Table of Contents

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-174945

PROSPECTUS SUPPLEMENT
(To Prospectus dated July 18, 2011)

$6,153,000

Common Stock

On June 16, 2011, we entered into an At Market Issuance Sales Agreement with MLV & Co. LLC ("MLV") (formerly McNicoll Lewis & Vlak), pursuant to which we may offer and sell shares of our common stock, no par value per share, having an aggregate offering price of up to $20,300,000 from time to time through MLV acting as agent. On November 29, 2013, we entered into an amendment to the Sales Agreement ("Amendment No. 1") to offer and sell our common stock under this prospectus supplement and the accompanying prospectus.

Our common stock is listed on The NASDAQ Capital Market under the symbol "ASTM" The last reported sale price of our common stock on November 26, 2013 was $3.21 per share.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus may be made in sales deemed to be "at the market" equity offerings as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, including sales made directly on or through The NASDAQ Capital Market, the existing trading market for our common stock, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices, and/or in any other method permitted by law. MLV will act as sales agent on a best efforts basis using commercially reasonable efforts consistent with its normal trading and sales practices. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The compensation payable to MLV for sales of common stock sold pursuant to the sales agreement will be an amount up to 3% of the gross proceeds of any shares of common stock sold. In connection with the sale of the common stock on our behalf, MLV may be deemed to be an "underwriter" within the meaning of the Securities Act of 1933, as amended, and the compensation of MLV may be deemed to be underwriting commissions or discounts.

As of October 2, 2013, the aggregate market value of our outstanding common stock held by non-affiliates was approximately $12,988,000, based on 4,474,661 outstanding shares of common stock, of which approximately 4,046,093 shares were held by non-affiliates, and a price of $5.80 per share on October 2, 2013. The aggregate market value of securities sold by or on our behalf pursuant to General Instruction I.B.6 of Form S-3 during the 12 calendar months prior to, and including, the date of this prospectus supplement is $1,668,882, which is not greater than one-third of the aggregate market value of our common stock held by our non-affiliates.

Before buying shares of our common stock, you should carefully consider the risk factors described in "Risk Factors" beginning on page S-10 of this prospectus supplement.

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

The date of this prospectus supplement is November 29, 2013.

Table of Contents

TABLE OF CONTENTS

PROSPECTUS SUPPLEMENT

ABOUT THIS PROSPECTUS SUPPLEMENT

Unless expressly stated otherwise, all references in this prospectus supplement and the accompanying prospectus to "the Company," "Aastrom" "we," "us," "our," or similar references mean Aastrom Biosciences, Inc. and its subsidiaries on a consolidated basis.

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of our common stock and supplements information contained in the accompanying prospectus and the documents incorporated by reference into the accompanying prospectus. The second part is the accompanying prospectus, which gives more general information about us and the shares of common stock we may offer from time to time under our shelf registration statement. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or any document incorporated by reference therein, on the other hand, the information in this prospectus supplement shall control.

You should read this document together with additional information described under the headings "Where You Can Find More Information" and "Incorporation of Certain Information by Reference" in this prospectus supplement. We have not authorized any dealer, salesperson or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and any related free writing prospectus. You should not rely upon any information or representation not contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any free writing prospectus that we may authorize to be provided to you. This prospectus supplement, the accompanying prospectus and any related free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy common stock, nor does this prospectus supplement, the accompanying prospectus and any related free writing prospectus constitute an offer to sell or the solicitation of an offer to buy common stock in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus supplement, the accompanying prospectus and any related free writing prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus supplement, the accompanying prospectus and any related free writing prospectus is delivered or common stock is sold on a later date.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference into the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents that we incorporate by reference, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (Securities Act) and Section 21E of the Securities Exchange Act of 1934, as amended (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 plans;
- 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; and
- revenue expectations and operating results.

Table of Contents

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights information contained elsewhere in, or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all of the information that you should consider in making your investment decision. You should read the entire prospectus supplement and the accompanying prospectus carefully, especially the discussion regarding the risks of investing in our securities under the heading "Risk Factors" beginning on page S-10 of this prospectus supplement and our financial statements and related notes incorporated by reference in this prospectus supplement, before investing in our securities. This prospectus supplement may add to, update or change information in the accompanying prospectus. Please refer to our Glossary at the end of this Prospectus for certain industry-specific and technical definitions.

