stock through brokers or otherwise. For example, neither Aastrom nor the Plan Administrator will pay interest on any cash held pending the next purchase date. Additionally, since the purchase price under the Plan is an average of recent closing prices for a few days prior to the purchase date, your purchase price may be higher than that which you could have obtained by directing a purchase through a broker or in an negotiated transaction. Shareholders will be required to deposit funds in advance of knowing the purchase price. Finally, any discount from the market prices at the time of the investment in common shares purchased under the Plan may create additional taxable income to the participant. Purchase of shares is subject to all of the risks of stock ownership, including those discussed in the Risk Factors section of this Prospectus.

Eligibility and Enrollment

4. How does an Aastrom shareholder enroll in the Plan?

- *Persons who are registered shareholders*

If you are already an Aastrom registered shareholder (i.e., if you own shares that are registered in your name, not your broker's), you may enroll in the Plan simply by completing and returning an Authorization and Enrollment Form, together with a check for $10.00 for the enrollment fee. You may obtain an Authorization and Enrollment Form from the Plan Administrator or directly from our website: http://www.aastrom.com/.

- *Persons who hold shares in a bank or brokerage account*

If your shares of Aastrom stock are held on your behalf by a bank or broker (i.e., "street name"), you can satisfy the eligibility requirements in either of two ways. First, you could arrange with your bank or broker to have at least one share registered directly in your name. Alternatively, you could provide Aastrom with a copy of the relevant portion of a brokerage account statement (as of a date within the last three months) that shows you owned shares of Aastrom in your account, and also complete and return a Share Ownership Certification Form, which is now also available on our website for your convenience.

In either case, you must also complete and return an Authorization and Enrollment Form, together with a check for $10.00 for the enrollment fee. All of these forms are available from the Plan Administrator or directly from our website: http://www.aastrom.com/.

5. I'm not currently a shareholder. May I participate in the Plan?

If you currently do not hold shares of Aastrom Common Stock, you must first purchase Aastrom stock and either (i) have it registered in your name, or (ii) complete and return the Share Ownership Certification form (which requires you to provide Aastrom with the relevant portions of an account statement as of a date within the last three months that shows that you owned Aastrom shares in your account).

6. Are there fees associated with enrollment?

Participation in the Plan is subject to the following fees. These fees may change at any time and you will be notified of any changes.

Fee Schedule:

One-time enrollment fee in direct purchase plan	$10.00
Fee for insufficient funds for check or automatic deductions	$50.00

7. Who may participate in the Plan?

All U.S. citizens who are shareholders of Aastrom are eligible to participate. Foreign citizens are eligible to participate as long as their participation would not violate any laws in their home countries. We may limit the participation of any shareholder if compliance with any applicable regulatory requirements of the shareholder's state or country of residence would be unduly burdensome in our determination.

Purchases and Sales

8. What are the minimum and maximum amounts for purchases?

The minimum amount for purchases is $250 and the maximum amount is $10,000 during any month.

9. How do I make a purchase?

You may send a Transaction Form and a check payable in U.S. dollars to Aastrom Biosciences Direct Stock Purchase Plan. Checks must be drawn against a U.S. bank or U.S. bank affiliate. We will accept wire transfers or debits from an account with a U.S. bank or U.S. bank affiliate. Cash, money orders and third-party checks are not allowed. For initial purchases, you must send an Authorization and Enrollment Form (and a check for the enrollment fee) with or before sending checks or wire transfers. Checks and forms should be mailed to Aastrom Biosciences Shareholder Direct Stock Purchase Plan, c/o Continental Stock Transfer and Trust Company (Attn: DRP), 17 Battery Place, New York, NY 10004-1125.

10. May I have funds for purchases automatically deducted from my bank account?

Yes. You may authorize monthly automatic deductions from an account at a financial institution that is a member of the National Automated Clearing House Association.

- To initiate this service, you must send an Authorization and Enrollment Form, with the "Automatic Deduction Service" section completed, to the Plan Administrator.
- To change any aspect of the instruction, you must send a revised Authorization and Enrollment Form, with the "Automatic Deduction Service" section completed, to the Plan Administrator.
- To terminate the deductions, you must notify the Plan Administrator in writing.

Initial set-up, changes and terminations to the automatic deduction instructions will be made as soon as practicable. Once effective, funds will be deducted from your designated account at least 2 days before each purchase date. You should contact the financial institution where you maintain your account to determine if they will impose any fees on automatic monthly deductions.

11. How are payments with “insufficient funds” handled?

If the Plan Administrator does not receive a payment because of insufficient funds or incorrect draft information, the requested purchase will be deemed void, and the Plan Administrator will immediately remove from your account any shares purchased in anticipation of receiving such funds. If the net proceeds from the sale of such shares are insufficient to satisfy the balance of the uncollected amounts, the Plan Administrator may sell additional shares from your account as necessary to satisfy the uncollected balance.

