



AS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION ON SEPTEMBER 22, 2003  
REGISTRATION NO. 333-

**SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549**

**FORM S-3**

**REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933**

**AASTROM BIOSCIENCES, INC.**

(Exact Name of Registrant as Specified in Its Charter)

**Michigan**  
(State or Other Jurisdiction  
of Incorporation or Organization)

**94-3096597**  
(IRS Employer  
Identification Number)

**24 FRANK LLOYD WRIGHT DRIVE  
P.O. BOX 376  
ANN ARBOR, MICHIGAN 48106  
(734) 930-5555**

(Address, Including Zip Code, and Telephone Number, Including  
Area Code, of Registrant's Principal Executive Offices)

**ALAN M. WRIGHT  
SENIOR VICE PRESIDENT, ADMINISTRATIVE  
AND FINANCIAL OPERATIONS, CFO  
AASTROM BIOSCIENCES, INC.  
24 FRANK LLOYD WRIGHT DRIVE  
P.O. BOX 376  
ANN ARBOR, MICHIGAN 48106  
(734) 930-5555**

(Name, Address, Including Zip Code, and Telephone Number, Including  
Area Code, of Agent for Service)

COPIES TO:

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**APPROXIMATE DATE OF COMMENCEMENT OF PROPOSED SALE TO THE PUBLIC:**

From time to time after the effective date of this registration statement.

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

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If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. [ X ]

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

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

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

**CALCULATION OF REGISTRATION FEE**

<b>TITLE OF SHARES TO BE REGISTERED</b>	<b>AMOUNT TO BE REGISTERED</b>	<b>PROPOSED MAXIMUM AGGREGATE PRICE PER UNIT (2)</b>	<b>PROPOSED MAXIMUM AGGREGATE OFFERING PRICE (2)</b>	<b>AMOUNT OF REGISTRATION FEE</b>
Common stock (\$0 par value)	897,595(1)	\$1.52	\$1,364,344	\$111

- (1) Consists of 897,595 shares of common stock issuable upon the exercise of outstanding warrants. In addition to the 897,595 shares set forth in the table above, this Registration Statement also covers such indeterminate number of additional shares as may be held (or acquired upon exercise of the warrants) as a result of any future stock splits, stock dividends or similar transactions covered by Rule 416.
- (2) Estimated, pursuant to Rule 457(c), solely for the purpose of calculating the registration fee based on the average of the high and low prices for the common stock, as reported on the Nasdaq SmallCap Market on September 12, 2003.

**THE REGISTRANT HEREBY AMENDS THIS REGISTRATION STATEMENT ON SUCH DATE OR DATES AS MAY BE NECESSARY TO DELAY ITS EFFECTIVE DATE UNTIL THE REGISTRANT SHALL FILE A FURTHER AMENDMENT WHICH SPECIFICALLY STATES THAT THIS REGISTRATION STATEMENT SHALL THEREAFTER BECOME EFFECTIVE IN ACCORDANCE WITH SECTION 8(a) OF THE SECURITIES ACT OF 1933 OR UNTIL THE REGISTRATION STATEMENT SHALL BECOME EFFECTIVE ON SUCH DATE AS THE COMMISSION, ACTING PURSUANT TO SAID SECTION 8(a), MAY DETERMINE.**

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SUBJECT TO COMPLETION, DATED SEPTEMBER 22, 2003

**THE INFORMATION IN THIS PROSPECTUS IS NOT COMPLETE AND MAY BE CHANGED. THE SELLING SHAREHOLDERS MAY NOT SELL THESE SECURITIES UNDER THIS PROSPECTUS UNTIL THE REGISTRATION STATEMENT FILED WITH THE SECURITIES AND EXCHANGE COMMISSION IS EFFECTIVE. THIS PROSPECTUS IS NOT AN OFFER TO SELL NOR DOES IT SEEK AN OFFER TO BUY THESE SECURITIES IN ANY STATE WHERE THE OFFER AND SALE WOULD NOT BE PERMITTED.**

**PROSPECTUS**

**897,595 Shares Of Common Stock  
Aastrom Biosciences, Inc.**

This prospectus relates to the offer and sale of 897,595 shares of common stock being offered by the selling shareholders identified in this prospectus. All of these shares are issuable upon exercise of warrants. The selling shareholders may sell their shares in a number of ways and at varying prices. Each selling shareholder will determine independent of us the price and manner it may offer or sell its shares. The selling shareholders may decide not to sell any of their shares under this prospectus. We are not selling any shares of our common stock under this prospectus and will not receive any proceeds from the sale of our shares by the selling shareholders.

Our common stock is quoted on the Nasdaq SmallCap Market under the symbol "ASTM." On September 18, 2003, the last reported sale price of our common stock was \$1.64.

