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As filed with the Securities and Exchange Commission on March 19, 2012.

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM S-3

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

AASTROM BIOSCIENCES, INC.

(Exact name of registrant as specified in its charter)

Michigan	**94-3096597**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification Number)

24 Frank Lloyd Wright Drive
P.O. Box 376
Ann Arbor, Michigan 48106
(800) 556-0311
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Timothy M. Mayleben
President and Chief Executive Officer
Aastrom Biosciences, Inc.
P.O. Box 376
Ann Arbor, Michigan 48106
(800) 556-0311
(Name, address, including zip code, and telephone number, including area code, of agent for service)

With copies to:
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Approximate date of commencement of proposed sale to the public: From time to time after this Registration Statement becomes effective.

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

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

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

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

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. o

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer o	Accelerated filer x	Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company o

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered (1)	Amount to be Registered (2)	Proposed Maximum Offering Price Per Share (2)	Proposed Maximum Aggregate Offering Price (2)	Amount of Registration Fee (3)
Common Stock	4,525,978	$ 2.52	$11,405,464.56	$1,308

(1) The securities being registered hereunder include such indeterminate number of shares of common stock that may be issuable with respect to the securities being registered hereunder as a result of stock splits, stock dividends or similar transactions, in each case determined in accordance with Rule 416 under the Securities Act.

(2) The shares of common stock registered hereunder are issuable upon the exercise of Class A warrants to purchase an aggregate of 4,525,978 shares of common stock at an exercise price of $2.52 per share (as adjusted from $2.97 per share for the anti-dilution provision triggered in our December 2010

financing), for an aggregate exercise price of $11,405,464.56 if all such Class A warrants are exercised. The Class A warrants were issued and previously registered pursuant to Registration Statement on Form S-3, File No. 333-155739 as amended by Post-Effective Amendment No. 1 on Form S-3/A filed by the Registrant on February 19, 2009.

(3) The Class A warrants, and the shares of common stock issuable upon the exercise of such Class A warrants, were previously registered pursuant to Registration Statement on Form S-3, File No. 333-155739. Pursuant to Rule 415(a)(6) under the Securities Act, the filing fees previously paid in connection with the securities being registered hereunder will continue to be applied to the same.

The Registrant has an existing "shelf" registration statement, File No. 333-155739, that was declared effective on March 19, 2009 and which expires on March 19, 2012 pursuant to Rule 415(a)(5) under the Securities Act, as amended. Class A warrants to purchase 4,525,978 shares of common stock issued under such registration statement remain outstanding. The Registrant is filing this new Registration Statement for the sole purpose of ensuring that an effective Registration Statement covers the exercise of such previously issued Class A warrants. Pursuant to Rule 415(a)(6) under the Securities Act of 1933, as amended, the filing fees previously paid in connection with the securities being registered hereunder will continue to be applied to such securities. In accordance with SEC rules, the Registrant may continue to offer and sell securities being registered hereunder during the grace period afforded by Rule 415(a)(5). If the Registrant sells any securities being registered hereunder during the grace period, the Registrant will identify in a pre-effective amendment to this Registration Statement the new amount of securities to be carried forward to this Registration Statement in reliance upon Rule 415(a)(6).

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The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED MARCH 19, 2012.
PROSPECTUS

AASTROM BIOSCIENCES, INC.
4,525,978 Shares of Common Stock

We are offering up to 4,525,978 shares of common stock that are issuable upon the exercise of Class A warrants previously offered and sold by us on January 21, 2010. Each Class A warrant represents the right to purchase 0.75 of a share of common stock at any time, and from time to time through July 21, 2015 at an exercise price of $2.52 per share (as adjusted from $2.97 per share for the anti-dilution provision triggered in our December 2010 financing).

Our common stock is traded on the Nasdaq Capital Market under the symbol "ASTM." On March 19, 2012, the closing price for our common stock was $1.99 per share.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" contained in this prospectus beginning on page 6 and any applicable prospectus supplement, and under similar headings in the other documents that are incorporated by reference into this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of 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 March 19, 2012.

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You may rely only on the information provided or incorporated by reference in this prospectus. We have not authorized anyone to provide information different from that contained in this prospectus. Neither the delivery of this prospectus nor the sale of the securities means that the information contained in this prospectus is correct after the date of this prospectus. This prospectus is not an offer to sell or solicitation to buy the securities in any circumstances under which the offer or solicitation is unlawful.

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EXPLANATORY STATEMENT

We have an existing "shelf" registration statement on Form S-3, File No. 333-155739, that was declared effective on March 19, 2009 and which expired on March 19, 2012 pursuant to Rule 415(a)(5) under the Securities Act, subject to an up-to 180 day grace period pending effectiveness of the registration statement of which this prospectus is a part. Of the securities issued under such registration statement, Class A warrants to purchase 4,525,978 shares of our common stock remain outstanding and unexercised. We have filed a registration statement of which this prospectus is a part for the sole purpose of ensuring that an effective registration statement covers the exercise of such Class A warrants.

PROSPECTUS SUMMARY

The following summary highlights information contained elsewhere in this prospectus. It may not contain all of the information that is important to you. You should read the entire prospectus carefully, especially the discussion regarding the risks of investing in our securities under the heading "Risk Factors," before investing in our securities. In this prospectus, "Aastrom," "we," "us," and "our" refer to Aastrom Biosciences, Inc. Please refer to our Glossary at the end of this Prospectus for certain industry-specific and technical definitions.

Business

Overview

We were incorporated in 1989 and are a regenerative medicine company focused on the development of innovative cell therapies to repair or regenerate damaged or diseased tissues. We are developing patient-specific, expanded multicellular therapies for use in the treatment of severe, chronic ischemic cardiovascular diseases. We believe ixmyelocel-T (the new generic name approved by the U.S. Food and Drug Administration (FDA) and United States Adopted Names (USAN) Council in March 2011 for our multicellular therapy) is a disease modifying therapy with multi-functional properties including: tissue remodeling, immuno-modulation and the promotion of angiogenesis. Our proprietary cell-manufacturing technology enables the manufacture of multicellular therapies, expanded from an adult's own bone marrow, and delivered directly to damaged tissues. Preclinical and clinical data suggest that ixmyelocel-T may be effective in treating patients with severe, chronic ischemic cardiovascular diseases such as CLI. Preliminary data utilizing ixmyelocel-T in dilated cardiomyopathy (DCM) have provided indications of efficacy and safety. Nearly 200 patients have been treated in recent clinical trials using ixmyelocel-T (over 400 patients safely treated since our inception). We recently released positive Phase 2b data from our RESTORE-CLI trial and launched our pivotal Phase 3 REVIVE trial in CLI in February 2012. We also plan to start a randomized, placebo-controlled, double-blinded Phase 2b trial in DCM by mid-2012.

Our Therapy

Ixmyelocel-T is a patient specific, expanded multicellular therapy developed using our proprietary, automated processing system. Ixmyelocel-T is a product derived from an adult's own bone marrow but it is significantly enhanced compared with the original bone marrow. Our process enhances the patient's bone marrow mononuclear cells by expanding the mesenchymal stromal cells and alternatively activated macrophages while retaining many of the hematopoietic cells. The manufacture of our patient specific, expanded multicellular therapies is done under current Good Manufacturing Practices (cGMP) and current Good Tissue Practices (cGTP) guidelines required by the FDA.

Our therapy has several features that we believe are primarily responsible for success in treating adult patients with severe, chronic cardiovascular diseases:

Patient specific (autologous) — we start with the patient's own cells, which are accepted by the patient's immune system allowing the cells to integrate into existing functional tissues. This characteristic of our therapy, we believe, eliminates both the risk of rejection and the risk of having to use immunosuppressive therapy pre- or post-therapy. Our data also suggests that ixmyelocel-T provides the potential for long-term engraftment and tissue repair.

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Expanded — we begin with a small amount of bone marrow from the patient (up to 60 ml) and significantly expand the number of certain cell types, primarily CD90+ (mesenchymal stromal cells or MSCs) and CD14+auto+ (alternatively activated macrophages) to far more than are present in the patient's own bone marrow (up to 200 times the number of certain cell types compared with the starting bone marrow aspirate). Ixmyelocel-T is derived from the patient's own bone marrow but it is significantly enhanced compared with the starting bone marrow.

Multicellular — we believe the multiple cell types in ixmyelocel-T, which are normally only found in bone marrow but in smaller quantities, possess the key functions required for tissue remodeling, immuno-modulation and the promotion of angiogenesis.