In addition, an “insufficient funds” fee of $50.00 will be charged. The Plan Administrator may place a hold on the Plan account until the “insufficient funds” fee is received from you, or may sell shares from your account to satisfy any uncollected amounts.

12. When will shares be purchased?

The Plan Administrator will buy shares on the first Wednesday after the 15th of each month if your funds and/or instructions are received no later than five business days before that day.

13. When must funds for purchases and instructions be received by the Plan Administrator?

For all purchases, your funds must be received by the Plan Administrator no later than five business days before the purchase date. For initial purchases, your Enrollment From must also be received by the Plan Administrator no later than five business days before the purchase date.

14. What is the price of shares purchased under the Plan?

The purchase price for shares is a 3% discount from the average of the closing sale prices for our common stock as reported by Nasdaq for three trading days ending two days before the purchase date. You will not earn any interest on funds held in your account and you bear the risk of any price changes in Aastrom stock during the pricing period and until the purchase date, as well as from the purchase date through the time you sell your shares.

The Plan Administrator will use your funds to purchase as many full shares as possible and will use any amount remaining to purchase a fraction of a share.

15. What happens if I deposit less than $250 or more than $10,000 by two business days before the monthly purchase date?

If your account has less than the $250 minimum purchase amount (or if your account has more than $10,000 maximum purchase amount) as of two business days before the purchase date, the Plan Administrator will promptly return those funds to you, without interest.

16. How do I sell my shares?

You can sell some or all of the Plan shares you hold in book-entry form by providing written instructions to the Plan Administrator through the mail or by facsimile. You can provide these instructions by completing, signing and submitting a Transaction Form. Sample forms that could be used for sales of shares are contained on our website: http://www.aastrom.com. If you prefer, you can withdraw shares from the Plan, at no cost to you, and sell them through a broker of your own choosing. Shares will normally be mailed to you or transferred to your broker (as you specify) within five business days of receipt of your instructions.

17. When will shares be sold under the Plan? What is the price of shares sold under the Plan?

The Plan Administrator will sell shares on each purchase date (the Wednesday after the 15th of each month). The sale price for your shares will be the average weighted price per share received by the Plan Administrator for all sales made that day for Plan participants.

18. When must sales instructions be received?

To sell your shares under the Plan, the Plan Administrator must receive your signed sales instructions (by completing and returning a Transaction Form) by the close of business at least two days before the sales date. Thus, if you want to sell your shares on a monthly sale date (which would occur on a Wednesday), the Plan Administrator must receive your sales instructions by the close of business on the preceding Monday.

19. Will I be charged brokerage fees for sales of shares under the Plan?

No. Aastrom will pay brokerage fees for shares sold under the Plan.

20. Are there restrictions on how quickly shares that are purchased under the Plan can be sold?

Shares that are purchased under the Plan or deposited into the Plan may not be sold under the Plan for at least 9 days after they are purchased or deposited into the Plan. Thus, someone purchasing shares under the Plan could not submit sale instructions so that shares would be purchased and sold on the same day. The first sale under the Plan of shares purchased under the Plan could take place on the next monthly sale date. This restriction does not apply to other shares that have been held under the Plan for at least 9 days. As a result, a participant could purchase shares under the Plan and sell different shares on the same date. This restriction also does not apply to shares that are withdrawn from the Plan; those shares could be sold at any time.

Source of Stock

21. What is the source of Aastrom stock purchased through the Plan?

Share purchases will be made directly from Aastrom. At Aastrom’s option, we may elect to have share purchases made in the market, although we do not expect to use this option in the near future.

How Shares Are Held

22. How does the safekeeping service (book-entry shares) work?

All shares of Aastrom stock that are purchased through the Plan will be held by the Plan Administrator and registered in book-entry form in your Plan account on the records of the Plan Administrator. If you hold Aastrom Common Stock certificates outside the Plan, you may also, at any time, deposit those certificates for safekeeping with the Plan Administrator, and the shares represented by the deposited certificates will be included in book-entry form in your Plan account.

23. How do I deposit my Aastrom stock certificates with the Plan Administrator?

To deposit certificates into the Plan, you should send your certificates, by registered and insured mail, to the Plan Administrator at Continental Stock Transfer and Trust Company (Attn: DRP) , 17 Battery Place, New York, NY 10004-1125, with written instructions to deposit those shares in your Plan account. The certificates should not be endorsed and the assignment section should not be completed.

24. Are there any direct charges to shareholders associated with this custodial service?

No. There is no cost to you either for having the Plan Administrator hold the shares purchased for you through the Plan or for having the Plan Administrator hold additional shares you deposit into your account. We may pay some minor fees to the Plan Administrator.

25. How can I receive a stock certificate?

Normally, stock certificates for shares purchased under the Plan will not be issued; rather shares will be registered in the name of the Plan Administrator or its nominee and credited to your Plan account. However, you may request a stock certificate by indicating your preference on the Transaction Form and forwarding it to the Plan Administrator. There is no charge for this service. Stock certificates for fractional shares will not be issued under any circumstances.

