

PROSPECTUS SUPPLEMENT
(To Prospectus dated October 11, 2005)

11,842,105 Shares
Warrants to Purchase 5,921,053 Shares

Aastrom

Common Stock

We are offering to unaffiliated institutional investors up to 11,842,105 shares of our common stock and warrants to purchase up to 5,921,053 shares of common stock in this offering (and the shares of common stock issuable from time to time upon exercise of these warrants). The common stock and warrants will be sold in units, with each unit consisting of one share of common stock and a warrant to purchase 0.5 shares of common stock at an exercise price of \$1.5875 per share of common stock. Each unit will be sold at a negotiated price of \$1.14 per unit. Units will not be issued or certificated. The shares of common stock and warrants are immediately separable and will be issued separately.

Our common stock is traded on the Nasdaq Capital Market under the symbol "ASTM." On October 15, 2007, the closing price of our common stock on the Nasdaq Capital Market was \$1.27 per share.

We have retained BMO Capital Markets Corp. to act as exclusive placement agent in this offering. We have agreed to pay BMO Capital Markets Corp. the placement agent's fees set forth in the table below. The placement agent is not required to sell any specific number or dollar amount of securities offered in this offering, but will use their commercially reasonable efforts to arrange for the sale of the securities offered.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying base prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	Per Unit	Total
Public offering price	\$ 1.14	\$13,500,000
Placement agent's fee	\$0.068	\$ 810,000
Proceeds to Aastrom Biosciences, Inc. (before expenses)	\$1.072	\$12,690,000

We estimate the total expenses of this offering, excluding the placement agent's fee, will be approximately \$200,000. Because there is no minimum offering amount required as a condition to closing in this offering, the actual public offering amount, placement agent's fee and net proceeds to us, if any, in this offering are not presently determinable and may be substantially less than the maximum offering amounts set forth in this prospectus supplement.

Delivery of the units to purchasers is expected to be made on or about October 16, 2007.

Investing in our securities involves significant risks. Please see the section entitled "Risk Factors" beginning on page S-4 of this prospectus supplement, page 3 of the accompanying base prospectus and page 15 of our Annual Report on Form 10-K for the fiscal year ended June 30, 2007.

BMO Capital Markets

As Placement Agent

October 16, 2007

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This prospectus supplement and the accompanying base prospectus, dated October 11, 2005, relate to the offer by us of up to 11,842,105 shares of our common stock and warrants to purchase up to 5,921,053 shares of common stock in this offering (and the shares of common stock issuable from time to time upon exercise of these warrants). You should rely only on the information contained in or incorporated by reference into this prospectus supplement and the accompanying base prospectus and any free writing prospectuses prepared by us or on our behalf. If anyone provides you with different or inconsistent information, you should not rely on it. We are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information contained in this prospectus supplement, the accompanying base prospectus and the documents incorporated by reference is accurate only as of their respective dates, regardless of the time of delivery of this prospectus supplement and accompanying base prospectus or of any sale of shares of our common stock and warrants to purchase shares of common stock in this offering (and the shares of common stock issuable from time to time upon exercise of these warrants). Our business, financial condition, results of operations and prospects may have subsequently changed.

No action is being taken in any jurisdiction outside the United States to permit a public offering of the shares of our common stock or warrants, or possession or distribution of this prospectus supplement and the accompanying base prospectus in that jurisdiction. Persons who come into possession of this prospectus supplement and the accompanying base prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus supplement and the accompanying base prospectus applicable to that jurisdiction.

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying base prospectus are part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, using a “shelf” registration process. Under this shelf registration process, we may offer and sell any combination of securities described in the accompanying base prospectus in one or more offerings, up to a total dollar amount of \$75 million. We previously sold securities under this shelf registration having an aggregate dollar amount of \$25,510,000, leaving a remaining available dollar amount of \$49,490,000. The accompanying base prospectus provides you with a general description of the securities we may offer. Each time we use the accompanying base prospectus to offer securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. This prospectus supplement, the accompanying base prospectus and the documents incorporated by reference herein and therein include important information about us, our common stock and warrants being offered and other information you should know before investing. The prospectus supplement may also add, update or change information contained in the base prospectus. This prospectus supplement describes the specific details regarding this offering, including the price, the amount of common stock and warrants being offered, the risks of investing in our common stock and warrants, and the placement arrangements. The accompanying base prospectus provides general information about us, some of which may not apply to this offering.

Unless the context requires otherwise, in this prospectus supplement and the accompanying base prospectus the terms “Aastrom,” “we,” “us” and “our” refer to Aastrom Biosciences, Inc. and its subsidiaries.

To the extent that any statement that we make in this prospectus supplement is inconsistent with statements made in the accompanying base prospectus, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying base prospectus. You should read both this prospectus supplement and the accompanying base prospectus together with additional information described under the heading, “Where You Can Find More Information.”

PROSPECTUS SUPPLEMENT SUMMARY

The following summary highlights selected information about us. 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.

We are a regenerative medicine company (a medical area that focuses on developing therapies that regenerate damaged or diseased tissues or organs) focused on the clinical development of autologous cell products (cells collected from a patient and returned to that same patient) for the repair or regeneration of multiple human tissues, based on proprietary Tissue Repair Cell (TRC) Technology. Our preclinical and clinical product development programs utilize patient-derived bone marrow stem and early progenitor cell populations, and are being investigated for their ability to aid in the regeneration of tissues such as bone, vascular, cardiac and neural. TRC-based products have been used in over 250 patients, and are currently in the following stages of development:

- Bone regeneration — Bone Repair Cells (BRCs):
 - Osteonecrosis of the femoral head:
 - U.S.: ON-CORE Phase III clinical trial; Orphan Drug Designation from the FDA for use in the treatment of osteonecrosis of the femoral head
 - Spain: Pivotal clinical trial

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- Germany: Positive interim compassionate use data reported in October 2007
- Non-union fractures:
 - U.S.: Patient enrollment completed in Phase I/II clinical trial; final patient results expected to be reported in October 2007
- Vascular regeneration — Vascular Repair Cells (VRCs):
 - Critical limb ischemia:
 - U.S.: RESTORE-CLI Phase IIb clinical trial
 - Germany: Phase I/II clinical trial; positive interim data reported in October 2007
- Cardiac regeneration — Cardiac Repair Cells (CRCs):
 - Chronic heart disease:
 - Preclinical research underway; clinical program under development; Orphan Drug Designation from the FDA for use in the treatment of dilated cardiomyopathy, a severe chronic disease of the heart
- Neural regeneration — Neural Repair Cells (NRCs):
 - Spinal cord injury:
 - Preclinical research underway; clinical program under development

Our platform TRC Technology is based on:

- Autologous cell products which are a unique cell mixture containing large numbers of stem and early progenitor cells produced outside of the body from a small amount of bone marrow taken from the patient, and
- The means to produce these products in an automated process.

We have developed a patented and proprietary manufacturing system to produce human cells for clinical use. This automated cell manufacturing system enables the “single-pass perfusion” cell culture process. Single-pass perfusion is our patented technology for growing large numbers of human cells. The cell component of TRC-based products include adult stem and early progenitor cell populations, which are capable of forming tissues such as bone, vascular, cardiac, neural, and the hematopoietic and immune system.

Since our inception, we have been in the development stage and engaged in research and product development, conducted principally on our own behalf. Our initial business plan was to pursue our targeted markets by commercializing our cell manufacturing system and supplies. Since that time we have phased out our marketing efforts promoting the cell manufacturing system as a commercial product in the U.S. Currently, we have product sales consisting of limited sales of manufacturing supplies to academic collaborators for research and limited revenue related to cell-based products.

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Our current focus is on utilizing our TRC Technology to produce autologous cell-based products for use in regenerative medicine. At such time as we satisfy applicable regulatory approval requirements, we expect the sales of our TRC-based products to constitute nearly all of our product sales revenues.

We do not expect to generate positive cash flows from our consolidated operations for at least the next several years and then only if more significant TRC-based cell product sales commence. Until that time, we expect that our revenue sources from our current activities will consist of only minor sales of our cell products, and dendritic cell and T-cell manufacturing supplies to our academic collaborators, grant revenue, research funding and potential licensing fees or other financial support from potential future corporate collaborators.

We are beginning to explore the possibility of entering into complementary regenerative medicine business activities, whether through acquisition or otherwise.