Minimally invasive — our procedure for taking bone marrow (an "aspirate") can be performed in an out-patient setting and takes approximately 15 minutes. For diseases such as CLI, the administration of ixmyelocel-T is performed in an out-patient setting (e.g. a physician's office) in a one-time, approximately 20 minute procedure.

Safe — bone marrow and bone marrow-derived therapies have been used safely and efficaciously in medicine for over three decades. Our product, ixmyelocel-T, a bone marrow-derived, patient specific, expanded multicellular therapy leverages this body of scientific study and medical experience.

Our therapy is produced at our cell manufacturing facility in the United States, located at our headquarters in Ann Arbor, Michigan.

Clinical Development Programs

Our clinical development programs are focused on addressing areas of high unmet medical needs in severe, chronic ischemic cardiovascular diseases. We have completed a successful Phase 2b clinical trial in CLI. We have reached agreement with the FDA on CMC which has allowed us to launch our pivotal Phase 3 REVIVE clinical trial in the first quarter of 2012 with a protocol approved by FDA through the Special Protocol Assessment (SPA) process. Our CLI development program has also received Fast Track Designation from the FDA. We have completed our Phase 1/2 clinical trials in DCM and plan to begin a randomized, placebo-controlled, double-blinded Phase 2b trial in mid-2012. Our DCM development program has received Orphan Disease Designation from the FDA.

Results to date in our clinical trials may not be indicative of results obtained from subsequent patients enrolled in those trials or from future clinical trials. Further, our future clinical trials may not be successful or we may not be able to obtain the required Biologic License Application (BLA) approval to commercialize our products in the United States in a timely fashion, or at all. See "Risk Factors".

Critical Limb Ischemia

Background

CLI is the most serious and advanced stage of peripheral arterial disease (PAD). PAD is a chronic atherosclerotic disease that progressively restricts blood flow in the limbs and can lead to serious medical complications. This disease is often associated with other serious clinical conditions including hypertension, cardiovascular disease, hyperlipidemia, diabetes, obesity and stroke. CLI is used to describe patients with the most severe forms of PAD: those with chronic ischemia-induced pain (even at rest) or tissue loss (ulcers or gangrene) in the limbs, often leading to amputation and death. Many CLI patients are considered "no option" patients as they have exhausted all other treatment options with the exception of amputation. The one-year and four-year mortality rates for no option CLI patients that progress to amputation are approximately 25% and 70%, respectively. Ixmyelocel-T, our disease modifying therapy with multiple functions, has shown significant promise in the treatment of CLI patients with existing tissue loss and no option for revascularization. Currently, there are an estimated 250,000 no option CLI patients in the U.S.

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Phase 2b Clinical Program — RESTORE CLI

Our U.S. Phase 2b RESTORE-CLI program was a multi-center, randomized, double-blind, placebo-controlled clinical trial. This clinical trial was designed to evaluate the safety and efficacy of ixmyelocel-T in the treatment of patients with CLI and no option for revascularization. It was the largest multi-center, randomized, double-blind, placebo-controlled cellular therapy study ever conducted in no option CLI patients. We completed enrollment of this trial in February 2010 with a total of 86 patients at 18 sites across the United States, with the last patient treated in March 2010. These patients were followed for a period of 12 months after treatment. In addition to assessing the safety of our product, efficacy endpoints included time to first occurrence of treatment failure — the trial's primary efficacy end-point — (defined as major amputation, all-cause mortality, doubling in wound surface area and de novo gangrene), amputation-free survival (defined as major amputation and all-cause mortality), major amputation rates, level of amputation, wound healing, patient quality of life and pain scores. The primary purpose of the trial was to assess performance of our therapy and, if positive, prepare for a Phase 3 program.

Results to date of the RESTORE-CLI trial have included two planned interim analyses and a final 12-month report:

- In June 2010, we reported interim results at the Society of Vascular Surgery Meeting. The interim analysis included the six-month results for the first 46 patients enrolled in the trial and twelve-month results for the first 30 patients enrolled in the trial. Results of this analysis demonstrated that the study achieved both its primary safety endpoint and primary efficacy endpoint of time to first occurrence of treatment failure. The results related to the primary endpoint were statistically significant (p=0.0053). Analysis of the data for amputation free survival, a secondary efficacy endpoint which the study was not powered to demonstrate, were positive and showed a statistically significant reduction in event rates in favor of our therapy (p=0.038). Other endpoints measured (e.g., major amputation rate, complete wound healing, change in Wagner wound scale) showed encouraging trends, but did not reach statistical significance at the interim analysis.

- In November 2010, we presented six-month data on all 86 patients enrolled in the trial and twelve-month data on the first 72 patients at the VEITHsymposium™ non-CME satellite session. Results of this analysis showed that the study again achieved both its primary safety endpoint and primary efficacy endpoint of time to first occurrence of treatment failure. The findings related to time to first occurrence of treatment failure were statistically significant (p=0.0132). Further analyses showed a clinically meaningful reduction of 56% in treatment failure events. Analysis of the data for amputation-free survival, showed a clinically meaningful reduction in event rates of 24%, but did not show statistical significance (p=0.5541).

- In November 2011, the final 12-month data on all patients from the RESTORE-CLI trial were presented at the American Heart Association Scientific Sessions. Patients in the treatment arm showed a 62% reduction in risk relative to placebo in the primary efficacy endpoint of time to first occurrence of treatment failure (p=0.0032). While the study was not powered to show statistical significance in the secondary endpoint of amputation free survival, results from a subgroup of 45 patients with wounds at baseline (the approximate profile of the Phase 3 patient population)

showed a positive trend in this measure (21% ixmyelocel-T treated vs 44% control event rate; p=0.0802). The study also met the primary safety endpoint with no meaningful differences between the treated and control groups.

Phase 3 Clinical Program — REVIVE

In February 2012, we began screening patients in the pivotal Phase 3 REVIVE clinical trial for patients with CLI and no option for revascularization. The first patient is expected to be randomized and aspirated in March 2012. Leading up to the launch of the REVIVE pivotal trial, we received Fast Track Designation from the FDA for use of ixmyelocel-T for CLI in October 2010 and reached agreement with the FDA on a Special Protocol Assessment (SPA) in July 2011. The Phase 3 REVIVE No Option Trial that we agreed to with the FDA under the SPA process includes 594 no option CLI patients with tissue loss (ulcers and gangrene) at baseline. Patients will be randomized 1:1 and followed for 12 months for the primary efficacy endpoint of amputation-free survival. Patients will be followed for an additional 6 months for safety. We anticipate that enrollment will occur at approximately 80 sites across the U.S.

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Dilated Cardiomyopathy

Background

DCM is a severe, chronic cardiovascular disease that leads to enlargement of the heart, reducing the pumping function of the heart to the point that blood circulation is impaired. Patients with DCM typically present with symptoms of congestive heart failure, including limitations in physical activity and shortness of breath. It is currently estimated that there are approximately 125,000 ischemic DCM patients in the U.S. There are two types of DCM: ischemic and non-ischemic. Ischemic DCM, the most common form representing an estimated 60% of all DCM patients, is associated with atherosclerotic cardiovascular disease. Patient prognosis depends on the stage and cause of the disease but is typically characterized by a very poor quality of life and a high mortality rate.

Current treatments for DCM patients include both heart transplantation and left ventricular assist devices (LVADs). There are less than 2,500 heart transplantations in the U.S. each year, many DCM patients are not eligible, and they're expensive at an estimated cost of over $750,000. LVADs are also expensive at an estimated cost of over $175,000 and have a mortality rate of 50% at 2 years.

In February 2007, the FDA granted Orphan Drug Designation to ixmyelocel-T for the treatment of DCM. Our DCM development program is currently in Phase 2. We recently completed follow up on two U.S. Phase 1/2 trials investigating surgical and catheter-based delivery for our product in the treatment of DCM in reporting stages. We plan to initiate a randomized, placebo-controlled, double-blinded Phase 2b trial using catheter delivery for 60 — 80 ischemic DCM patients in the U.S. in mid-2012.