Overview

We are a clinical-stage biotechnology company focused on developing innovative cell therapies that repair and regenerate damaged tissue for use in the treatment of severe, chronic ischemic cardiovascular diseases. We are developing patient-specific (autologous) multicellular therapies utilizing our proprietary, highly automated and scalable manufacturing system. Our manufacturing technology platform, the Aastrom Replicell System (ARS), enables the expansion of a variety of cell types, including the production of multicellular therapies expanded from an adult patient's own bone marrow, which can be delivered directly to damaged tissues using conventional syringes and cell injection catheter systems.

Our lead product, ixmyelocel-T, has demonstrated multiple biological activities that promote tissue repair and regeneration by reducing inflammation, promoting angiogenesis and remodeling ischemic tissue. Preclinical and clinical data suggest that ixmyelocel-T is safe and effective in treating patients with severe, chronic ischemic cardiovascular diseases such as advanced heart failure due to dilated cardiomyopathy (DCM), the third leading cause of heart failure, and critical limb ischemia (CLI), the most severe form of peripheral arterial disease (PAD).

Our lead ixmyelocel-T clinical development program is for the treatment of advanced heart failure due to ischemic DCM. Ixmyelocel-T has been granted a U.S. Orphan Drug designation by the U.S. Food and Drug Administration (FDA) for the treatment of DCM, which we believe provides an efficient and cost-effective path to approval for ixmyelocel-T in this heart failure indication. We are currently enrolling our phase 2b ixCELL-DCM study, which is a randomized, double-blind, placebo-controlled clinical trial for patients with advanced heart failure due to ischemic DCM. The study is designed to enroll 108 patients at approximately 35 sites across the United States and Canada. We also have ongoing ixmyelocel-T clinical programs for the treatment of CLI and craniofacial reconstruction, as well as preclinical research and development programs for the treatment of cardiovascular diseases.