To date, we have financed our operations primarily through public and private sales of our equity securities, and we expect to continue obtaining required capital in a similar manner. As a development stage company, we have never been profitable and do not anticipate having net income unless and until significant product sales commence. With respect to our current activities, this is not likely to occur until we obtain significant additional funding, complete the required clinical trials for regulatory approvals, and receive the necessary approvals to market our products. Through June 30, 2007, we have accumulated a net loss of approximately \$159 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, obtain the required regulatory approvals, 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

Securities offered	11,842,105 shares of common stock and warrants to purchase 5,921,053 shares of common stock
Common stock to be outstanding immediately after this offering	132,716,168 shares
Offering price	\$1.14
Warrants:	The warrants will be exercisable for cash on or after about April 17, 2008 through and including about April 17, 2013, at an exercise price of \$1.5875 per share of common stock.
Use of proceeds	Proceeds from the offering will be used to fund: (i) clinical trials and research and development; (ii) manufacturing development and expansion; and (iii) other working capital and general corporate purposes. See "Use of Proceeds" on page S-13.
The Nasdaq Capital Market Symbol	ASTM

The number of shares of common stock to be outstanding after this offering is based on 120,874,063 shares outstanding as of August 31, 2007, plus the 11,842,105 shares covered by this offering. This number excludes:

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- a total of 10,837,936 shares of our common stock subject to outstanding options under our current and previous equity incentive plans as of June 30, 2007, having a weighted average exercise price of \$1.47 per share (since June 30, 2007, an additional 1,701,200 options have been issued at an average exercise price of \$1.14 per share);
- 5,047,667 shares of our common stock issuable upon exercise of outstanding warrants as of June 30, 2007, having a weighted average exercise price of \$1.62 per share (since June 30, 2007, 808,824 warrants were exercised at an exercise price of \$1.23 per share);
- 5,912,095 shares of our common stock available for future grants or awards under our 2004 Equity Incentive Plan as of June 30, 2007; and
- 5,921,053 shares of common stock issuable upon the exercise of the warrants to be issued in offering.

RISK FACTORS

You should carefully consider the following risk factors before purchasing our common stock and warrants. 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 supplement 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 supplement. See "Where You Can Find More Information."

Risks Related To Our Business

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, 2007, we have incurred a cumulative net loss totaling approximately \$159 million, and we have continued incur losses since that date. These losses have resulted principally from costs incurred in the research and development of our cell culture technologies and our cell manufacturing system, general and administrative expenses, and the prosecution of patent applications. We expect to incur significant operating losses at least until, and probably after, product sales increase, primarily owing to our research and development programs, including preclinical studies and clinical trials, and the establishment of marketing and distribution capabilities necessary to support commercialization efforts for our products. We cannot predict with any certainty the amount of future losses. Our ability to achieve profitability will depend, among other things, on successfully completing the development of our product candidates, timely initiation and completion of clinical trials, obtaining regulatory approvals, establishing manufacturing, sales and marketing arrangements with third parties, maintaining supplies of key manufacturing components, acquisition and development of complementary activities and raising sufficient cash to fund our operating activities. In addition, we may not be able to achieve or sustain profitability.

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 and cell manufacturing facilities. We expect that our available cash, cash equivalents, short-term investments and interest income available as of June 30, 2007 will be sufficient to finance currently planned activities beyond the end of fiscal year 2008 (ending June 30, 2008). However, in order to grow and expand our business, to introduce our new product candidates into the marketplace and to acquire or develop complementary business activities, we will need to raise additional funds. We will also need

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additional funds or a collaborative partner, or both, to finance the research and development activities of our cell product candidates for additional indications. 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, clinical 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
- the effect of commercialization activities and facility expansions, if and as required
- complementary business acquisition or development opportunities

Because of our long-term funding requirements, we intend to access the public or private equity markets if conditions are favorable to complete a financing, even if we do not have an immediate need for additional capital at that time, or whenever we require additional operating capital. 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.

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 U.S., which we believe will ultimately be the largest market for our products. We will also be required to obtain additional approvals from various foreign regulatory authorities to initiate sales activities of cell products in those jurisdictions, including certain countries in the EU. If we cannot demonstrate the safety and efficacy of our cell product candidates, or of the cells produced in our manufacturing system, we may not be able to obtain required regulatory approvals. If we cannot demonstrate the safety and efficacy of our technologies and product candidates, 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. Because our product development programs are designed to satisfy the standards applicable to 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. Each of these cell mixtures (such as our TRC-based products) is, under current regulations, regulated as a biologic product, which requires a Biological License Application (BLA).

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EU Directives and regulations (laws) have become effective, and have influenced the requirements for manufacturing cell products and the conduct of clinical trials. Recent changes to the EU Medicinal Products Prime Directive (including added annexes and new regulations) shifted patient-derived cells to the medicinal products category, which will require Marketing Authorizations in order to market and sell these products. These new requirements have delayed some of our current planned clinical trials with TRC-based products in the EU, and will require clinical trials with data submission and review by one or more European regulatory bodies. There is uncertainty about which clinical trial activities and data are required, and because of the recent nature of these new directives, laws and regulations, there is no established precedent to understand the timeline or other requirements for Marketing Authorization.

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

Commercialization in the U.S. and the EU of our cell product candidates will require completion of substantial clinical trials, and obtaining sufficient safety and efficacy results to support required registration approval and market acceptance of our cell product candidates. We may not be able to successfully complete the 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 cell 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 must successfully complete our clinical trials to be able to market certain of our products.

To be able to market therapeutic cell products in the U.S. and across the EU, we must demonstrate, through extensive preclinical studies and clinical trials, the safety and efficacy of our processes and product candidates. 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.

Our research programs are currently directed at improving TRC-based product functionality for certain clinical indications, improving product shelf life, and decreasing the cost of manufacturing our TRC-based products. These production process changes may alter the functionality of our cells, and require various additional levels of experimental and clinical testing and evaluation. Any such testing could lengthen the time before these products would be commercially available.

Even if successful clinical results are reported for a product from a completed clinical trial, this does not mean that the results will be sustained over time, or are sufficient for a marketable or regulatory approvable product.

Failure of third parties to manufacture component parts, provide limited source supplies or meet our specifications or quality standards, or imposition of additional regulation, would impair our new product development and our sales activities.

We rely solely on third parties such as Astro, Ethox, Moll and Lonza to manufacture or supply certain of our devices/manufacturing equipment, as well as component parts and other materials used in the cell product manufacturing 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 fails to perform their respective obligations or if our supply of 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.

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.

Manufacturing our cell products in centralized facilities may increase the risk that we will not have adequate quantities of our cell products for clinical programs.

We rely on a third party manufacturer, Fraunhofer Institute for Interfacial Engineering and Biotechnology in Stuttgart, Germany, to supply our TRC-based cell products for certain EU clinical trials. Reliance on third party manufacturers entails risks including regulatory compliance and quality assurance and the possible breach of the manufacturing agreement by the third party. We are subject to similar regulatory and compliance risks at our site in Ann Arbor, Michigan. Both sites could be subject to ongoing, periodic, unannounced inspection by regulatory agencies to ensure strict compliance with cGMP regulations and other governmental regulations and corresponding foreign standards. Our present and future manufacturers might not be able to comply with these regulatory requirements. We do not have redundant cell manufacturing sites. In the event our cell manufacturing facilities are damaged or destroyed or are subject to regulatory restrictions, our clinical trial programs and other business prospects would be adversely affected.

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

We will be seeking to obtain regulatory approvals to market our TRC-based cell products for tissue repair and regeneration treatments. Even if we obtain all required regulatory approvals, we cannot be certain that our products and processes will be accepted in the market place at a level that would allow us to operate profitably. Our products may be unable to achieve commercial acceptance for a number of reasons such as the availability of alternatives that are less expensive, more effective, or easier to use, the perception of a low cost-benefit ratio for the product amongst physicians and hospitals, or an inadequate level of product support from ourselves or a commercial partner. 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.

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 U.S. 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

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reimbursement from third party payors may reduce the demand for, or negatively affect the price of, our products. For example, in the past, published studies suggested that stem cell transplantation for breast cancer, which 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 has negatively affected the marketability of our products in this indication in the past.

Use of animal-derived materials could harm our product development and commercialization efforts.

Some of the manufacturing materials and/or components we use in, and are critical to, implementation of our TRC Technology involve the use of animal-derived products, including fetal bovine serum. Suppliers or regulatory changes may limit or restrict the availability of such materials for clinical and commercial use. We currently purchase all of our fetal bovine sera from protected herds in Australia and New Zealand. These sources are considered to be the safest and raise the least amount of concern from the global regulatory agencies. If, for example, the so-called “mad cow disease” occurs in New Zealand or in Australia, it may lead to a restricted supply of the serum currently required for the TRC-based product manufacturing processes. Any restrictions on these materials would impose a potential competitive disadvantage for our products or prevent our ability to manufacture TRC-based cell products. Regulatory authorities in the EU are reviewing the safety issues related to the use of animal-derived materials, which we currently use in our production process. The FDA has issued draft regulations for controls over bovine materials. These proposed regulations do not appear to affect our ability to purchase the manufacturing materials we currently use. However, the FDA may issue final regulations that could affect our operations. We do not know what actions, if any, the authorities may take as to animal derived materials specific to medicinal products distributed in the EU. Our inability to develop or obtain alternative compounds would harm our product development and commercialization efforts. There are certain limitations in the supply of certain animal-derived materials, which may lead to delays in our ability to complete clinical trials or eventually to meet the anticipated market demand for our cell products.