Surgical Trial Program — DCM

We completed enrollment of 40 DCM patients in the IMPACT-DCM clinical trial in January 2010 and the final patient was treated in March 2010. Participants in the IMPACT-DCM clinical trial were required to have New York Heart Association (NYHA) functional class III or IV heart failure, a left ventricular ejection fraction (LVEF) of less than or equal to 30% (60-75% is typical for a healthy person), and meet other eligibility criteria, including optimized medical therapy. Patients were randomized in an approximate 3:1 ratio of treatment to control group. Patients in the treatment group received our therapy through direct injection into the heart muscle during minimally invasive-surgery (involving a chest incision of approximately 2 inches). The primary objective of this study was to assess the safety of ixmyelocel-T in patients with DCM. Efficacy measures include cardiac dimensions and tissue mass, cardiac function (e.g. cardiac output, LVEF, cardiopulmonary exercise testing parameters), cardiac perfusion and viability, as well as other efficacy endpoints. NYHA functional class and quality of life are also assessed. Patients were followed for 12 months after treatment.

Six-month data from the IMPACT-DCM interim analysis were presented at The Sixth International Conference on Cell Therapy for Cardiovascular Disease in January 2011. Results indicated that ixmyelocel-T is safe and showed that serious adverse events were associated with the surgical procedure and not the cellular therapy. Adverse events after the initial peri-operative period were roughly equal between the control and treatment groups. Efficacy findings include positive trends in clinical endpoints, quality of life, functional, and structural parameters in the treatment group as compared with the control group.

Twelve-month data on all 40 patients enrolled in the IMPACT-DCM trial were presented at the 15th Annual Heart Failure Society of America Scientific Meeting in September 2011. Results were consistent with the six-month interim analysis, indicating that ixmyelocel-T is safe and showed that serious adverse events were associated with the surgical procedure and not the therapy. Efficacy results were also consistent with the six-month results and demonstrated promising efficacy results in patients with ischemic DCM.

Catheter Trial Program — DCM

The Catheter-DCM clinical trial was designed to explore catheter-based direct injection delivery of ixmyelocel-T to treat DCM patients. This multi-center, randomized, controlled, prospective, open-label, Phase 2 study enrolled approximately 11 patients with ischemic DCM and 10 patients with non-ischemic DCM at clinical sites across the United States. Participants met the same criteria as stated above for the IMPACT-DCM surgical trial. The first patient was enrolled into the trial in April 2010 and enrollment concluded in December 2010 with 21 patients enrolled.

In September 2011, we reported results from a six-month interim analysis of patients treated in the Catheter-DCM Phase 2 trial. In this analysis, efficacy parameters were consistent with those seen in the IMPACT-DCM trial results. In addition, the adverse event profile suggests that catheter administration of ixmyelocel-T is safe and appears to cause fewer adverse events compared to surgical

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administration. We expect to report 12-month results from the Catheter-DCM Phase 2 trial in Q2 2012. We plan to launch a randomized, placebo-controlled, double-blind Phase 2b trial in mid-2012 in approximately 60 — 80 ischemic DCM patients in the U.S. and using catheter administration.

Corporate Information

Aastrom was incorporated in 1989 under the laws of the State of Michigan. Our principal executive offices are located at Domino's Farm, Lobby K, 24 Frank Lloyd Wright Drive, Ann Arbor, Michigan 48105 and our mailing address is 24 Frank Lloyd Wright Drive, P.O. Box 376, Ann Arbor, Michigan 48106. Our telephone number is (734) 418-4400. The address of our website is www.aastrom.com. Information contained on or accessible through our website is not part of this prospectus.

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RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the risks described below and in the documents incorporated by reference in this prospectus and any prospectus supplement, as well as other information we include or incorporate by reference into this prospectus and any applicable prospectus supplement, before making an investment decision. Our business, financial condition or results of operations could be materially adversely affected by the materialization of any of these risks. The trading price of our securities could decline due to the materialization of any of these risks, and you may lose all or part of your investment. This prospectus and the documents incorporated herein by reference also contain forward-looking statements that involve risks and uncertainties. Actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks described below and in the documents incorporated herein by reference, including (i) our Annual Report on Form 10-K for the year ended December 31, 2011 and (ii) other documents we file with the SEC that are deemed incorporated by reference into this prospectus.

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 December 31, 2011, we have incurred a cumulative net loss totaling approximately $240,880,000 and we have continued to incur losses since that date. These losses have resulted principally from costs incurred in the research and development (including clinical trials) of our cell culture technologies and our cell manufacturing system, general and administrative expenses, and the prosecution of patent applications. We expect to continue to incur significant operating losses over the next several years and 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. Therefore, 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 and commercialize our products.

Despite the proceeds we received from our March 2012 financing, we will require substantial additional capital resources in order to conduct our operations, complete our product development programs, complete our clinical trials needed to market our products (including a Phase 3 clinical trial for CLI), and commercialize these products and cell manufacturing facilities. 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 a significant amount of additional funds. We will also need significant 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;

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- avoiding infringement and misappropriation of third-party intellectual property;
- obtaining valid and enforceable patents that give us a competitive advantage;
- our ability to establish additional collaborative relationships;
- our ability to effectively launch a commercial product;
- the effect of commercialization activities and facility expansions, if and as required; and
- complementary business acquisition or development opportunities.

In November 2010, we terminated the common stock purchase agreement with Fusion Capital Fund II entered into June 2009. As a result, we no longer have access to the potential funding from Fusion Capital under that agreement. We entered into an At the Market Sales Agreement (ATM) on June 16, 2011, which allows us to raise approximately $20,000,000 through sales of our common stock from time to time. However, there are certain factors, such as

volume of trading in our stock and the stock price, which limit the amount that can be raised in a short period of time through the ATM. Regardless of the usage of the ATM, we need to raise additional capital in order to fund the phase 3 clinical trial of ixmyelocel-T for CLI, complete our product development programs, complete clinical trials needed to market our products and commercialize these products. We believe that with our existing cash and cash equivalents and the net proceeds of $37,800,000 from the financing that closed in March 2012, we have adequate liquidity to finance our operations, including development of our products and product candidates, through at least December 31, 2012. While our budgeted cash usage and operating plan through December 31, 2012 does not currently contemplate taking additional actions to reduce the use of cash over that period, we could, if necessary, delay or forego certain budgeted discretionary expenditures such as anticipated hiring plans or certain non-critical research and development expenditures, as well as slow down or delay certain clinical trial activity such that we believe that we will have sufficient cash on hand through at least December 31, 2012.

Notwithstanding the proceeds we received from our March 2012 financing, we will need to raise additional funds in order to complete our product development programs, complete clinical trials needed to market our products (including clinical trials for our CLI and DCM programs), and commercialize these products. Because of our long-term funding requirements, we may try 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. In addition, we may seek collaborative relationships, incur debt and access other available funding sources. This additional funding may not be available to us on reasonable terms, or at all. Some of the factors that will impact our ability to raise additional capital and our overall success include:

- the rate and degree of progress for our product development;
- the rate of regulatory approval to proceed with clinical trial programs;
- the level of success achieved in clinical trials;
- the requirements for marketing authorization from regulatory bodies in the United States and other countries;
- the liquidity and market volatility of our equity securities; and
- regulatory and manufacturing requirements and uncertainties, technological developments by competitors.

If adequate funds are not available in the future, we may not be able to develop or enhance our products, take advantage of future opportunities, or respond to competitive pressures or unanticipated requirements and we may be required to delay or terminate research and development programs, curtail capital expenditures, and reduce business development and other operating activities. Should the financing we require to sustain our working capital needs be unavailable or prohibitively expensive when we

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require it, the consequences could have a material adverse effect on our business, operating results, financial condition and prospects.

Failure to obtain and maintain required regulatory approvals would severely limit our ability to sell our products.

We must obtain the approval of the FDA before commercial sales of our cell product candidates may commence in the United States, which we believe will 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. If we cannot demonstrate the safety, purity and potency of our product candidates, including our cell product candidates, produced in our production system, 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.

Our product development programs are based on novel technologies and are inherently risky.

We are subject to the risks of failure inherent in the development of products based on new technologies. The novel nature of our therapeutics creates significant challenges in regard to product development and optimization, manufacturing, government regulation, third party reimbursement and market acceptance. For example, if regulatory agencies have limited experience in approving cellular therapies for commercialization, the development and commercialization pathway for our therapies may be subject to increased uncertainty, as compared to the pathway for new conventional drugs.

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 products is, under current regulations, regulated as a biologic, which requires a BLA.

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

In order to commercialize our cell product candidates in the United States, we must complete substantial clinical trials and obtain sufficient safety, purity and potency 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 results. 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 any issues delaying commercialization and we may not be able to raise capital to finance our continued operation during the period required for resolution of any such issues.