Transfers of Shares

26. Can I transfer shares that I hold in the Plan to someone else?

Yes. You may transfer ownership of some or all of your Plan shares by sending the Plan Administrator written transfer instructions. Your signature must be "Medallion Guaranteed" by a financial institution. Most banks and brokers participate in the Medallion Guarantee program. The Medallion Guarantee program ensures that the individual signing is in fact the owner of the participant's account.

You may transfer shares to new or existing Aastrom shareholders. However, a new Plan account will not be opened for a transferee as a result of a transfer of less than one full share. If you are opening a new Plan account for a transferee, you must include an Authorization and Enrollment Form with the transfer instructions, and the transferee must complete an Enrollment Form.

Withdrawal from the Plan

27. How do I close my Plan account?

You may terminate your participation in the Plan either by giving written notice to the Plan Administrator or by completing the appropriate section of your account statement and returning it to the Plan Administrator. Upon termination, you must elect either to receive a certificate for the number of whole shares held in your Plan account and a check for the value of any fractional shares, or to have all of the shares in your Plan account sold for you as described above. The Plan Administrator will send you your proceeds, without interest, or your certificates as soon as is practicable.

Administration

28. Who administers the Plan?

The Plan is administered by Continental Stock Transfer and Trust Company, Aastrom's stock transfer agent. As Plan Administrator, Continental Stock Transfer and Trust Company acts as agent for Plan participants and keeps records, sends statements and performs other duties relating to the Plan.

29. What are some of the other duties of the Plan Administrator?

The Plan Administrator will do the following:

- receive and hold funds pending the purchase of shares
- issue shares to the account of participants shortly after each purchase date

- hold shares in the Plan through book-entries
- receive any deposits of additional shares in the Plan
- following receipt of instructions, sell shares on the applicable sales date and remit payment to the participant
- distribute shares to the participant or upon withdrawals of shares from the Plan
- remit payment to Aastrom for shares purchased from us under the Plan

30. How do I contact the Plan Administrator?

To request enrollment packages or for other questions, please call (800) 509-5586

or write to: Aastrom Biosciences Shareholder Direct Stock Purchase Plan
c/o Continental Stock Transfer and Trust Company
17 Battery Place
New York, NY 10004-1125

When communicating with the Plan Administrator, you should have available your account number and taxpayer identification number.

31. What kind of reports will be sent to participants in the Plan?

You will receive a quarterly statement of account activity. Supplemental account statements will be provided for any month in which you make a cash investment, withdraw or sell shares. You should retain these statements in order to establish the cost basis of shares purchased under the Plan for income tax and other purposes.

Additional Information

32. How would a stock split or stock dividend affect my account?

Any shares resulting from a stock split or stock dividend paid on shares held in custody for you by the Plan Administrator will be credited to your book-entry position. Of course, you may request a certificate at any time for any or all of your shares.

33. Can I vote my Plan shares?

You will be sent a proxy statement, together with a proxy card. This proxy card, when duly signed and returned, will be voted as you indicate. Fractional shares will be aggregated and voted in accordance with the participant’s directions. If the proxy card is not returned or if it is returned unsigned, the shares will not be voted.

34. Can the Plan be changed?

We may add to, modify or discontinue the Plan at any time. We will send you written notice of any significant changes.

Upon discontinuance of the Plan, we will return to you any uninvested automatic deductions from your bank account, and any uninvested cash investments. We will also issue you free of charge a certificate for full shares credited to your account and pay you in cash for any fractional shares credited to your account.

35. What are the responsibilities of Aastrom and the Plan Administrator?

Neither Aastrom Biosciences nor the Plan Administrator, will be liable for any act, or for any failure to act as long as they have made good faith efforts to carry out the terms of the Plan, as described in this Prospectus and on the forms that accompany each investment or activity.

Participants should recognize that neither Aastrom Biosciences nor the Plan Administrator can promise a profit or protect against a loss on the Common Stock purchased under the Plan.

Federal Income Tax Consequences

You should consult with your tax advisor for a complete analysis of the tax consequences of participating in the Plan.

The Internal Revenue Service has indicated in somewhat similar situations that a participant who purchases shares under the Plan will be treated as having received a distribution equal to the excess, if any, of the fair market value of the common shares on the purchase date over the amount of the cash payment made by the participant. Such a distribution would be taxable as ordinary dividend income to the extent that we have current or accumulated “earnings and profits” as of the end of the taxable year in which the distribution occurs. If the distribution exceeds the holder’s allocable share of those earnings and profits, then the excess will generally be treated first as a tax-free return of basis, and thereafter as capital gain.

You will not realize a gain or loss for U.S. Federal income tax purposes upon a transfer of shares to the Plan or the withdrawal of whole shares from the Plan. You will, however, generally realize a gain or loss when shares are sold. The amount of gain or loss will be the difference between the amount that you receive for the shares sold and your tax basis in these shares. In order to determine the tax basis for shares in your account, you should retain all account and transaction statements.

LEGAL MATTERS

The validity of the common stock offered hereby has been 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, 2003, 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.