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

We have only limited internal manufacturing, sales, marketing and distribution capabilities. As market needs develop, we intend to establish and operate commercial-scale manufacturing facilities, which will need to comply with all applicable regulatory requirements. We will also need to develop new configurations of our cell manufacturing system for these facilities to enable processes and cost efficiencies associated with large-scale manufacturing. Establishing these facilities will require significant capital and expertise. Any delay in establishing, or difficulties in operating, these facilities will limit our ability to meet the anticipated market demand for our cell products. We intend to get assistance to market some of our future cell products through collaborative relationships with companies with established sales, marketing and distribution capabilities. 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. We may market one or more of our TRC-based products through our own sales force. Our inability to develop and retain a qualified sales force could limit our ability to market, sell and distribute our cell products.

If we do not keep pace with our competitors and with technological and market changes, our products may become obsolete and our business will suffer.

The markets for our products are very competitive, subject to rapid technological changes, and vary for different 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 use for bone marrow transplantation, following marrow ablation due to chemotherapy, 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 the practical elimination of this market for our cell-based product for this application.

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Our cell manufacturing system is 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, the cost or process of treatment and other factors may cause researchers and practitioners to not use our products and we could suffer a competitive disadvantage. Finally, to the extent that others develop new technologies that address the targeted application for our products, our business will suffer.

We have experienced significant management turnover, and 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 previous occasions. As a result of these and other factors, we may not be successful in hiring or retaining key personnel. On July 17, 2006 we announced that George W. Dunbar had joined the Company as CEO, President and a Director. Our inability to replace any key employee, including but not limited to Mr. Dunbar, 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. Certain patent equivalents to the U.S. patents have also been issued in other jurisdictions including Australia, Japan, the Republic of Korea, Canada and under the European Convention. Certain of these foreign patents are due expire beginning in 2008. Furthermore, we rely on 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, each of 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 established guidelines and have certain rights in the technology developed with the grant. 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.

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 manufacture and/or use of TRC-based products during clinical trials, or after commercialization, results in adverse events. 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.

We are required to evaluate our internal control over financial reporting under Section 404 of the Sarbanes-Oxley Act of 2002 and any adverse results from such evaluation could have a negative market reaction.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002 (Section 404), we are required to furnish a report by our management on our internal control over financial reporting. That report must contain, among other matters, an assessment of the design and operating effectiveness of our internal controls over financial reporting as of the end of the fiscal year. This assessment must include disclosure of any material weaknesses in our internal control over financial reporting identified by management. That report must also contain a statement that our independent registered public accounting firm has issued an attestation report on the design and operating effectiveness of our system of internal accounting controls over financial reporting. If in the future we are unable to assert that our internal control over financial reporting is effective as of the end of the then current fiscal year (or, if our independent registered public accounting firm is unable to express an unqualified opinion on the design and operating effectiveness of our internal controls), we could lose investor confidence in the accuracy and completeness of our financial reports, which would have a negative effect on our stock price and our ability to raise capital.

Risks Related To Our Common Stock and Warrants

Our corporate documents and Michigan law contain provisions that may make it more difficult for us to be acquired.

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

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

We are required to meet certain qualitative and 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 Capital Market. In May 2003 and in July 2004, we received notification from Nasdaq of potential delisting as a result of our stock trading below \$1.00 for more than thirty consecutive business days. While in each case our stock price recovered within the permitted grace periods and Nasdaq notified us that we were again in full compliance, we cannot provide any assurance that our stock price would again recover within the specified

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times if future closing bid prices below \$1.00 triggered another potential delisting. The qualitative tests we must meet address various corporate governance matters, including Audit Committee and Board composition. In the past, we experienced director resignations and are devoting increased resources to Board member recruitment and retention. If we do not maintain compliance with the Nasdaq requirements within specified periods and subject to permitted extensions, our common stock may be recommended for delisting (subject to any appeal we would file). 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.

The issuance of additional common stock or warrants 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. We may enter into financing transactions at prices which are at a substantial discount to market and which may include the issuance of warrants. Such an equity issuance would cause a substantially larger number of shares to be outstanding and would dilute the ownership interest of existing shareholders.

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

The market price of shares of our common stock has been volatile, ranging in closing price between \$1.13 and \$1.60 during the twelve month period ended June 30, 2007. 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
- news or reports from other stem cell, cell therapy or tissue engineering companies
- reports by securities analysts
- status of the investment markets
- concerns related to management transitions

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.

Risks Related To This Offering

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

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Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not necessarily improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, financial condition, operating results and cash flow, and could cause the price of our common stock to decline.

Substantial future sales of our common stock in the public market may depress our stock price.

As of August 31, 2007, we had approximately 121 million shares of common stock outstanding. The market price of our common stock could drop due to sales of a large number of shares or the perception that such sales could occur. These factors also could make it more difficult to raise funds through future offerings of common stock or warrants.

The exercise of our outstanding options and warrants will dilute shareholders and could decrease our stock price.

The existence of our outstanding options and warrants, including any warrants to be issued pursuant to this offering, may adversely affect our stock price due to sales of a large number of shares or the perception that such sales could occur. These factors also could make it more difficult to raise funds through future offerings of common stock or warrants, and could adversely impact the terms under which we could obtain additional equity capital. Exercise of outstanding options and warrants, or any future issuance of additional shares of common stock or other equity securities, including but not limited to options, warrants or other derivative securities convertible into our common stock, may result in significant dilution to our shareholders and may decrease our stock price.

FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying base prospectus, including the documents that we incorporate by reference, contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as “anticipates,” “estimates,” “plans,” “projects,” “trends,” “opportunity,” “comfortable,” “current,” “intention,” “position,” “assume,” “potential,” “outlook,” “remain,” “continue,” “maintain,” “sustain,” “seek,” “achieve,” “continuing,” “ongoing,” “expects,” “management believes,” “we believe,” “we intend” and similar words or phrases, or future or conditional verbs such as “will,” “would,” “should,” “could,” “may,” or similar expressions. Accordingly, these statements involve estimates, assumptions and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus, and in particular those factors listed under the section entitled “Risk Factors.”

Because the factors referred to in the preceding paragraph could cause actual results or outcomes to differ materially from those expressed in any forward-looking statements we make, you should not place undue reliance on any such forward-looking statements. Further, any forward-looking statement speaks only as of the date on which it is made, and we undertake no obligation to update any forward-looking statement or statements to reflect events or circumstances after the date on which such statement is made or to reflect the occurrence of unanticipated events. New factors emerge from time to time, and it is not possible for us to predict which factors will arise. In addition, we cannot assess the impact of each factor on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements.

USE OF PROCEEDS

We estimate that the net proceeds we will receive from this offering, assuming an offering price of \$1.14 per share, will be approximately \$12.5 million after deducting the placement agent's fee and estimated offering expenses and assuming that we sell the maximum number of shares offered hereby. We will not receive any proceeds from the sale of common stock issuable upon exercise of the warrants we are offering unless and until such warrants are exercised. If the warrants are fully exercised for cash, we will receive additional proceeds of approximately \$9.4 million. We will not pay the placement agent any fee with respect to shares of our common stock issued upon exercise of the warrants.

We intend to use any net proceeds from this offering, together with other available funds, for clinical trials and research and development, manufacturing development and expansion and working capital and general corporate purposes, which may include the cost of a possible acquisition or the development of complementary business activities.

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 trials and other product development activities, other cell therapy application programs and changing assessments of potential market opportunities and competitive developments. 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.

DILUTION

If you invest in our common stock and warrants in this offering, your interest will be diluted to the extent of the difference between the public offering price per share of our common stock and the net tangible book value per share of our common stock immediately after this offering.

As of June 30, 2007, we had a net tangible book value of \$28,251,000, or \$0.24 per share of common stock based upon 120,012,869 shares outstanding. Net tangible book value per share is equal to our total tangible assets (total assets less intangible assets) less total liabilities, divided by the number of shares of our outstanding common stock.

Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock and warrants in this offering and the net tangible book value per share of common stock immediately after the completion of this offering. Without taking into account any other changes in our net tangible book value since June 30, 2007, after giving effect to our sale of units consisting of 11,842,105 shares of common stock and warrants to purchase 5,921,053 shares of common stock in this offering at the public offering price of \$1.14 per unit and after deducting the placement agent's fee and estimated offering expenses payable by us (but excluding any proceeds received upon exercise of warrants), our pro forma net tangible book value as of June 30, 2007 would have been \$40,741,000, or \$0.31 per share. This amount represents an immediate increase in net tangible book value of \$0.07 per share to our existing shareholders and an immediate dilution in net tangible book value of \$0.83 per share to new investors purchasing our common stock and warrants in this offering. The following table illustrates this per share dilution:

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Public offering price per unit		\$	1.14
Net tangible book value per share as of June 30, 2007	\$28,251,000		
Increase in net tangible book value per share attributable to this offering	\$12,490,000		
Pro forma net tangible book value per share as of June 30, 2007 after giving effect to this offering		\$40,741,000	
Dilution per share to new investors in this offering		\$	0.83

These calculations exclude:

- a total of 10,837,936 shares of our common stock subject to outstanding options under our current and previous equity incentive plans as of June 30, 2007, having a weighted average exercise price of \$1.47 per share (since June 30, 2007, an additional 1,701,200 options have been issued at an average exercise price of \$1.14 per share);
- 5,047,667 shares of our common stock issuable upon exercise of outstanding warrants as of June 30, 2007, having a weighted average exercise price of \$1.62 per share (since June 30, 2007, 808,824 warrants were exercised at an exercise price of \$1.23 per share);
- 5,912,095 shares of our common stock available for future grants or awards under our 2004 Equity Incentive Plan as of June 30, 2007; and
- 5,921,053 shares of common stock issuable upon the exercise of warrants to be issued in this offering.

To the extent that any of these options or warrants are exercised, there will be further dilution to new investors. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our shareholders.

DESCRIPTION OF WARRANTS

Each warrant represents the right to purchase up to 0.5 shares of common stock at an exercise price equal to \$1.5875 per share, subject to adjustment as described below. Each warrant may be exercised for cash on or after about April 17, 2008 through and including about April 17, 2013.

The exercise price and the number of shares underlying the warrants are subject to appropriate adjustment in the event of stock splits, stock dividends on our common stock, stock combinations or similar events affecting our common stock. In addition, in the event we consummate any merger, consolidation, sale or other reorganization event in which our common stock is converted into or exchanged for securities, cash or other property, then following such event, the holders of the warrants will be entitled to receive upon exercise of the warrants the kind and amount of securities, cash or other property which the holders would have received had they exercised the warrants immediately prior to such reorganization event.

No fractional shares of common stock will be issued in connection with the exercise of a warrant. In lieu of fractional shares, we will pay the holder an amount in cash equal to the fractional amount multiplied by the market value of a share of common stock.

A warrant may be transferred by a holder without our consent, upon surrender of the warrant to us, properly endorsed (by the holder executing an assignment in the form attached to the warrant) and upon payment of any necessary tax or other governmental charge imposed upon such transfer.

The warrants will not be listed on any securities exchange or automated quotation system and we do not intend to arrange for any exchange or quotation system to list or quote the warrants.

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The above summary of certain terms and provisions of the warrants is qualified in its entirety by reference to the detailed provisions of the warrants, the form of which will be filed as an exhibit to a Current Report on Form 8-K that will be incorporated by reference herein.

PLAN OF DISTRIBUTION

We are offering the shares of our common stock and warrants to purchase our common stock through a placement agent. Subject to the terms and conditions contained in the placement agency agreement dated October 15, 2007, BMO Capital Markets Corp. has agreed to act as the exclusive placement agent for the sale of up to 11,842,105 shares of our common stock and warrants to purchase up to 5,921,053 shares of our common stock. The placement agent is not purchasing or selling any shares or warrants by this prospectus supplement or accompanying base prospectus, nor are they required to arrange the purchase or sale of any specific number or dollar amount of units, but has agreed to use commercially reasonable efforts to arrange for the sale of all 11,842,105 shares and 5,921,053 warrants.

The placement agency agreement provides that the obligations of the placement agent and the investors are subject to certain conditions precedent, including the absence of any material adverse change in our business and the receipt of certain opinions, letters and certificates from our counsel, our independent auditors and us.

Confirmations and definitive prospectuses will be delivered, or otherwise made available, to all investors who agree to purchase shares of the common stock and warrants to purchase shares of the common stock, informing investors of the closing date as to such shares and warrants. We currently anticipate that closing of the sale of 11,842,105 shares of common stock and warrants to purchase 5,921,053 shares of common stock will take place on or about October 16, 2007. Investors will also be informed of the date and manner in which they must transmit the purchase price for their shares.

On the scheduled closing date, the following will occur:

- we will receive funds in the amount of the aggregate purchase price; and
- BMO Capital Markets Corp. will receive the placement agent's fee in accordance with the terms of the placement agency agreement.

Pursuant to a requirement of the Financial Industry Regulatory Authority, or FINRA, the maximum commission or discount to be received by any FINRA member or independent broker/dealer may not be greater than eight percent (8.0%) of the gross proceeds received by us for the sale of any securities being registered pursuant to SEC Rule 415.

We will pay the placement agent a fee equal to 6.0% of the gross proceeds of the sale of units in the offering, without taking into account any proceeds from the exercise of the warrants. The following table shows the per unit and total fees we will pay to the placement agent assuming the sale of all of the units offered pursuant to this prospectus supplement.

Per unit	\$ 0.068
Total	\$ 810,000

Because there is no minimum offering amount required as a condition to closing, the actual total may be less than the maximum amount set forth above.

The estimated offering expenses payable by us, in addition to the placement agent's fee, are approximately \$200,000, which includes legal, accounting and printing costs and various other fees associated with registering and listing the shares of common stock. After deducting certain fees due to the placement agent and our estimated offering expenses, we expect the net proceeds from this offering to be up to approximately \$12,490,000.

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We have agreed to indemnify the placement agent against certain liabilities, including liabilities under the Securities Act of 1933, as amended. We have also agreed to contribute to payments the placement agent may be required to make in respect of such liabilities.

Our executive officers and directors have agreed to a 90-day “lock-up” with respect to our common stock, including securities convertible into or exercisable for our common stock. This means that, subject to certain exceptions, for a period of 90 days following the date of this prospectus supplement, these persons may not offer, sell, pledge or otherwise dispose of these securities without the prior written consent of BMO Capital Markets Corp. We also have agreed to a 90-day “lock-up” with respect to our common stock, including securities convertible into or exercisable for our common stock. This means that, subject to certain exceptions, for a period of 90 days following the date of this prospectus supplement, we may not offer, sell or otherwise dispose of these securities without the prior written consent of BMO Capital Markets Corp.

This is a brief summary of the material provisions of the placement agency agreement and does not purport to be a complete statement of its terms and conditions. A copy of the placement agency agreement will be filed with the SEC and incorporated by reference into the registration statement of which this prospectus supplement forms a part. See “Where You Can Find More Information” on page S-16.

LEGAL MATTERS

The validity of the common stock and warrants offered hereby will be passed upon for Aastrom by Dykema Gossett PLLC, Ann Arbor, Michigan acting as special counsel to Aastrom. Seyfarth Shaw LLP, Chicago, Illinois, has acted as counsel to Aastrom in connection with this offering. Certain legal matters will be passed upon for the placement agent by Morgan, Lewis & Bockius LLP, New York, New York.

EXPERTS

The financial statements and management’s assessment of the effectiveness of internal control over financial reporting (which is included in Management’s Report on Internal Control over Financial Reporting) incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended June 30, 2007, have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

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 100 F Street, N.E., Room 1580, 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 Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, until we sell all of the common stock and warrants offered hereby, are incorporated by reference in this prospectus:

1. Our Annual Report on Form 10-K for the fiscal year ended June 30, 2007;

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2. Our proxy statement for our annual shareholders' meeting to be held on November 7, 2007;
3. Our Current Reports on Form 8-K filed with the SEC on September 10, 2007, September 11, 2007 and September 12, 2007;
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); and
5. All of the filings pursuant to the Securities Exchange Act that we may make after the date of this prospectus supplement and prior to the termination of this offering.

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

SUBJECT TO COMPLETION, DATED OCTOBER 11, 2005

The information in this prospectus is not complete and may be changed. We 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

\$75,000,000

AASTROM BIOSCIENCES, INC.