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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 United States, 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. The results of early stage clinical trials do not ensure success in later clinical trials, and interim results are not necessarily predictive of final results.

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. For example, patients enrolling in our studies need to provide an adequate amount of bone marrow to process and expand for injection and some patients may not be able to provide sufficient starting material despite our study inclusion and exclusion criteria designed to prevent this. Bone marrow is an inherently variable starting material. We have experienced delays in patient accrual in our previous clinical trials. If we experience future delays in patient enrollment, 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 product functionality for certain clinical indications, improving product shelf life, and decreasing the cost of manufacturing our 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 will be sufficient for a marketable or regulatory approvable product.

We will rely on third parties to conduct some of our clinical trials, and their failure to perform their obligations in a timely or competent manner may delay development and commercialization of our product candidates.

We have engaged and we may use clinical research organizations to assist in conduct of our clinical trials. There are numerous alternative sources to provide these services. However, we may face delays outside of our control if these parties do not perform their obligations in a timely or competent fashion or if we are forced to change service providers. Any third party that we hire to conduct clinical trials may also provide services to our competitors, which could compromise the performance of their obligations to us. If we experience significant delays in the progress of our clinical trials, the commercial prospects for product candidates could be harmed and our ability to generate product revenue would be delayed or prevented. In addition, we and any provider that we retain will be subject to Good Clinical Practice, or GCP requirements. If GCP and other regulatory requirements are not adhered to by us or our third-party providers, the development and commercialization of our product candidates could be delayed.

Any failure of such CRO to successfully accomplish clinical trial monitoring, data collection, safety monitoring and data management and the other services it provides for us in a timely manner and in compliance with regulatory requirements could have a material adverse effect on our ability to complete clinical development of our products and obtain regulatory approval. Problems with the timeliness or quality of the work of a CRO may lead us to seek to terminate the relationship and use an alternate service provider. However, making such changes may be costly and may delay our trials, and contractual restrictions may make such a change difficult or impossible. Additionally, it may be difficult to find a replacement organization that can conduct our trials in an acceptable manner and at an acceptable cost.

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Failure of third parties, including Vention Medical (formerly ATEK Medical, LLC), to manufacture or supply certain components, equipment, disposable devices and other materials used in our cell manufacturing process would impair our cell product development.

We rely on third parties, including Vention Medical (Vention), to manufacture and/or supply certain of our devices/manufacturing equipment and to manufacture and/or supply certain components, equipment, disposable devices and other materials used in our cell manufacturing process to develop our cell products. Vention is our sole supplier of cell cassettes for which it would be difficult to obtain alternate sources of supply on a short-term basis. If any of our manufacturers or suppliers fails to perform their respective obligations, or if our supply of certain components, equipment, disposable devices and other materials is limited or interrupted, it could impair our ability to manufacture our products, which would delay our ability to conduct our clinical trials or market our product candidates on a timely and cost-competitive basis, if at all.

In addition, 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 of 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 are subject to regulatory compliance and quality assurance requirements at our production site in Ann Arbor, Michigan. This site could be subject to ongoing, periodic, unannounced inspection by regulatory agencies to ensure strict compliance with GMP regulations and other governmental regulations. We do not have redundant cell manufacturing sites. In the event our cell production facility is damaged or destroyed or is 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 cell products for tissue repair treatments. Even if we obtain all required regulatory approvals, we cannot be certain that our products and processes will be accepted in the marketplace 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 payers will pay for our products and related treatments.

Reimbursement by third party payers depends on a number of factors, including the payer's determination that use of the product is safe and effective, not experimental or investigational, medically necessary, appropriate for the specific patient and cost-effective. Reimbursement in the United States or foreign countries may not be available or maintained for any of our product candidates. If we do not obtain approvals for adequate third party reimbursements, we may not be able to establish or maintain price levels sufficient to realize an appropriate return on our investment in product development. Any limits on reimbursement from

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third party payers 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 payers has negatively affected the marketability of our products in this indication in the past.

Managing and reducing health care costs has been a general concern of federal and state governments in the United States and of foreign governments. In addition, third party payers are increasingly challenging the price and cost-effectiveness of medical products and services, and many limit reimbursement for newly approved health care products. In particular, third party payers may limit the indications for which they will reimburse patients who use any products that we may develop. Cost control initiatives could decrease the price for products that we may develop, which would result in lower product revenues to us.

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 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 our product manufacturing processes. Any restrictions on these materials would impose a potential competitive disadvantage for our products or prevent our ability to manufacture our cell products. 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. 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. We may need to make such expenditures when there are significant uncertainties as to the market opportunity. 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 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 will 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

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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 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.

The current credit and financial market conditions may exacerbate certain risks affecting our business.

We rely upon third parties for certain aspects of our business, including collaboration partners, wholesale distributors, contract clinical trial providers, contract manufacturers and third-party suppliers. Because of the recent tightening of global credit and the volatility in the financial markets, there may be a delay or disruption in the performance or satisfaction of commitments to us by these third parties, which could adversely affect our business.

If we cannot attract and retain key personnel, our business may 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 three previous occasions, most recently in fiscal 2008. As a result of these and other factors, we may not be successful in hiring or retaining key personnel. Our inability to replace any key employee could harm our operations.

Risks Related to Intellectual Property

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 intellectual property rights to protect our proprietary products and technologies. This involves complex legal, scientific, and factual questions and uncertainties. We rely upon patent, trade secret, copyright and contract laws to protect proprietary technology and trademark law to protect brand identities. However, we cannot assure you that any patent applications filed by, assigned to, or licensed to us will be granted, and that the scope of any of our issued or licensed patents will be sufficiently broad to offer meaningful protection. In addition, our issued patents or patents licensed to us could be successfully challenged, invalidated, held to be unenforceable, or circumvented so that our patent rights would not create an effective competitive barrier. We also cannot assure you that the inventors of the patents and applications that we own or license were the first to invent or the first to file on the inventions, or that a third party will not claim ownership in one of our patents or patent applications. We cannot assure you that a third party does not have or will not obtain patents that dominate the patents we own or license now or in the future. Furthermore, we rely on exclusive, world-wide licenses relating to the production of human cells granted to us by the University of Michigan. 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. Once the patents expire, third parties may be able to practice the inventions covered by those patents and thus compete with us.

Patent law relating to the scope of claims in the biotechnology field is evolving and our patent rights in this country and abroad are subject to this uncertainty.

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We also rely on trade secrets and un-patentable 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. Our competitors may also independently develop technologies substantially equivalent or superior to ours. 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. Our cell processing system and cell compositions utilize a wide variety of technologies and we can give no assurance that we have identified or can identify all inventions and patents that may be infringed by development and manufacture of our cell compositions. Although we have not been subject to any filed infringement claims, 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. Such litigation is typically protracted and the results are unpredictable. 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 including treble damages and the opposing party's attorney fees, and force us to pay significant license fees and royalties or cease the development and sale of our products and processes.

We have hired and will continue to hire individuals who have experience in cell culture and cell based therapeutics and may have confidential trade secret or proprietary information of third parties. We caution these individuals not to use or reveal this third-party information, but we cannot assure you that these individuals will not use or reveal this third-party information. Thus, we could be sued for misappropriation of proprietary information and trade secrets. Such claims are expensive to defend and could divert our attention and could result in substantial damage awards and injunctions that could have a material adverse effect on our business, financial condition or results of operations.

We may need to initiate lawsuits to protect or enforce our patents or other proprietary rights, which would be expensive and, if unsuccessful, may cause us to lose some of our intellectual property rights.

To protect or enforce our patent rights, it may be necessary for us to initiate patent litigation proceedings against third parties, such as infringement suits or interference proceedings. These lawsuits would be expensive, take significant time and would divert management's attention from other business concerns. These lawsuits could put our patents at risk of being invalidated, held unenforceable, or interpreted narrowly, and our patent applications at risk of not being issued. Further, these lawsuits may provoke the defendants to assert claims against us. The patent position of biotechnology firms is highly uncertain, involves complex legal and factual questions and recently has been the subject of much litigation. We cannot assure you that we will prevail in any of such suits or proceedings or that the damages or other remedies awarded to us, if any, will be commercially valuable.