**Investing in our 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 SEPTEMBER \_\_, 2003.

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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 and do not refer to the selling shareholders.

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## SUMMARY

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.

### Our Business

We are a late-stage development company focused on human cell-based therapies. We have identified multiple paths to revenue based on our proprietary *ex vivo* cell production technology, including the near-term Cell Production Products business, and an active Prescription Cell Product pipeline for stem cell tissue repair and cancer and infectious disease treatments.

Our core technology is based on our 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. In addition, this system provides 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 markets the AastromReplicell™ System and cell production kits to researchers and companies for their production of cells for clinical trials. The initial kits are used for the production of dendritic cells used for developing cancer vaccines. 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, 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 product being evaluated is our OCG-I cells for bone grafting (fusions, fractures or dental defects). We are currently preparing for 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 product has been CE marked and is currently being used by a limited number of centers in Europe to evaluate its use. In the United States, the SC-I therapy reached Phase III trials, although we halted these trials due to a shift in medical practice that reduced patient need and availability. The OC-I therapy is currently in a Phase I/II clinical trial. 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.

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. The first Dendricell™ clinical trials are planned at Stanford University for a multiple myeloma cancer vaccine and at Duke University for a colorectal cancer vaccine. In addition, we have been in the pre-clinical stage for a T-cell therapeutic targeting the Epstein-Barr Virus.

The recent commercialization of our automated cell production instruments and cell-specific production kits should generate revenues in the near term, although we are not yet able to project the market size and potential growth for those products. While we have initiated marketing activities in Europe for the CE Marked SC-I, DC-I and the DCV-I 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 more significant product sales commence. Until that time, 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, milestone payments and licensing fees from existing and potential future corporate collaborators. To date, we have financed our operations through public and

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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. Through March 31, 2003, we have accumulated losses of approximately \$100 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, or complete a corporate partnering or acquisition transaction necessary for us to continue our operation at current levels.

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**

Common stock offered by the selling shareholders

897,595 shares (all of which are issuable upon exercise of warrants)



## 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 June 30, 2003, we have incurred cumulative net losses totaling approximately \$102.4 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.

### **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.

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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. Pursuant to previously approved shareholder resolutions, the Board of Directors has the authority to increase the maximum number of authorized shares from 100 million to 150 million.

### **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 \$1.45 during the fiscal year ended June 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 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.

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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.

### **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 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, 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.**

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 Aastrom Replicell™ 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

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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 and DCV-I 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.

### **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. Other countries are adopting new strict policies and requirements for cell products. These new requirements may delay, restrict or prevent the sale or use of our products.

### **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

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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

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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.

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### **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 Current Reports on Form 8-K filed with SEC on July 10, 2003 and September 2, 2003; and
3. 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



## SELLING SHAREHOLDERS

This prospectus relates to the offering by the selling shareholders named below of up to 897,595 shares of common stock. All of these shares are issuable upon exercise, from time to time, of the warrants that they hold. The table below sets forth the following information with respect to the selling shareholders as of September 15, 2003:

- the number of Aastrom's outstanding shares of common stock beneficially owned by each selling shareholder (including shares obtainable under options or warrants exercisable within sixty days of such date) prior to the offering hereby. (However, the selling shareholders may have acquired additional shares or sold or otherwise disposed of some portion of their shares since that date.);
- the number of such shares being offered hereby; and
- the number and percentage of Aastrom's outstanding shares of common stock to be beneficially owned by each selling shareholder after completion of the sale of common stock being offered hereby.

Except as set forth in the footnotes to the following table, no selling shareholder has held a position or office or had a material relationship with us within the past three years, other than as an owner of our securities. We cannot be sure that any selling shareholder will exercise any of the warrants or sell any or all of the shares offered hereby.

Selling Shareholders	Number of Shares Beneficially Owned	Number of Such Shares Being Offered	Number of Shares Beneficially Owned After the Offering (1)	Percentage of Aastrom Stock Owned After the Offering (1)
Susan Ladue (2) 4632 Coleman Creek Road Medford, OR 97501	600,000 (3)	600,000 (3)	0	*
T. Bresner & Associates (4) 1776 Broadway, Suite 1206 New York, NY 10019	40,000 (3)	40,000 (3)	0	*
Lee Skowblow (5) 1776 Broadway, Suite 1206 New York, NY 10019	257,595 (3)	257,595 (3)	0	*

\* less than 1%

- (1) Assumes that all shares offered are sold. This registration statement will permit, but not require, the selling shareholders to sell their shares from time to time. The selling shareholders may decide not to exercise their warrants and, even if the warrants are exercised, the selling shareholders may decide not to sell their shares pursuant to this registration statement.
- (2) Ms. Ladue has provided public and investor relations services to Aastrom and received the warrants that may be exercised for these shares as partial compensation for those services.
- (3) All shares of common stock are issuable upon exercise of warrants.