**Common Stock
Preferred Stock
Debt Securities
Warrants**

We may from time to time issue, in one or more series or classes, up to \$75,000,000 in aggregate principal amount of our common stock, preferred stock, debt securities and/or warrants. We may offer these securities separately or together. We will specify in the accompanying prospectus supplement the terms of the securities being offered. We may sell these securities to or through underwriters and also to other purchasers or through agents. We will set forth the names of any underwriters or agents, and any fees, conversions, or discount arrangements, in the accompanying prospectus supplement. We may not sell any securities under this prospectus without delivery of the applicable prospectus supplement.

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

Our common stock is traded on the Nasdaq SmallCap Market under the symbol "ASTM." On October 10, 2005, the last reported sale price for our common stock was \$2.18 per share.

INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISK. SEE "RISK FACTORS" BEGINNING ON PAGE 5 FOR A DISCUSSION OF MATERIAL RISKS YOU SHOULD CONSIDER BEFORE YOU INVEST IN OUR SECURITIES.

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 October 11, 2005.

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

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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 working 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 generally. In light of these risks and uncertainties, the events anticipated in the forward-looking statements may not occur.

PROSPECTUS 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

We are a development stage company focused on the development of the *ex vivo* production and sale of proprietary human cell products for use in cell therapy and tissue regeneration. Our pre-clinical and clinical product development programs utilize bone marrow-derived adult stem and progenitor cell mixtures being investigated for aiding in the growth of tissues such as bone, vascular tissue and cartilage, as well as blood and immune system cells.

In the expanding fields of cell therapy and tissue regeneration, we are developing proprietary adult bone marrow cell-based products, some of which are now in the clinical stage, for the regenerative repair of damaged human tissues and other medical disorders. Our lead products contain TRCs, which are a unique mixture of bone marrow-derived adult stem and progenitor cells, produced outside of the body or “*ex vivo*” from a small amount of bone marrow taken from the patient. In clinical trials involving approximately 200 patients, our TRCs have been demonstrated to be safe and reliable, and appeared to regenerate certain normal healthy human tissues.

We have also developed our proprietary AastromReplicell System®, which is a patented, integrated system of instrumentation and single-use consumable kits for the commercial production of human cells. The AastromReplicell System was developed to provide a manufacturing platform for our proprietary cell products, such as our TRCs. The AastromReplicell System technology has also been applied to the production of dendritic cells and dendritic cell vaccines for third parties requiring automated cell production supporting GMP (Good Manufacturing Practice) compliance. Since this third-party development activity is minimal at present, active development and marketing activities targeting developers of dendritic cells and dendritic cell vaccines have been halted.

Our commercial production pathway for our TRC cell products is in part enabled through the AastromReplicell System platform. This proprietary and automated clinical cell production system combines patented GMP-compliant automated cell production with patented “single-pass perfusion.” Single-pass perfusion is our technology for growing large quantities of highly robust human cells outside the body. These cells include adult stem and progenitor cell mixtures, which are the cells believed to be required for forming tissues such as bone, vascular, cartilage, blood, and immune system cells.

Our primary business model is to establish a core infrastructure for the manufacturing and distribution of TRC cell products for use in multiple medical indications. Initially, we intend to pursue TRC based cell products for the following therapeutic areas:

- Local bone regeneration such as is needed in fractures, spinal fusion, and jaw bone reconstruction
- Vascular (blood vessel) regeneration in limb ischemia resulting from diabetes and other diseases

In the future, we may develop and/or support the development by third parties of products for other areas such as cartilage regeneration, cardiac tissue regeneration, and dendritic cell based vaccines.

We do not have the sales or marketing organization that would be needed to commercialize our therapeutic products. We intend to seek partnerships with other companies who have this capability, as well

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as to develop our own ability to either support these relationships and, if necessary, to complete some pilot level of sales and marketing activity ourselves.

In the EU, our business development activities are aided through our small, wholly-owned subsidiaries located in Dublin, Ireland and Berlin, Germany.

Since our inception, we have been in the development stage and engaged in research and product development, conducted principally on our own behalf, but also in connection with various collaborative research and development agreements with others. Our initial business plan was to pursue the bone marrow transplantation markets. At approximately the same time (late fiscal year 1999) that we intended to commence our initial pilot-scale product launch in the EU of the AastromReplicell System with the SC-I kit, data was released at international meetings that resulted in the majority of the patients who would otherwise have been candidates for the SC-I product, to no longer require the use of the product. This loss of market for the SC-I caused us to reorganize our operations and suspend all external activities in October 1999, pending the receipt of additional financing and the completion of the reorganization process. We expanded the capabilities of the AastromReplicell System to include dendritic cell production and initiated pilot marketing activities for the CE Marked DC-I, DCV-I and the DCV-II products. However, only minimal and irregular revenue has been generated from these products, and as a result it is no longer a priority area for us. Therefore, we plan to limit our marketing efforts promoting the AastromReplicell System as a stand-alone product. Rather our focus is on utilizing the AastromReplicell System technology in cell manufacturing facilities to support our TRC development programs. At such time as we satisfy applicable regulatory approval requirements, we expect the sales of our TRC and our related cell-based products will constitute nearly all of our product sales revenues.

We do not expect to generate positive cash flows from our consolidated operations for at least the next several years and then only if more significant TRC cell product sales commence. Until that time, we expect that our revenue sources will consist of only minor sales from our dendritic cell kits to academic and commercial research centers, grant revenue and research funding, and potential licensing fees, or other financial support from potential future corporate collaborators. To date, we have financed our operations primarily through public and private sales of our equity securities, and we expect to continue obtaining required capital in a similar manner. As a development-stage company, we have never been profitable and do not anticipate having net income unless and until significant product sales commence. This is not likely to occur until we obtain significant additional funding and complete the required clinical trials for regulatory approvals, and receive the necessary approvals to market our products. Through, June 30, 2005, we have accumulated losses of approximately \$125 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, obtain the required regulatory approvals, 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.

This Prospectus

This prospectus is part of a registration statement that we filed with the SEC utilizing a “shelf” registration process. Under this shelf process, we may sell the securities described in this prospectus in one or more offerings up to a total dollar amount of \$75 million. We have provided in this prospectus a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. We may also add, update or change in the prospectus supplement any of the information contained in this prospectus. This prospectus, together with applicable prospectus supplements, includes all material information relating to this offering. You should read both this prospectus and any prospectus supplement together with the additional information described under the heading “Where You Can Find More Information.”

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 securities offered.

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, 2005, we have incurred cumulative net losses totaling approximately \$125 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 at least until, and probably after, 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, maintaining supplies of key manufacturing components, 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 U.S., which we believe will ultimately be the largest market for our products. We will also be required to obtain additional approvals from various foreign regulatory authorities to initiate sales activities of cell products, and continue or increase sale of equipment, in those jurisdictions, such as the EU. If we cannot demonstrate the safety, reliability and efficacy of our cell product candidates, or of the cells produced in our device products, we may not be able to obtain required regulatory approvals. 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. Although the AastromReplicell System is currently considered to be unregulated manufacturing equipment in the U.S., the FDA may reconsider this and classify the System as a Class III medical device, or may ultimately choose to regulate the AastromReplicell System under another category. Because our product development programs are designed to satisfy the standards applicable to 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 (such as the Tissue Repair Cells) may, under current regulations be regulated as a biologic product, which requires a Biologic License Application (BLA).

The new EU Directives (laws) have become effective, and have influenced the requirements for manufacturing cell products and the conduct of clinical trials. These changes have delayed or in some cases temporarily halted clinical trials of cellular products in the EU. The recent changes to the European Union Medicinal Products Prime Directive shifted patient-derived cells to the medicinal products category, which will require license approvals in order to market and sell these products. These new laws may delay some of our current planned clinical trials with Tissue Repair Cells in the EU, and will require clinical trials with data submission and review by European regulatory bodies. There is uncertainty as to the level of trials and data needed and because of the recent nature of these regulations; there is no established precedent to understand the timeline or other requirements for licensure.

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

Commercialization in the U.S. and the EU of our cell product candidates will require completion of substantial clinical trials, and obtaining sufficient safety and efficacy results to support required registration approval and market acceptance of our cell product candidates. 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 cell 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 must successfully complete our clinical trials to be able to market certain of our products.

To be able to market therapeutic cell products in the U.S. and in the EU, 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.

Our research programs are currently developing and evaluating new variations of TRCs that are intended to improve the functionality for certain clinical indications, to improve shelf life, and to decrease the cost of manufacturing our TRC products. These production process changes may alter the functionality of our TRCs, and would require various levels of experimental and clinical testing and evaluation. Any such testing or clinical study may affect regulatory review process and lengthen the time before TRC products would be commercially available.

Even if successful clinical results are reported for a product from a completed clinical trial, this does not mean that the results will be sustained over time, or are sufficient for a marketable or regulatory approvable product.