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 has certain rights in the technology developed with the grant. These rights include a non-exclusive, fully paid-up, worldwide license under such inventions for any governmental purpose. In addition, the U.S. Government has the right to require us to grant an exclusive license under any of such inventions to a third party if the U.S. Government determines that: (i) adequate steps have not been taken to commercialize such inventions; (ii) such action is necessary to meet public health or safety needs; or (iii) such action is necessary to meet requirements for public use under federal regulations. Additionally, under the federal Bayh Dole Act, a party which acquires an exclusive license for an invention that was partially funded by a federal research grant is subject to the following government rights: (i) products using the invention which are sold in the

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United States are to be manufactured substantially in the United States, unless a waiver is obtained; (ii) the government may force the granting of a license to a third party who will make and sell the needed product if the licensee does not pursue reasonable commercialization of a needed product using the invention; and (iii) the U.S. Government may use the invention for its own needs. If we fail to meet these guidelines, we would lose our exclusive rights to these products, and we would lose potential revenue derived from the sale of these products.

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 our 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 adversely affect our financial condition.

Risks Related to an Investment in our Common Stock

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

The market price of shares of our common stock has been volatile, ranging in closing price between $1.79 and $3.27 during the period ended December 31, 2011. 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;
- regulatory developments in both the United States and abroad;
- 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 regenerative medicine companies;
- reports by securities analysts;
- status of the investment markets;
- concerns related to management transitions; and
- delisting from the NASDAQ Capital Market.

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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 recently 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.

The sale of our common stock through future equity offerings may cause dilution and could cause the price of our common stock to decline.

We have registered $100,000,000 of securities for public sale pursuant to our registration statement on Form S-3 declared effective in July 2011. In addition, we registered $75,000,000 of securities for public sale pursuant to our registration statement on Form S-3 filed in November 2010. In December 2010, we offered 10,000,000 shares of common stock and warrants to purchase up to 10,000,000 shares of common stock under such registration statement and pursuant to a prospectus supplement first made available on December 10, 2010. Additionally, we entered into an At the Market Sales Agreement (ATM) on June 16, 2011, which allows us to raise approximately $20,000,000 through sales of our common stock from time to time under such registration statement. However, there are certain factors, such as volume of trading in our stock and the stock price, which limit the amount that can be raised in a short period of time through the ATM.

Sales of our common stock offered through future equity offerings may result in substantial dilution to the interests of other holders of our common stock. The sale of a substantial number of shares of our common stock to investors, or anticipation of such sales, could make it more difficult for us to sell equity or equity-related securities in the future at a time and at a price that we might otherwise wish to effect sales.

Eastern Capital Limited, the investor in Aastrom's March 2012 financing, holds a large percentage of our outstanding capital stock and, should they choose to, or should we elect to, convert their capital stock into shares of voting stock, will have significant influence over the outcome of corporate actions requiring shareholder approval; and such shareholder's priorities for our business may be different from other shareholders.

All of our outstanding Series B-1 non-voting preferred stock, representing a significant amount of our outstanding capital stock on a fully-converted basis, is held by Eastern Capital Limited, the investor in our March 2012 financing. These shares are exchangeable for shares of Series B-2 voting preferred stock and, in March 2017, are convertible into shares of our common stock. If we or Eastern Capital elect to exchange or convert its shares of Series B-1 Preferred Stock into a series of our voting shares, based solely on the number of shares of Series B-1 Preferred Stock that Eastern Capital purchased at the closing of the transaction, Eastern Capital will have beneficial ownership of up to approximately twenty-four percent (24%) (calculated on an as converted to common stock basis and excluding any shares that will accrue as a dividend on the shares of Series B-1 Preferred) of our voting securities based on the approximately fifty-one million shares of common stock and Series B-1 Preferred Stock outstanding as of the date of this report. Furthermore, in connection with the March 2012 financing, we amended our Shareholder Rights Plan to allow Eastern Capital to acquire beneficial ownership of up to 49.9% of the Company's outstanding securities without being deemed an "Acquiring Person" for purposes of our Shareholder Rights Plan. As a result of their current ownership and their ability to acquire more of our securities, they will be able to significantly influence the outcome of any financing transaction or other matter submitted to our shareholders for approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets or any other significant corporate transaction. The interests of Eastern Capital may differ from the interests of our other shareholders. For example, Eastern Capital could delay or prevent a change of control of Aastrom even if such a change of control would benefit Aastrom's other shareholders. The significant concentration of stock ownership may adversely affect the trading price of Aastrom's common stock due to our investors' perception that conflicts of interest may exist or arise.

In addition, the shares of Series B-1 Preferred Stock and the shares of Series B-2 Preferred Stock which may be issued upon exchange of the shares of Series B-1 Preferred Stock have certain rights, preferences and privileges that rank senior to the shares of

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our common stock. For example, the shares of Series B-1 Preferred Stock and Series B-2 Preferred Stock are entitled to receive a liquidation preference prior to any payment being made to holders of common stock upon a voluntary or involuntary liquidation, dissolution or winding up of the Company, or we experience a change of control. Furthermore, if the shares of Series B-1 Preferred Stock are never exchanged for shares of Series B-2 Preferred Stock and/or converted into shares of our common stock, at any time after March 2017, we may be required to redeem the then outstanding shares of Series B-1 Preferred Stock and any dividend shares accrued thereon at a price equal to the greater of (A) $3,250 (subject to adjustments for stock splits and similar events) plus all accrued dividends and (B) the then fair market value of a share of common stock multiplied by the number of shares of common stock into which such share of Series B-1 Preferred Stock is then convertible. Such redemption would be completed in three annual installments beginning not more than 120 days after we receive a request for redemption. The requirement for us to redeem Eastern Capital's shares of Series B-1 Preferred Stock in cash could diminish our working capital, the consequences of which could have a material adverse effect on our business, operating results, financial condition and prospects.

Provisions in our corporate documents, Michigan law and our shareholder rights plan 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. Michigan law contains a provision that makes it more difficult for a 10% shareholder, or its officers, to acquire a company. This authority, together with certain provisions of our charter documents, may have the effect of making it more difficult for a third party to acquire, or of discouraging a third party from attempting to acquire, control of our company. This effect could occur even if our shareholders consider the change in control to be in their best interest. We have adopted a shareholder rights plan, the purpose of which is, among other things, to enhance our Board's ability to protect shareholder interests and to ensure that shareholders receive fair treatment in the event any coercive takeover attempt of our company is made in the future. The shareholder rights plan could make it more difficult for a third party to acquire, or could discourage a third party from acquiring, our company or a large block of our company's common stock.

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CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This 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,” “believe,” “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 report, and in particular those factors referenced in the section “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. These forward-looking statements include, but are not limited to, 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 plan;
- features and successes of our cellular therapies;
- manufacturing and facility capabilities;
- clinical trial plans and anticipated results, including the publication thereof;
- anticipation of future losses;
- replacement of manufacturing sources;
- commercialization plans; or
- revenue expectations and operating results.

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HOW WE INTEND TO USE THE PROCEEDS

The estimated net proceeds we will receive from this offering will be approximately $11,405,464.56 if all of the Class A warrants are exercised.

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, including continuing to conduct our clinical development programs, 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 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 financings, as well as collaborative relationships, incurring debt and other available sources. Please see the discussion of the risks associated with our liquidity in the section “Risk Factors.”

PLAN OF DISTRIBUTION

We are offering up to 4,525,978 shares of our common stock issuable upon the exercise of outstanding Class A warrants to purchase 4,525,978 shares of common stock. We are not offering any new warrants or any other shares pursuant to the registration statement of which this prospectus is a part.

Exercise of Class A Warrants. The Class A warrants were issued on January 21, 2010 and are exercisable at any time up through July 21, 2015. If an effective registration statement is available for the issuance of the shares of common stock issuable upon exercise of the Class A warrants, the Class A warrants are exercisable at the option of each holder by delivering to us a duly executed exercise notice accompanied by payment in cash for the number of common stock purchased upon such exercise.

In the event that a registration statement covering shares of common stock underlying the Class A warrants, or an exemption from registration is not available for the issuance or resale of such shares of common stock underlying the Class A warrants, the holder may, in its sole discretion, exercise the Class A warrant and, in lieu of making the cash payment otherwise contemplated to be made to us upon such exercise in payment of the aggregate exercise price, elect instead to receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the Class A warrant.

Prior Offer and Sale of the Class A Warrants. The Class A warrants were offered and sold pursuant to the Registration Statement on Form S-3, File No. 333-155739, as supplemented by a prospectus supplement filed January 15, 2010.

In connection with such offering, we agreed to indemnify the underwriter and its affiliates against certain liabilities, including liabilities under the Securities Act of 1933, as amended, and liabilities arising from breaches of representations and warranties contained in the underwriter agreement. We have also agreed to contribute to payments the underwriter and its affiliates may be required to make in respect of such liabilities.