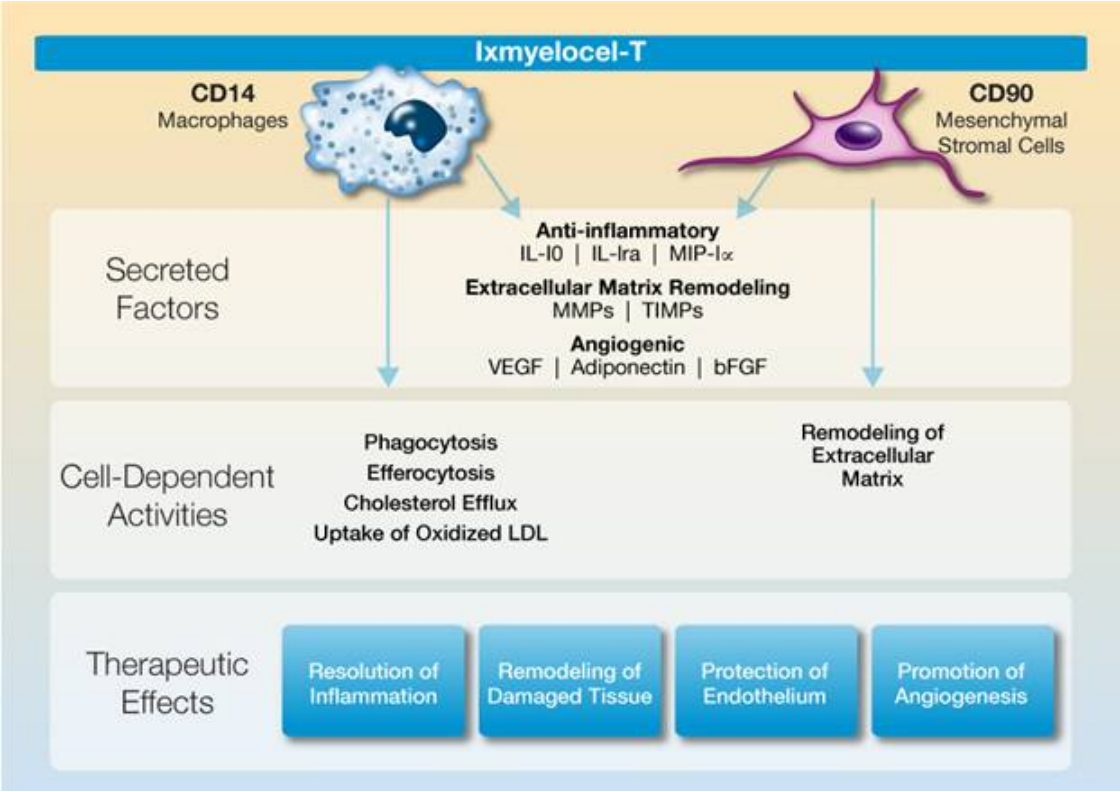
Our Therapy

Ixmyelocel-T is a unique multicellular product derived from an adult patient's own bone marrow. Our proprietary cell manufacturing process significantly expands the mesenchymal stromal cells (MSCs) and M2-like anti-inflammatory macrophages in the patient's bone marrow mononuclear cells while retaining many of the hematopoietic cells. These cell types are known to regulate the immune response and play a key role in tissue repair and regeneration by resolving pathologic inflammation, promoting angiogenesis, and remodeling ischemic tissue. Ixmyelocel-T is the only multicellular product known to have expanded cell populations of both MSCs and M-2 like anti-inflammatory macrophages.

MSCs and M2-like macrophages have a wide range of biological activities that promote repair and regeneration of damaged tissues through the paracrine effects of their secreted factors, as well as their direct cell activities. These cells produce high levels of potent anti-inflammatory and angiogenic factors, as well as factors involved in extracellular matrix remodeling. These cells also have direct activities such as phagocytosis of cellular debris and apoptotic cells, which control the inflammatory response, uptake of LDL and removal of cholesterol, and remodeling of extracellular matrix. We believe that, together, these paracrine effects and direct cell activities are responsible for ixmyelocel-T's demonstrated therapeutic effects of resolving inflammation, promoting angiogenesis, and remodeling and repairing damaged tissue.

Table of Contents

The following illustration summarizes the multiple biological activities of ixmyelocel-T that promote repair and regeneration of ischemic tissue:



Ixmyelocel-T has several features that we believe are primarily responsible for success in treating adult patients with severe ischemic cardiovascular diseases such as DCM and critical limb ischemia:

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. We believe that this characteristic of our therapy eliminates both the risk of rejection and the need 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.

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 MSCs and M2-like anti-inflammatory macrophages, to a substantially greater number 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).

Multicellular — we believe the multiple cell types in ixmyelocel-T, which are normally found in bone marrow but in smaller quantities, possess the key functions required for reducing chronic inflammation and promoting angiogenesis and tissue repair. By reducing inflammation, we believe that ixmyelocel-T provides the ideal conditions to allow for the growth of new tissue and blood vessels.

Minimally invasive — our procedure for collecting bone marrow can be performed in an out-patient setting and takes approximately 15 minutes. Administration of ixmyelocel-T for the treatment of DCM is performed in the cardiac catheterization laboratory using a cell injection catheter system in a one-time procedure. For diseases such as CLI, administration of ixmyelocel-T is performed with a syringe in an outpatient setting in a one-time, approximately 20 minute procedure.

Table of Contents

Safe — bone marrow and bone marrow-derived therapies have been used safely and efficaciously in medicine for over three decades. Ixmyelocel-T leverages this body of scientific study and medical experience, and appears well tolerated in over 200 patients treated to date.

Our Technology Platform

Our patient-specific multicellular therapies are manufactured using the Company's proprietary Aastrom Repicell System (ARS) cell manufacturing system. Our manufacturing process is conducted in a highly-automated, fully-closed and rigorously controlled system. Our system is highly scalable and reproducible and located in a 5,000-square-foot centralized manufacturing facility in Ann Arbor, Michigan. Production is conducted under current Good Manufacturing Practices (cGMP) guidelines required by the FDA with current annual capacity to treat up to 3,000 patients.