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

We will be seeking to obtain regulatory approvals to market our TRC cell products for tissue repair and regeneration 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 TRCs 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.

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 U.S. 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.

Use of animal-derived materials could harm our product development and commercialization efforts.

Some of the compounds we use in, and are critical to, our TRC manufacturing processes involve the use of animal-derived products, including fetal bovine serum. However, animal-derived cells are not used as "feeder cells" in the growth of human TRCs. Suppliers or regulatory authorities may limit or restrict the availability of such compounds for clinical and commercial use. For example, the occurrence of so-called "mad cow disease" in the U.S. or in New Zealand may lead to a restricted supply of the serum currently required for the TRC manufacturing process. Any restrictions on these compounds would impose a potential competitive disadvantage for our products or prevent our ability to manufacture TRC cell products. Regulatory authorities in the EU are reviewing the safety issues related to the use of animal-derived materials, which we currently use in our production process. It is unknown at this time what actions, if any, the authorities may take as to animal derived materials specific to medicinal products

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distributed in the EU. Our inability to develop or obtain alternative compounds would harm our product development and commercialization efforts. There are certain limitations in the supply of certain animal-derived materials, which may lead to delays in our ability to complete clinical trials or eventually to meet the anticipated market demand for our cell products.

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

We have only limited internal manufacturing, sales, marketing and distribution capabilities. As market needs develop, we intend to establish and operate commercial-scale manufacturing facilities, which will need to comply with all applicable regulatory requirements. We expect to develop new configurations of the AastromReplicell System for these centralized facilities to enable process and cost efficiencies associated with large-scale manufacturing. Establishing these facilities will require significant capital and expertise. Any delay in establishing, or difficulties in operating, these facilities will limit our ability to meet the anticipated market demand for our cell products. We intend to get assistance to market our future cell products through collaborative relationships with companies with established sales, marketing and distribution capabilities. 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. We may market our TRCs through our own sales force. Our inability to develop and retain a qualified sales force could limit our ability to market, sell and distribute our cell products.

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 and cell manufacturing facilities. We expect that our available cash and interest income, including that raised in the recent sale of common stock, described above, will be sufficient to finance currently planned activities beyond the end of fiscal year 2006 (ending June 30, 2006). However, in order to grow and expand our business, and to introduce our new product candidates into the marketplace, following sale of all of the securities offered hereby, we will raise additional capital. 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, clinical 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 intend to access the public or private equity markets if conditions are favorable to complete a financing, even if we do not have an immediate need for additional capital at that time, or whenever we require additional operating capital. 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 such time, we may enter into financing transactions at prices, which are at a substantial discount to market. 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 \$0.63 and \$4.05 during the twelve month period ended June 30, 2005. 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 news or reports from other stem cell, cell therapy or tissue engineering companies
- reports by securities analysts
- 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.

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

We are required to meet certain qualitative and 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. In May 2003, and July 2004, we received notification from Nasdaq of potential delisting as a result of our stock trading below \$1.00 for more than thirty consecutive business days. While in each case our stock price recovered within the permitted grace periods and Nasdaq notified us that we were again in full compliance, we cannot provide any assurance that our stock price would again recover within the specified times if future closing bid prices below \$1.00 triggered another potential delisting. The qualitative tests we must meet address various corporate governance matters, including Audit Committee and Board composition. We have experienced recent director resignations and are devoting increased resources to Board member recruitment and retention. If we do not maintain compliance with the Nasdaq requirements within specified periods and subject to permitted extensions, our common stock may be recommended for delisting (subject to any appeal we would file). If our common stock were delisted, it could be more

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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.

Failure of third parties to manufacture component parts or provide limited source supplies, or imposition of additional regulation, 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 or supply certain of our component parts, growth factors and other materials used in the cell product manufacturing 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.

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.

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 markets for our products are very competitive, subject to rapid technological changes, and vary for different 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 use for bone marrow transplantation, following marrow ablation due to chemotherapy, 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 the practical elimination of this market for our cell-based product for this application.

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, the cost or process of treatment and other factors may cause researchers and practitioners to not use our products and we could suffer a competitive disadvantage. As a result, we may be unable to recover the net book value of our inventories. 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, Chief Executive Officer and Chairman of Aastrom. Our inability to replace any 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

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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 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 established guidelines and have certain rights in the technology developed with the grant. 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.

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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We are required to evaluate our internal control over financial reporting under Section 404 of the Sarbanes-Oxley Act of 2002 and any adverse results from such evaluation could have a negative market reaction.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, we are required to furnish a report by our management on our internal control over financial reporting. That report must contain, among other matters, an assessment of the effectiveness of our internal control over financial reporting as of the end of the fiscal year, including a statement as to whether or not our internal control over financial reporting is effective. This assessment must include disclosure of any material weaknesses in our internal control over financial reporting identified by management. That report must also contain a statement that our independent registered public accounting firm has issued an attestation report on management's assessment of such internal controls. If in the future we are unable to assert that our internal control over financial reporting is effective as of the end of the then current fiscal year (or, if our independent registered public accounting firm are unable to attest that our management's report is fairly stated or they are unable to express an opinion on the effectiveness of our internal controls), we could lose investor confidence in the accuracy and completeness of our financial reports, which would have a negative effect on our stock price and our ability to raise capital.

Forward-looking statements

This registration statement 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
- adequacy of existing capital to support operations for a specified time
- product development and marketing plans
- clinical trial plans and anticipated results
- anticipation of future losses
- replacement of manufacturing sources
- commercialization plans
- revenue expectations and operating results

These statements are subject to risks and uncertainties, including those set forth in this Risk Factors section and in the materials incorporated by reference into this prospectus, 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 or in any prospectus supplement are made as of the date hereof or thereof. We assume no obligation to update any such forward-looking statement or to update any reason why actual results might differ.

RATIO OF EARNINGS TO FIXED CHARGES (1)

The following table sets forth ratios of earnings to fixed charges for the periods shown.

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Twelve Months Ended				
June 30 2005	June 30 2004	June 30 2003	June 30 2002	June 30 2001
N/A (2)	N/A (2)	N/A (2)	N/A (2)	N/A (2)

- (1) The ratio of earnings to fixed charges was computed by dividing earnings by fixed charges. For this purpose, earnings consist of net loss before fixed charges. Fixed charges consist of interest expense plus the interest factor in lease expenses. During the fiscal years covered by this table, we did not have any material fixed charges or preferred stock dividends. However, our total lease expenses, which comprised most of our total commitments, were \$626,000, \$616,000, \$602,000, \$547,000 and \$495,000 for the twelve months ended June 30, 2005, 2004, 2003, 2002 and 2001.
- (2) Earnings have been inadequate to cover fixed charges and total commitments. The dollar amount of the coverage deficiency was approximately \$11.8 million, \$10.5 million, \$9.6 million, \$7.9 million and \$5.9 million for the twelve months ended June 30, 2005, 2004, 2003, 2002 and 2001.

USE OF PROCEEDS

We cannot guarantee that we will receive any proceeds in connection with this offering because we may choose not to issue any securities covered by this prospectus.

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

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

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

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 100 F Street, N.E., 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 Sections 13(a), 13(c) 14 or 15(d) of the Securities Exchange Act of 1934, until we sell all of the common stock offered hereby, are incorporated by reference in this prospectus:

1. Our Annual Report on Form 10-K for the fiscal year ended June 30, 2005;

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2. Our Current Reports on Form 8-K, as amended, originally filed with SEC on July 5, 2005; August 2, 2005 (and the amendment thereto filed on September 8, 2005); August 25, 2005; September 8, 2005 (relating to the resignation of a director); September 30, 2005; and October 11, 2005; and the amendment filed on September 8, 2005 to the 8-K originally filed on June 20, 2005;
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).

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

THE SECURITIES WE MAY OFFER

The descriptions of the securities contained in this prospectus, together with the applicable prospectus supplements, summarize all the material terms and provisions of the various types of securities that we may offer. We will describe in the applicable prospectus supplement the particular terms of the securities offered by that prospectus supplement. If we indicate in the applicable prospectus supplement, the terms of the securities may differ from the terms we have summarized below. We will also include in the prospectus supplement information, where applicable, about material United States federal income tax considerations relating to the securities, and the securities exchange, if any, on which the securities will be listed.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock and certain provisions of our articles of incorporation and bylaws is a summary and is qualified in its entirety by the provisions of our articles of incorporation and bylaws.

Our authorized capital stock consists of 200,000,000 shares of common stock, no par value per share, and 5,000,000 shares of preferred stock, no par value per share.