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CERTAIN PROVISIONS OF MICHIGAN LAW AND OF OUR CHARTER AND BYLAWS; SHAREHOLDER RIGHTS PLAN; TRANSFER AGENT AND REGISTRAR

We are subject to certain anti-takeover provisions of the MBCA that 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 that could have anti-takeover effects.

Our Charter does not provide shareholders with the right to act without a meeting and does 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 a majority of the shares of our outstanding common stock.

These and other provisions of our Charter or Bylaws 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.

Shareholder Rights Plan

On August 11, 2011, Aastrom's Board of Directors adopted a Shareholder Rights Plan, as set forth in the Shareholder Rights Agreement between Aastrom and the rights agent, the purpose of which is, among other things, to enhance the Board's ability to protect shareholder interests and to ensure that shareholders receive fair treatment in the event any coercive takeover attempt of Aastrom is made in the future. The Shareholder Rights Plan could make it more difficult for a third party to acquire, or could discourage a third party from acquiring, Aastrom or a large block of our common stock. The following summary description of the Shareholder Rights Plan should be read in conjunction with the Shareholder Rights Plan, which was filed with the Securities and Exchange Commission as an exhibit to a Registration Statement on Form 8-A on August 12, 2011.

In connection with the adoption of the Shareholder Rights Plan, the Board of Directors declared a dividend distribution of one preferred stock purchase right (a "Right") for each outstanding share of common stock to shareholders of record as of the close of business on August 15, 2011. In addition, one Right will automatically attach to each share of common stock issued between August 15, 2011 and the distribution date. The Rights currently are not exercisable and are attached to and trade with the outstanding shares of common stock. Under the Shareholder Rights Plan, the Rights become exercisable if a person or group becomes an "acquiring person" by acquiring 15% or more of the outstanding shares of common stock or if a person or group commences a tender offer that would result in that person owning 15% or more of the common stock. If a person or group becomes an "acquiring person," each holder of a Right (other than the acquiring person and its affiliates, associates and transferees) would be entitled to purchase, at the then-current exercise price, such number of shares of our preferred stock which are equivalent to shares of common stock having a value of twice the exercise price of the Right. If Aastrom is acquired in a merger or other business combination transaction after any such event, each holder of a Right would then be entitled to purchase, at the then-current exercise price, shares of the acquiring company's common stock having a value of twice the exercise price of the Right.

The Rights may be redeemed in whole, but not in part, at a price of $0.001 per Right (payable in cash, common stock or other consideration deemed appropriate by the Board of Directors) by the Board of Directors only until the earlier of (i) the time at which any person becomes an "acquiring person" or (ii) the expiration date of the Rights Agreement. Immediately upon the action of the Board of Directors ordering redemption of the Rights, the Right will terminate and thereafter the only right of the holders of Rights will be to receive the redemption price. The Rights will expire at the close of business on August 15, 2021, unless previously redeemed or exchanged by Aastrom as described above.

Transfer Agent and Registrar

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

THE SECURITIES WE MAY OFFER

We are offering a maximum of 4,525,978 shares of common stock upon the exercise of outstanding Class A warrants to purchase shares of our common stock. The following briefly summarizes the general terms and provisions of our shares of common stock, and the Class A warrants pursuant to which such shares of common stock may be issued. You should read the provisions of our articles of incorporation, as amended, bylaws and other relevant instruments and agreements relating to our securities before you make an investment decision with respect to our shares of common stock.

Description of Capital Stock

The following description of our common stock and certain provisions of our Charter and our amended and restated bylaws, or Bylaws, is a summary and is qualified in its entirety by the provisions of our Charter and Bylaws.

Our authorized capital stock consists of 150,000,000 shares of common stock, no par value per share, and 5,000,000 shares of preferred stock, no par value per share. Please see "Certain Provisions of Michigan Law and of Our Charter and Bylaws; Shareholder Rights Plan; Transfer Agent and Registrar" for a description of those provisions in our Charter and Bylaws that would have an effect of delaying, deferring or preventing a change in control of Aastrom and that would operate only with respect to an extraordinary corporate transaction involving us or our subsidiaries.

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. We do not have a classified board of directors and shareholders 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,

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dissolution or winding up, holders of common stock are entitled to share ratably in assets available for distribution, subject to any prior distribution rights of any preferred stock then outstanding. Holders of common stock are entitled to receive proportionately any such dividends declared by our Board, 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 Charter, which may be amended by the holders of a majority of the outstanding shares of common stock. We have adopted a shareholder rights plan, which could make it more difficult for a third party to acquire, or could discourage a third party from acquiring, our company or a large block of our common stock. Please see the description above in "Certain Provisions of Michigan Law and of our Charter and Bylaws; Shareholder Rights Plan; Transfer Agent and Registrar."

Description of Outstanding Class A Warrants Pursuant to which the Offered Shares of Common Stock may be Issued

The following description summarizes the material terms and provisions of the Class A warrants. Each Class A warrant has an exercise price of $2.52 per share (as adjusted from $2.97 per share for the anti-dilution provision triggered in our December 2010 financing), subject to adjustment as summarized below, and is exercisable at any time beginning six months after issuance until 5:30 p.m. (New York time) on the date that is five years from the date of exercisability, which is July 21, 2015. Each Class A warrant is exercisable for 0.75 shares of common stock.

Each Class A warrant provides that the share ratio and exercise price of the Class A warrants is subject to adjustment in the event of a subdivision or consolidation of our common stock. Each Class A warrant also provides that if there is: (i) any reclassification or

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change of our common stock into other shares; (ii) any consolidation, amalgamation, arrangement or other business combination resulting in any reclassification or change of our common stock into other shares; or (iii) any sale, lease, exchange or transfer of our assets in their entirety or substantially in their entirety to another entity, then each holder of a Class A warrant which is thereafter exercised shall receive, in lieu of common stock, the kind and number or amount of other securities or property which such holder would have been entitled to receive as a result of such event if such holder had exercised such Class A warrants prior to the event.

Subject to certain exceptions, if we sell or issues shares of common stock, rights, options or warrants to purchase shares of common stock, other rights for shares of the common stock, or securities convertible or exchangeable into shares of common stock, in any case at a price per share less than the Class A warrant exercise price, then the Class A warrant exercise price will be reduced to the price determined by multiplying the exercise price in effect immediately prior to such issuance by a fraction, (A) the numerator of which will be the number of shares of common stock outstanding immediately prior to such issuance plus the number of shares which the aggregate consideration received for such issuance would purchase at the exercise price in effect immediately prior to such issuance, and (B) the denominator of which will be the number of shares of common stock outstanding immediately after such issuance.

We also covenanted in each Class A warrant that, during the period in which the Class A warrants are exercisable, it will give public notice of its intention to fix a record date for the issuance of rights, options or warrants (other than the warrants) to all or substantially all of the holders of our common stock at least 10 days prior to the record date of such event.

LEGAL MATTERS

Certain legal matters, including the legality of the securities offered, will be passed upon for us by Dykema Gossett PLLC, Ann Arbor, Michigan, acting as special counsel to the Company.

EXPERTS

The consolidated 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 December 31, 2011 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 are subject to the information requirements of the Exchange Act and, in accordance therewith, 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 Room at 100 F Street, N.E., Washington, D.C. 20549. You may call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room. These documents also may be accessed through the SEC's electronic data gathering, analysis and retrieval system, or EDGAR, via electronic means, including the SEC's home page on the Internet (www.sec.gov).

We have the authority to designate and issue more than one class or series of stock having various preferences, conversion and other rights, voting powers, restrictions, limitations as to dividends, qualifications, and terms and conditions of redemption. See “Description of Capital Stock.” We will furnish a full statement of the relative rights and preferences of each class or series of our stock which has been so designated and any restrictions on the ownership or transfer of our stock to any shareholder upon request and without charge. Written requests for such copies should be directed to Aastrom Biosciences, Inc., 24 Frank Lloyd Wright Drive, P.O. Box 376, Ann Arbor, Michigan 48106, attention: Investor Relations or by telephone request to (734) 418-4400. Our website is

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located at http://www.aastrom.com. Information contained on our website is not incorporated by reference into this prospectus and, therefore, is not part of this prospectus or any accompanying prospectus supplement.