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- (4) T. Bresner & Associates has provided public and investor relations services to Aastrom and received the warrants that may be exercised for these shares as partial compensation for those services. Trudi Bresner exercises investment and voting control over the shares. Ms. Bresner disclaims beneficial ownership of the common stock owned by this selling shareholder.
- (5) Mr. Skowblow has provided financing consulting and investor relations services to Aastrom and received the warrants that may be exercised for these shares as partial compensation for those services.

The number of shares set forth in the table represents the maximum number of shares of common stock to be offered by the selling shareholders. The number of shares set forth in the table includes 897,595 shares the selling shareholders would receive under the warrants. The actual number of shares of common stock that will be issued upon exercise of the warrants is indeterminate. Therefore, the actual number of shares offered and sold hereunder could be materially less than this maximum amount. The actual number of shares of common stock offered hereby, and included in the Registration Statement of which this prospectus is a part, also includes an additional number of shares of common stock that may be issued or issuable upon exercise of the warrants by reason of any stock split, stock dividend or similar transaction involving the common stock, in order to prevent dilution, in accordance with Rule 416 under the Securities Act.

### **PLAN OF DISTRIBUTION**

The selling shareholders and any of their pledgees, assignees and successors-in-interest may, from time to time, sell any or all of their shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These sales may be at fixed or negotiated prices. The selling shareholders may use any one or more of the following methods when selling shares:

- ordinary brokerage transactions and transactions in which the broker dealer solicits purchasers;
- block trades in which the broker dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker dealer as principal and resale by the broker dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- settlement of short sales;
- broker dealers may agree with the selling shareholders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted pursuant to applicable law.

The selling shareholders may also sell shares under Rule 144 under the Securities Act, if available, rather than under this prospectus.

Broker dealers engaged by the selling shareholders may arrange for other brokers dealers to participate in sales. Broker dealers may receive commissions or discounts from the selling shareholders (or, if any broker dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated. The selling shareholders do not expect these commissions and discounts to exceed what is customary in the types of transactions involved.

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The selling shareholders may from time to time pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time under this prospectus, or under an amendment to this prospectus filed under Rule 424(b)(3) or other applicable provision of the Securities Act of 1933 amending the list of selling shareholders to include the pledgee, transferee or other successors in interest as selling shareholders under this prospectus.

The selling shareholders and any broker dealers or agents that are involved in selling the shares may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker dealers or agents and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. The selling shareholders have informed the Company that they do not have any agreement or understanding, directly or indirectly, with any person to distribute the common stock.

The selling shareholders and any other persons participating in a distribution of the shares will be subject to applicable provisions of the Securities Exchange Act and the rules and regulations thereunder, including Regulation M, which may restrict certain activities of, and limit the timing of purchases and sales of the shares by the selling shareholders and other persons participating in a distribution of the shares. Furthermore, under Regulation M, persons engaged in a distribution of the shares are prohibited from simultaneously engaging in market making and certain other activities with respect to the shares for a specified period of time prior to the commencement of such distributions subject to specified exceptions or exemptions. All of the foregoing may affect the marketability of the shares offered hereby.

### **USE OF PROCEEDS**

We will not receive any proceeds from sales of the shares. We may receive up to approximately \$638,800 million upon exercise of the warrants. This is based on a potential full exercise of the warrants to purchase 897,595 shares of common stock. We intend to apply any net proceeds received from exercise of the warrants to general working capital purposes.

### **LEGAL MATTERS**

The validity of the common stock offered hereby will be passed upon for Aastrom by its special counsel, Pepper Hamilton LLP, Detroit, Michigan. 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.

**PART II****INFORMATION NOT REQUIRED IN PROSPECTUS****ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION.**

Other expenses in connection with the registration of the common stock hereunder will be substantially as follows (all expenses other than the SEC Registration Fee are estimates):

Item	Company Expense
SEC Registration Fee	\$ 111
Blue Sky Fees	\$ 1,000
Printing and engraving expenses	\$ 1,000
Legal fees and expenses	\$15,000
Accounting fees and expenses	\$ 5,000
Miscellaneous	\$ 7,889
Total	\$30,000

**ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS.**

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

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

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

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

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

### ITEM 16. EXHIBITS.

EXHIBIT NUMBER	DESCRIPTION OF DOCUMENT
5.1	Consent and Opinion of Pepper Hamilton LLP
23.1	Consent of PricewaterhouseCoopers LLP, independent accountants
23.2	Consent of Gray Cary Ware & Freidenrich LLP
23.3	Consent of Pepper Hamilton LLP (included in Exhibit 5.1)
24.1	Power of Attorney (see Signature page)

### ITEM 17. UNDERTAKING.

A. The undersigned Registrant hereby undertakes:

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

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

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

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

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

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

B. The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the Registrant's annual report pursuant to section 13(a) or section 15(d) of the Securities Exchange Act of 1934 that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

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

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

E. The undersigned Registrant hereby undertakes that:

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

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

**SIGNATURES**

Pursuant to the requirements of the Securities Act, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements of filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized in the City of Ann Arbor, State of Michigan, on September 19, 2003.