Common Stock

Holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of shareholders and do not have cumulative voting rights. Holders of common stock have no preemptive, redemption or conversion rights and are not subject to future calls or assessments. No sinking fund provisions apply to our common stock. All outstanding shares are fully-paid and non-assessable. In the event of our liquidation, dissolution or winding up, holders of common stock are entitled to share ratably in assets available for distribution, subject to prior distribution rights of any preferred stock then outstanding. Holders of common stock are entitled to receive proportionately any such dividends declared by the board of directors, out of legally available funds for dividends, subject to any preferences that may be applicable to any shares of preferred stock that may be outstanding at that time. The rights, preferences and privileges of holders of common stock are set forth in our restated articles of incorporation, which may be amended by the holders of at least two-thirds of the outstanding shares of common stock.

Preferred Stock

Our Board of Directors is authorized to issue up to 5,000,000 shares of preferred stock in one or more series without shareholder approval. Our Board of Directors may determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences of each series of preferred stock.

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The purpose of authorizing our Board of Directors to issue preferred stock in one or more series and determine the number of shares in the series and its rights and preferences is to eliminate delays associated with a shareholder vote on specific issuances. Examples of rights and preferences that the Board of Directors may fix are: (1) dividend rights, (2) dividend rates, (3) conversion rights, (4) voting rights, (5) terms of redemption, and (6) liquidation preferences. The issuance of preferred stock, while providing desirable flexibility in connection with possible acquisitions and other corporate purposes, could make it more difficult for a third party to acquire, or could discourage a third party from acquiring, a majority of our outstanding voting stock. The rights of holders of our common stock described above, will be subject to, and may be adversely affected by, the rights of any preferred stock that we may designate and issue in the future.

We will incorporate by reference as an exhibit to the registration statement which includes this prospectus the form of any certificate of designation which describes the terms of the series of preferred stock we are offering. This description and the applicable prospectus supplement will include:

- the title and stated value;
- the number of shares authorized;
- the liquidation preference per share;
- the purchase price;
- the dividend rate, period and payment date, and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;
- voting rights, if any, of the preferred stock;
- preemptive rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- whether interests in the preferred stock will be represented by depositary shares;

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- a discussion of any material United States federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

When we issues share of preferred stock under this prospectus, the shares will fully be paid and nonassessable and will not have, or be subject to, any preemptive or similar rights.

The Michigan Business Corporation Act provides that the holders of preferred stock will have the right to vote separately as a class on any proposal involving an increase or decrease in the authorized number of shares of that class, or changes in the powers, preferences or special rights of holders of that preferred stock so as to affect the class adversely. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Michigan Law and Certain Charter and By-Law Provisions

We are subject to certain anti-takeover provisions of the Michigan Business Corporation Act (the “MBCA”) which could delay or make more difficult a merger or tender offer involving Aastrom. Chapter 7A of the MBCA prevents, in general, an “interested shareholder” (defined generally as a person owning 10% or more of a corporation’s outstanding voting shares) from engaging in a “business combination” (as defined therein) with a Michigan corporation unless: (a) the Board of Directors issues an advisory statement, holders of 90% of the shares of each class of stock entitled to vote approve the transaction, and holders of two-thirds of the “disinterested” shares of each class of stock approve the transaction; or (b) the interested shareholder has been an interested shareholder for at least five years and has not acquired beneficial ownership of any additional shares of the corporation subsequent to the transaction which resulted in such shareholder being classified as an interested shareholder, and meets certain requirements, including provisions relating to the fairness of the price and the form of consideration paid; or (c) the Board of Directors, by resolution, exempts a particular interested shareholder from these provisions prior to the interested shareholder becoming an interested shareholder. The MBCA also contains certain other provisions which could have anti-takeover effects.

Our bylaws provide that the Board of Directors is divided into three classes of directors, with each class serving a staggered three-year term. The classification system of electing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of Aastrom and may maintain the incumbency of the Board of Directors, as it generally makes it more difficult for shareholders to replace a majority of the directors. Our restated articles of incorporation eliminate the right of shareholders to act without a meeting and do not provide for cumulative voting in the election of directors. The amendment of any of these provisions would require approval by holders of at least two-thirds of the shares of outstanding common stock.

These and other provisions of our restated articles of incorporation could have the effect of deterring certain takeovers or delaying or preventing certain changes in control or management of Aastrom, including transactions in which shareholders might otherwise receive a premium for their shares over then-current market prices.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Continental Stock Transfer & Trust Company.

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the debt securities that we may offer under this prospectus. While the terms we have summarized below will apply generally to any future debt securities we may offer, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. If we indicate in a prospectus supplement, the terms of any debt securities we offer under that prospectus supplement may differ from the terms we describe below.

We will issue any senior notes under the senior indenture which we will enter into with a trustee to be named in the senior indenture. We will issue any subordinated notes under the subordinated indenture which we will enter into with a trustee to be named in the subordinated indenture. We have filed forms of these documents as exhibits to the registration statement which includes this prospectus. We use the term “indentures” to refer to both the senior indenture and the subordinated indenture. The indentures will be qualified under the Trust Indenture Act. We use the term “debenture trustee” to refer to either the senior trustee or the subordinated trustee, as applicable.

The following summaries of material provisions of the senior notes, the subordinated notes and the indentures are subject to, and qualified in their entirety by reference to, all the provisions of the indenture applicable to a particular series of debt securities. Except as we may otherwise indicate, the terms of the senior indenture and the subordinated indenture are identical.

We conduct some of our operations through a subsidiary formed under the laws of Germany. Our rights and the rights of our creditors, including holders of debt securities, to the assets of any subsidiary of ours upon that subsidiary’s liquidation or reorganization or otherwise would be subject to the prior claims of that subsidiary’s creditors, except to the extent that we may be a creditor with recognized claims against the subsidiary. Our subsidiary’s creditors would include trade creditors, debt holders, secured creditors and taxing authorities. Except as we may provide in a prospectus supplement, neither the debt securities nor the indentures restrict us or our subsidiary from incurring indebtedness.

General

We will describe in each prospectus supplement the following terms relating to a series of notes:

- the title;
- any limit on the amount that may be issued;
- whether or not we will issue the series of notes in global form, the terms and who the depository will be;
- the maturity date;
- the annual interest rate, which may be fixed or variable, or the method for determining the rate;
- the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;

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- whether or not the notes will be secured or unsecured, and the terms of any security;
- the terms of the subordination of any series of subordinated debt;
- the place where payments will be payable;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- the date, if any, after which, and the price at which, we may, at our option, redeem the series of notes pursuant to any optional redemption provisions;
- the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund provisions or otherwise, to redeem, or at the holder's option to purchase, all or a portion of the series of notes;
- whether the indenture will restrict our ability to pay dividends, or will require us to maintain any asset ratios or reserves;
- whether we will be restricted from incurring any additional indebtedness;
- a discussion of any material United States federal income tax considerations applicable to the notes;
- the denominations in which we will issue the series of notes, if other than denominations of \$1,000 and any integral multiple thereof; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities.

Conversion or Exchange Rights

We will set forth in the prospectus supplement the terms on which a series of notes may be convertible into or exchangeable for common stock or other securities of ours. We will include in that prospectus supplement provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of common stock or other securities of ours that the holders of the series of notes receive would be subject to adjustment.

Consolidation, Merger or Sale

The indentures do not contain any covenant which restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the notes, as appropriate.

Events of Default Under the Indenture

The following are events of default under the indentures with respect to any series of notes that we may issue:

- if we fail to pay interest when due and our failure continues for 60 days and the time for payment has not been extended or deferred;

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- if we fail to pay the principal, or premium, if any, when due and the time for payment has not been extended or delayed;
- if we fail to observe or perform any other covenant contained in the notes or the indentures, other than a covenant specifically relating to another series of notes, and our failure continues for 60 days after we receive notice from the debenture trustee or holders of at least 50% in aggregate principal amount of the outstanding notes of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur as to us.

If an event of default with respect to notes of any series occurs and is continuing, the debenture trustee or the holders of at least 50% in aggregate principal amount of the outstanding notes of that series, by notice to us in writing, and to the debenture trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, due and payable immediately.

The holders of a majority in principal amount of the outstanding notes of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the debenture trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of notes, unless such holders have offered the debenture trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding notes of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the debenture trustee, or exercising any trust or power conferred on the debenture trustee, with respect to the notes of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the debenture trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.
- a holder of the notes of any series will only have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies if:
 - the holder has given written notice to the debenture trustee of a continuing event of default with respect to that series;
 - the holders of at least 50% in aggregate principal amount of the outstanding notes of that series have made written request, and such holders have offered reasonable indemnity to the debenture trustee to institute the proceeding as trustee; and
 - the debenture trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding notes of that series other conflicting directions within 60 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of notes if we default in the payment of the principal, premium, if any, or interest on, the notes.