INCORPORATION BY REFERENCE

This prospectus incorporates by reference important business and financial information that we file with the SEC and that we are not including in or delivering with this prospectus. As the SEC allows, incorporated documents are considered part of this prospectus, and we can disclose important information to you by referring you to those documents.

- our annual report on Form 10-K for the period ended December 31, 2011, filed with the SEC on March 15, 2012;
- portions of our definitive Proxy Statement for the Annual Meeting of Shareholders that have been incorporated by reference into the Form 10-K;
- our current reports on Form 8-K filed with the SEC on March 9, 2012; and
- the description of our common stock contained in our registration statement on Form S-1, which was filed with the SEC on November 1, 1996, including any amendment or report filed for the purpose of updating such description.

All documents we file with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, except as to any portion of any report or document that is not deemed filed under such provisions, (i) on or after the date of filing of the registration statement containing this prospectus and prior to the effectiveness of the registration statement and (ii) on or after the date of this prospectus until the earlier of the date on which all of the securities registered hereunder have been sold or the registration statement of which this prospectus is a part has been withdrawn, shall be deemed incorporated by reference in this prospectus and to be a part of this prospectus from the date of filing of those documents.

You may request a copy of any or all of these filings, at no cost, by writing to us at: Aastrom Biosciences, Inc., 24 Frank Lloyd Wright Drive, P.O. Box 276, Ann Arbor, Michigan 48106, attention: Investor Relations or by telephoning us at (734) 418-4400. These filings may also be obtained through our website located at http://www.aastrom.com.

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

We advise that there have been no material changes in our affairs that have occurred since the end of the latest fiscal period for which audited financial statements were included in the latest Form 10-K or 10-KT and that have not been described in a Form 10-Q or Form 8-K filed under the Exchange Act.

DISCLOSURE OF COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITIES

As permitted by the MBCA, our Bylaws contain provisions that permit us to indemnify our directors and officers to the full extent permitted by Michigan law and our Charter contains provisions that eliminate the personal liability of our directors in each case for monetary damages to us or our shareholders for breach of their fiduciary duties, except to the extent that Michigan law prohibits indemnification or elimination of liability. These provisions do not limit or eliminate our rights or the rights of any shareholder to seek an injunction or any other non-monetary relief in the event of a breach of a director’s or officer’s fiduciary duty. In addition, these provisions apply only to claims against a director or officer arising out of his or her role as a director or officer and do not

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relieve a director or officer from liability if he or she engaged in willful misconduct or a knowing violation of the criminal law or any federal or state securities law.

The rights of indemnification provided in our Bylaws are not exclusive of any other rights that may be available under any insurance or other agreement, by vote of shareholders or disinterested directors or otherwise.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling us pursuant to the foregoing provisions, we have been informed that in the opinion of the SEC this type of indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

GLOSSARY

TERM	DEFINITION
Adverse Event	Any adverse change in health or “side-effect” that occurs in a person participating in a clinical trial, from the time they consent to joining the trial until a pre-specified period of time after their treatment has been completed.
Autologous (Patient Specific)	Originating from the patient receiving treatment. (Aastrom uses only autologous cells)
BLA — Biologics License Application	An application containing product safety, efficacy and manufacturing information required by the FDA to market biologics products in the U.S.
CLI — Critical Limb Ischemia	A vascular disease characterized by insufficient blood flow in the lower extremities that causes severe pain, tissue loss or both.
CMC — Chemistry, Manufacturing, and Control	The composition, manufacture, and control of the drug substance and the drug product. It is information on the identification, quality, purity, and strength of the investigational product.
Controlled Clinical Trial	A clinical study that compares patients receiving a specific treatment to patients receiving an alternate treatment for the condition of interest. The alternate treatment may be another active treatment, standard of care for the condition and/or a placebo (inactive) treatment.
DCM — Dilated Cardiomyopathy	A chronic cardiac disease where expansion of the patient’s heart reduces the pumping function to a point that the normal circulation of blood cannot be maintained.
Double-Blind Clinical Trial	Clinical trials in which neither the patient nor the physician know if the patient received the experimental treatment or a control/placebo.
Ex vivo	Outside the body.
FDA — Food & Drug Administration	The U.S. FDA ensures that medicines, medical devices, and radiation-emitting consumer products are safe and effective. Authorized by Congress to enforce the Federal Food, Drug, and Cosmetic Act and several other public health laws, the agency monitors the manufacture, import, transport, storage, and sale of $1 trillion worth of goods annually.
GMP — Good Manufacturing Practice	GMP regulations require that manufacturers, processors, and packagers of drugs, medical devices, some food, and blood take proactive steps to ensure that their products are safe, pure, and effective. GMP regulations require a quality approach to manufacturing, enabling companies to minimize or eliminate instances of contamination, mix-ups, and errors.
Hematopoietic Stem Cells	Stem cells that give rise to all the blood cell types including myeloid (monocytes and macrophages, neutrophils, basophils, eosinophils, erythrocytes, megakaryocytes/platelets, dendritic cells), and lymphoid lineages (T-cells, B-cells, NK-

	cells).
IMPACT-DCM	Aastrom’s U.S. Phase 2 clinical trial investigating surgical delivery of our product in the treatment of dilated cardiomyopathy.
IND — Investigational New Drug	An application submitted to the FDA for a new drug or biologic that, if allowed, will be used in a clinical trial.
Ischemia	A shortage or inadequate flow of blood to a body part (commonly an organ or tissue) caused by a constriction or obstruction of the blood vessels supplying it.
LVEF — Left Ventricular Ejection Fraction	The fraction of blood pumped out of the left ventricle with each heart beat.
Open-label Clinical Trial	A trial in which both the treating physician and the patient know whether they are receiving the experimental treatment or control/placebo treatment.
Orphan Drug Designation	“Orphan drug” refers to a drug or biologic that is intended for use in the treatment of a rare disease or condition. Orphan drug designation from the U.S. Food and Drug Association (FDA) qualifies the sponsor to receive certain benefits from the Government in exchange for developing the drug for a rare disease or condition. The drug must then go through the FDA marketing approval process like any other drug or biologic which evaluates for safety and efficacy. Usually a sponsor receives a quicker review time and lower application fees for an orphan product.
Phase 1 Clinical Trial	A Phase 1 trial represents an initial study in a small group of patients to test for safety and other

	relevant factors.
Phase 2 Clinical Trial	A Phase 2 trial represents a study in a moderate number of patients to assess the safety and efficacy of a product.
Phase 2b Clinical Trial	A Phase 2b trial is a moderately-sized Phase 2 trial that is more specifically designed assess the efficacy of a product than a Phase 2a trial.
Phase 3 Clinical Trial	Phase 3 studies are initiated to establish safety and efficacy in an expanded patient population at multiple clinical trial sites and are generally larger than trials in earlier phases of development.
Progenitor Cells	A “parent” cell that gives rise to a distinct cell lineage by a series of cell divisions.
Prospective Clinical Trial	A clinical trial in which participants are identified and then followed throughout the study going forward in time.
Randomized Clinical Trial	A clinical trial in which the participants are assigned randomly to different treatment groups.
Somatic Cell	Any of the cells responsible for forming the body of an organism such as internal organs, bones, skin, connective tissues and blood.
Stem Cell	Unspecialized (undifferentiated) cells that retain the ability to divide throughout a

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	lifetime and give rise to more specialized (differentiated) cells which take the place of cells that die or are lost. In culture, these undifferentiated cells possess the ability to divide for indefinite periods in culture and may give rise to highly specialized cells.

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AASTROM BIOSCIENCES, INC.
4,525,978 Shares of Common Stock

PROSPECTUS
March 19, 2012

We have not authorized any dealer, salesperson or other person to give any information or represent anything not contained in this prospectus. You must not rely on any unauthorized information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus does not offer to sell any shares in any jurisdiction where it is unlawful. Neither the delivery of this prospectus, nor any sale made hereunder, shall create any implication that the information in this prospectus is correct after the date hereof.

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Part II—INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The expenses payable by Aastrom Biosciences, Inc. (the “Registrant” or the “Company”) in connection with the issuance and distribution of the securities being registered (other than underwriting discounts and commissions, if any) are set forth below. Each item listed is estimated, except for the Securities and Exchange Commission (the “SEC”) registration fee.