**AASTROM BIOSCIENCES, INC.**

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

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

**POWER OF ATTORNEY**

KNOW ALL MEN BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints R. Douglas Armstrong and Alan M. Wright, or either of them, as his or her attorney-in-fact, each with full power of substitution for him or her in any and all capacities, to sign any and all amendments to this registration statement, including, but not limited to, post-effective amendments and any and all new registration statements filed pursuant to Rule 462 under the Securities Act of 1933 in connection with or related to the offer contemplated by this registration statement, as amended, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming our signatures as they may be signed by our said attorney to said registration statement and any and all amendment thereto.

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

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ R. Douglas Armstrong, Ph.D.</u> R. Douglas Armstrong, Ph.D.	President, Chief Executive Officer, and Chairman of the Board of Directors (Principal Executive Officer)	September 19, 2003
<u>/s/ Alan M. Wright</u> Alan M. Wright	Senior Vice President, Administrative and Financial Operations, Chief Financial Officer (Principal Financial and Accounting Officer)	September 19, 2003
<u>/s/ Mary L. Campbell</u> Mary L. Campbell	Director	September 19, 2003
<u>/s/ Arthur F. Staubitz</u> Arthur F. Staubitz	Director	September 19, 2003
<u>/s/ Joseph A. Taylor</u> Joseph A. Taylor	Director	September 19, 2003
<u>/s/ Susan L. Wyant</u> Susan L. Wyant	Director	September 19, 2003

**INDEX TO EXHIBITS**

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24.1	Power of Attorney (see signature page)



September 19, 2003

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

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

Gentlemen:

We have acted as special counsel to Aastrom Biosciences, Inc., a Michigan corporation (the "Company"), in connection with the filing with the Securities and Exchange Commission (the "Commission") of a registration statement on September 19, 2003 (the "Registration Statement") of the Company on Form S-3 under the Securities Act of 1933, as amended (the "Act"). The Registration Statement relates to the sale of up to 897,585 shares of the Company's Common Stock that would be issued upon exercise of outstanding warrants (the "Warrant Shares"), covered by the Registration Statement.

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

In our examination, we have assumed the legal capacity of all natural persons, the genuineness of all signatures, the conformity to original documents of all photostatic and facsimile copies submitted to us, and the due execution and delivery of all documents by any party where due execution and delivery are a prerequisite to the effectiveness thereof. As to any facts material to the opinion expressed herein that were not independently established or verified, we have relied upon statements and representations of officers and other representatives of the Company. We have assumed that payment and delivery of the Warrant Shares is made in accordance with the terms set forth in the agreements and other documents relating to the issuance and sale of the Warrant Shares. In addition, we have assumed that the certificates representing the Warrant Shares will be duly executed and delivered and that the Restated Articles of Incorporation and the By-Laws of the Company, amended to date, and resolutions of the Company's Board of Directors specifically authorizing the issuance and sale of the Warrant Shares remain in effect and unmodified, except as may be required as set forth in this opinion.

On the basis of the foregoing, we are of the opinion that the Warrant Shares will be duly authorized, validly issued, fully paid, and non-assessable.

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

Very truly yours,

PEPPER HAMILTON LLP

CONSENT OF INDEPENDENT ACCOUNTANTS

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of our report dated August 8, 2003 relating to the financial statements and financial statement schedule, which appears in Aastrom Biosciences, Inc.'s Annual Report on Form 10-K for the year ended June 30, 2003. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

PRICEWATERHOUSECOOPERS LLP

Minneapolis, Minnesota  
September 22, 2003

[GRAY CARY WARE & FREIDENRICH LETTERHEAD]

September 18, 2003

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

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

Ladies and Gentlemen:

As counsel to Aastrom Biosciences, Inc., a Michigan corporation (the "Company"), in connection with the proposed offer and sale of those certain shares of the Company's Common Stock, \$0 par value, as set forth in the Registration Statement on Form S-3 (the "Registration Statement"), we hereby consent to the use of our name under the caption "Legal Matters" in the Registration Statement, including the Prospectus constituting a part thereof, as originally filed or as subsequently amended.

Very truly yours,

/s/ GRAY CARY WARE & FREIDENRICH LLP  
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