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We will periodically file statements with the debenture trustee regarding our compliance with specified covenants in the indentures.

Modification of Indenture; Waiver

We and the debenture trustee may change an indenture without the consent of any holders with respect to specific matters, including:

- to fix any ambiguity, defect or inconsistency in the indenture; and
- to change anything that does not materially adversely affect the interests of any holder of notes of any series.

In addition, under the indentures, the rights of holders of a series of notes may be changed by us and the debenture trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding notes of each series that is affected. However, we and the debenture trustee may only make the following changes with the consent of each holder of any outstanding notes affected:

- extending the fixed maturity of the series of notes;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or any premium payable upon the redemption of any notes; or
- reducing the percentage of notes, the holders of which are required to consent to any amendment.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for obligations to:

- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the debenture trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange, and Transfer

We will issue the notes of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indentures provide that we may issue notes of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust

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Company or another depository named by us and identified in a prospectus supplement with respect to that series. See “Legal Ownership of Securities” for a further description of the terms relating to any book-entry securities.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the notes of any series can exchange the notes for other notes of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the notes may present the notes for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the notes that the holder presents for transfer or exchange, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any notes. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the notes of each series.

If we elect to redeem the notes of any series, we will not be required to:

- issue, register the transfer of, or exchange any notes of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any notes that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any notes so selected for redemption, in whole or in part, except the unredeemed portion of any notes we are redeeming in part.

Information Concerning the Debenture Trustee

The debenture trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the debenture trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the debenture trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of notes unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any notes on any interest payment date to the person in whose name the notes, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the notes of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check which we will mail to the holder. Unless we otherwise indicate in a prospectus supplement, we will designate the corporate trust office of the debenture trustee in the City of New York as our sole paying agent for payments with respect to notes of

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each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the notes of a particular series. We will maintain a paying agent in each place of payment for the notes of a particular series.

All money we pay to a paying agent or the debenture trustee for the payment of the principal of or any premium or interest on any notes which remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the security thereafter may look only to us for payment of those amounts.

Governing Law

The indentures and the notes will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

Subordination of Subordinated Notes

The subordinated notes will be unsecured and will be subordinate and junior in priority of payment to some or all of our other indebtedness to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of subordinated notes which we may issue. It also does not limit us from issuing any other secured or unsecured debt.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the warrants that we may offer under this prospectus and the related warrant agreements and warrant certificates. While the terms summarized below will apply generally to any warrants that we may offer, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any warrants offered under that prospectus supplement may differ from the terms described below. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement which includes this prospectus.

General

We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from these securities.

We will evidence each series of warrants by warrant certificates that we will issue under a separate warrant agreement. We will enter into the warrant agreement with a warrant agent. Each warrant agent will be a bank that we select which has its principal office in the United States and a combined capital and surplus of at least \$50,000,000. We will indicate the name and address of the warrant agent in the applicable prospectus supplement relating to a particular series of warrants.

We will describe in the applicable prospectus supplement the terms of the series of warrants, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;

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- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreement and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreement and warrants may be modified;
- federal income tax consequences of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

- in the case of warrants to purchase debt securities, the right to receive payments of principal of, or any premium or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture; or
- in the case of warrants to purchase common stock or preferred stock, the right to receive any dividends or payments upon our liquidation, dissolution or winding up or to exercise any voting rights.

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to 5:00 P.M. New York time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required

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amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent upon exercise.

Upon receipt of the required payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Enforceability of Rights By Holders of Warrants

Each warrant agent will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue or series of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee maintain for this purpose as the “holders” of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as “indirect holders” of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depositary on behalf of other financial institutions that participate in the depositary’s book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Securities issued in global form will be registered in the name of the depositary or its participants. Consequently, for securities issued in global form, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depositary and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a book-entry security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depositary’s book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in “street name.” Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we will recognize only the banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee and of any third parties employed by us or a trustee, run only to the holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depositary participants or customers or by law, to pass the payment or notice along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, such as to relieve us of the consequences of a default or of our obligation to comply with a particular provision of the indenture or for other purposes. In such an event, we would seek approval only from the holders, and not the indirect holders, of the securities. Whether and how the holders contact the indirect holders is up to the holders.

Special Considerations for Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form or in street name, you should check with your own institution to find out:

- how it handles securities payments and notices;
- whether it imposes fees or charges;
- how it would handle a request for the holders’ consent, if ever required;
- whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;
- how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and
- if the securities are in book-entry form, how the depositary’s rules and procedures will affect these matters.

Global Securities

A global security is a security held by a depository which represents one or more individual securities. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depository. Unless we specify otherwise in the applicable prospectus supplement, The Depository Trust Company, New York, New York, known as DTC, will be the depository for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depository, its nominee or a successor depository, unless special termination situations arise. We describe those situations below under “—Special Situations When a Global Security Will Be Terminated.” As a result of these arrangements, the depository, or its nominee, will be the sole registered owner and holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depository or with another institution that does. Thus, an investor whose security is represented by a global security will not be a holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations for Global Securities

As an indirect holder, an investor’s rights relating to a global security will be governed by the account rules of the investor’s financial institution and of the depository, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depository that holds the global security.

If securities are issued only in the form of a global security, an investor should be aware of the following:

- An investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;
- An investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe under this section;
- An investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;
- An investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;
- The depository’s policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor’s interest in a global security. We and any applicable trustee have no responsibility for any aspect of the

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depository's actions or for its records of ownership interests in a global security. We and the trustee also do not supervise the depository in any way;

- The depository may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and
- Financial institutions that participate in the depository's book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities. There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When a Global Security will be Terminated

In a few special situations described below, the global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own name, so that they will be direct holders. We have described the rights of holders and street name investors above.

The global security will terminate when the following special situations occur:

- if the depository notifies us that it is unwilling, unable or no longer qualified to continue as depository for that global security and we do not appoint another institution to act as depository within 90 days;
- if we notify any applicable trustee that we wish to terminate that global security; or
- if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the prospectus supplement. When a global security terminates, the depository, and not we or any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

PLAN OF DISTRIBUTION

The securities being offered may be sold in one or more transactions at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market prices, at varying prices determined at the time of sale, or at negotiated prices. These sales may be effected at various times in one or more of the following transactions, or in other kinds of transactions:

- through underwriters for resale to the public or investors;
- transactions on the Nasdaq Stock Market or on any national securities exchange or U.S. inter-dealer system of a registered national securities association on which our common stock may be listed or quoted at the time of sale;
- in the over-the-counter market;
- in private transactions and transactions otherwise than on these exchanges or systems or in the over-the-counter market;

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- in connection with short sales of the shares;
- by pledge to secure debt and other obligations;
- through the writing of options, whether the options are listed on an options exchange or otherwise;
- in connection with the writing of non-traded and exchange-traded call options, in hedge transactions and in settlement of other transactions in standardized or over-the-counter options;
- through a combination of any of the above transactions; or
- any other method permitted by law.

We may sell our securities directly to one or more purchasers, or to or through underwriters, dealers or agents or through a combination of those methods. The related prospectus supplement will set forth the terms of each offering, including:

- the name or names of any agents, dealers, underwriters or investors who purchase the securities;
- the purchase price of the securities being offered and the proceeds we will receive from the sale;
- the amount of any compensation, discounts commissions or fees to be received by the underwriters, dealer or agents;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any discounts or concessions allowed or reallocated or paid to dealers;
- any securities exchanges on which such securities may be listed.
- the terms of any indemnification provisions, including indemnification from liabilities under the federal securities laws; and
- the nature of any transaction by an underwriter, dealer or agent during the offering that is intended to stabilize or maintain the market price of the securities.

In addition, any securities covered by this prospectus which qualify for sale pursuant to Regulation S, may be sold pursuant to Regulation S rather than pursuant to this prospectus.

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

We may agree to indemnify underwriters, dealers and agents who participate in the distribution of our common stock against various liabilities, including liabilities under the Securities Act of 1933. We may also agree to contribute to payments which the underwriters, dealers or agents may be required to make in

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

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

LEGAL MATTERS

The validity of the common stock offered hereby will be passed upon for Aastrom by Dykema Gossett PLLC, Ann Arbor, Michigan acting as special counsel to Aastrom. DLA Piper Rudnick Gray Cary US LLP, San Diego, California, has acted as counsel to Aastrom in connection with this offering.

EXPERTS

The financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended June 30, 2005, have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

11,842,105 Shares

Warrants to Purchase 5,921,053 Shares

Aastrom

Common Stock

PROSPECTUS SUPPLEMENT

BMO Capital Markets

October 16, 2007