Securities and Exchange Commission registration fee	$	1,308
Legal fees and expenses		10,000
Accounting fees and expenses		5,000
Printing fees and expenses		3,000
Transfer agent and trustee fees		*
Miscellaneous		*
Total	$	19,308

* Estimated expenses not presently known

Item 15. Indemnification of Directors and Officers

Sections 1561 through 1571 of the Michigan Business Corporation Act (the "MBCA") authorize a corporation to grant or a court to award, indemnity to directors, officers, employees and agents in terms sufficiently broad to permit such indemnification under certain circumstances for liabilities (including reimbursement for expenses incurred) arising under the Securities Act of 1933, as amended (the "Securities Act of 1933").

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

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

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

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

Item 16. Exhibits

A list of exhibits filed with this registration statement on Form S-3 is set forth on the Exhibit Index and is incorporated herein by reference.

Item 17. Undertakings

The undersigned registrant hereby undertakes:

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

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

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

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (a)(l)(i), (a)(l)(ii) and (a)(l)(iii) of this section do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Securities and Exchange Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are

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incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement;

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof;

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

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(l)(i), (vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof; provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date;

(5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;

(ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;

(iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and

(iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser;

(6) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant’s annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan’s annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in

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the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof;

(7) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue;

(8) That, for purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act of 1933 shall be deemed to be part of this registration statement as of the time it was declared effective;

(9) That, for the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof; and

(10) To file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act of 1939 in accordance with the rules and regulations prescribed by the Securities and Exchange Commission under Section 305(b)(2) of the Trust Indenture Act of 1939.

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SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in Ann Arbor, Michigan on March 19, 2012.

AASTROM BIOSCIENCES, INC.

By: /s/ Timothy M. Mayleben
Timothy M. Mayleben

President and Chief Executive Officer

Each person whose signature appears below hereby constitutes and appoints Timothy M. Mayleben and Brian D. Gibson, and each of them singly, his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him and in his name, place and stead, in any and all capacities, to sign any or all amendments (including, without limitation, post-effective amendments) to this Registration Statement and any subsequent registration statement filed by the Registrant pursuant to Rule 462(b) of the Securities Act of 1933, which relates to this Registration Statement, and to file the same, with all exhibits thereto, and all documents in connection herewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his substitutes, may lawfully do or cause to be done by virtue hereof.

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

Signature	Title	Date
/s/ Timothy M. Mayleben Timothy M. Mayleben	President, Chief Executive Officer and Director (Principal Executive Officer)	March 19, 2012
/s/ Brian D. Gibson Brian D. Gibson	Vice President of Finance, Chief Accounting Officer and Treasurer (Principal Financial and Accounting Officer)	March 19, 2012
/s/ Nelson M. Sims Nelson M. Sims	Lead Director	March 19, 2012
/s/ Ronald M. Cresswell, Ph.D. Ronald M. Cresswell, Ph.D.	Director	March 19, 2012
/s/ Alan L. Rubino Alan L. Rubino	Director	March 19, 2012
/s/ Harold C. Urschel, Jr., M.D. Harold C. Urschel, Jr., M.D.	Director	March 19, 2012
/s/ Robert L. Zerbe, M.D. Robert L. Zerbe, M.D.	Director	March 19, 2012

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EXHIBIT INDEX

Exhibit No.	Description
3.1	Restated Articles of Incorporation of Aastrom, filed as Exhibit 4.1 to Aastrom's Current Report on Form 8-K filed on December 17, 2009 and incorporated herein by reference.
3.2	Certificate of Amendment to Restated Articles of Incorporation of Aastrom dated February 9, 2010, filed as Exhibit 3.2 to Aastrom's Post Effective Amendment No. 1 to Form S-1 filed on March 31, 2010 and incorporated herein by reference.
3.3	Certificate of Amendment to Restated Articles of Incorporation of Aastrom dated March 22, 2011, filed as Exhibit 3.1 to Aastrom's Current Report on Form 8-K, filed on March 25, 2011 and incorporated herein by reference.
3.4	Amended and Restated Bylaws, filed as Exhibit 3.1 to Aastrom's Current Report on Form 8-K filed on November 12, 2010 and incorporated herein by reference.
3.5	Certificate of Designations, Preferences and Rights, of Aastrom Biosciences, Inc. classifying and designating the Series B Non-Voting Convertible Preferred Stock and the Series B-2 Voting Convertible Preferred Stock, attached as Exhibit 3.1 to the Company's Current Report on Form 8-K filed on March 9, 2012, incorporated herein by reference.
4.1	Specimen Common Stock Certificate, filed as Exhibit 4.1 to Amendment No. 2 to Aastrom's Registration Statement on Form S-1/A filed on December 20, 1996 and incorporated herein by reference.
4.2	Class A Warrant Agreement, dated as of January 21, 2010, by and between Registrant and Continental Stock Transfer & Trust Company

	(incorporated herein by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed with the SEC on January 27, 2010).
4.3	Shareholder Rights Agreement, dated as of August 11, 2011, between Aastrom Biosciences, Inc. and Continental Stock Transfer & Trust Company, as Rights Agent, attached as Exhibit 4.3 to the Company's Current Report on Form 8-A filed on August 12, 2011, incorporated herein by reference.
4.4	Amendment to Shareholder Rights Agreement, dated as of March 9, 2012, between Aastrom Biosciences, Inc. and Continental Stock Transfer & Trust Company, as Rights Agent, attached as Exhibit 4.1 to the Company's Current Report on Form 8-K filed on March 9, 2012, incorporated herein by reference.
5.1	Opinion of Dykema Gossett PLLC.
23.1	Consent of PricewaterhouseCoopers LLP
23.2	Consent of Dykema Gossett PLLC (included in Exhibit 5.1 hereto)
24.1	Power of Attorney (included in Part II of this registration statement)

Dykema Gossett PLLC
Suite 300
39577 Woodward Avenue
Bloomfield Hills, Michigan 48304

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Tel: (248) 203-0700
Fax: (248) 203-0763

March 19, 2012

Aastrom Biosciences, Inc.
Domino's Farm, Lobby K
24 Frank Lloyd Wright Dr.
Ann Arbor, Michigan 48105

Re: Registration Statement on Form S-3

Ladies and Gentlemen:

As special counsel to Aastrom Biosciences, Inc., a Michigan corporation (the "Company"), we are rendering this opinion in connection with the filing with the Securities and Exchange Commission (the "Commission") of the Company's registration statement on Form S-3, (the "Registration Statement"), under the Securities Act of 1933, as amended (the "Act"). The Registration Statement relates to 4,525,978 shares of common stock (the "Warrant Shares") that are issuable upon the exercise of Class A warrants (the "Class A Warrants") previously offered and sold by the Company pursuant to the Class A Warrant Agreement dated January 21, 2010 between the Company and Continental Stock Transfer & Trust Company (the "Class A Warrant Agreement").

In rendering our opinion, we have examined the Registration Statement (including the exhibits thereto), the Class A Warrant Agreement and the form of Class A Warrants, the originals or copies, certified or otherwise identified to our satisfaction, of the Restated Articles of Incorporation and the Bylaws of the Company as amended to date, resolutions of the Company's Board of Directors and such other documents and corporate records relating to the Company and the issuance and sale of the Warrant Shares as we have deemed appropriate.

In our examination, we have assumed the legal capacity of all natural persons, the genuineness of all signatures, the conformity to original documents of all photostatic and facsimile copies submitted to us, and the due execution and delivery of all documents by any party where due execution and delivery are a prerequisite to the effectiveness thereof. As to any facts material to the opinion expressed herein that were not independently established or verified, we have relied upon statements and representations of officers and other representatives of the Company. We have assumed that payment and delivery of the Warrant Shares is made in

accordance with the terms set forth in the Class A Warrant Agreement and the Class A Warrants and that the terms set forth in such agreements are in accordance with the resolutions of the Company's Board of Directors approving the issuance and sale of the Warrant Shares. In addition, we have assumed that the certificates representing the Warrant Shares will be duly executed and delivered.

On the basis of the foregoing, we are of the opinion that the Warrant Shares have been duly authorized and, when and to the extent issued against payment of the exercise price therefore and in accordance with the terms of the Class A Warrants and the Class A Warrant Agreement, will be validly issued, fully paid, and non-assessable.

The opinion expressed herein is based exclusively on the applicable provisions of the Michigan Business Corporation Act as in effect on the date hereof.

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

Very truly yours,

DYKEMA GOSSETT PLLC

/WWK

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of our report dated March 15, 2012 relating to the consolidated financial statements and the effectiveness of internal control over financial reporting, which appears in Aastrom Bioscience, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2011. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/PricewaterhouseCoopers LLP
Detroit, Michigan
March 19, 2012