Our Strategy

Our objective is to become the leading global biotechnology company in the development, manufacture, and commercialization of autologous multicellular therapies for the treatment of severe ischemic cardiovascular diseases. To achieve this objective, we intend to:

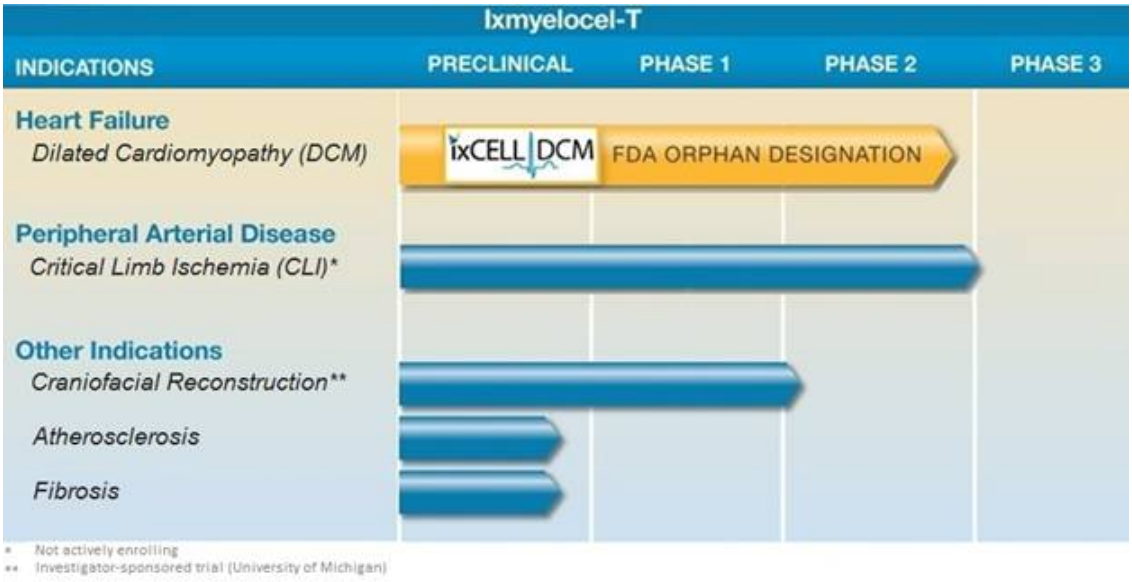
- Complete our phase 2b ixCELL-DCM clinical study for the treatment of advanced heart failure due to ischemic DCM and, if successful, progress ixmyelocel-T into pivotal phase 3 clinical studies for this orphan indication.
- Complete patient follow-up in the REVIVE-CLI study to evaluate safety and efficacy endpoints, and pursue opportunities through investigator-sponsored studies and strategic relationships to continue to develop ixmyelocel-T as a stand-alone and/or adjunct therapy for the treatment of critical limb ischemia.
- Conduct additional preclinical and clinical studies of ixmyelocel-T to pursue additional high-value indications for the treatment of severe ischemic cardiovascular diseases.
- Utilize our proprietary ARS cell-expansion manufacturing platform to expand our product portfolio of cell therapies for the treatment of immune/inflammatory, cardiovascular and fibrovascular diseases.
- Leverage our leading proprietary cell manufacturing platform and expertise to provide manufacturing services and capabilities to other development and commercial-stage biopharmaceutical companies.
- Prepare to commercialize ixmyelocel-T through continued development of our internal commercialization capabilities and/or strategic partnerships for North America, Europe and Asia.

Table of Contents

Our Clinical Development Programs

Our clinical development programs are focused on addressing areas of high unmet medical need in severe, chronic ischemic cardiovascular diseases. We have completed our Phase 1/2 clinical trials in DCM and we are currently enrolling our phase 2b ixCELL-DCM study, which is a randomized, double-blind, placebo-controlled clinical trial for patients with advanced heart failure due to ischemic DCM. Ixmyelocel-T has been granted a U.S. Orphan Drug designation by the FDA for the treatment of DCM. We also have ongoing ixmyelocel-T clinical programs for the treatment of CLI and craniofacial reconstruction.

The following summarizes the status of our clinical programs:



Heart Failure Due to Dilated Cardiomyopathy

Heart failure represents a significant unmet medical need and a growing public health problem. The American Heart Association reports that there are approximately 6 million patients currently suffering from heart failure in the United States and an estimated 650,000 new cases in the U.S. each year. Current medical costs to treat these patients exceed $25 billion and this is expected to more than triple to nearly $80 billion by 2030 as a result of a growing patient population and the high cost of the limited treatment alternatives for advanced heart failure patients, as described below.

DCM is the third leading cause of heart failure and the leading cause of heart transplantation in the United States. DCM is a disease characterized by weakening of the heart muscle, thinning of the heart walls, enlargement of the heart chambers, and the inability to sufficiently pump blood throughout the body. Patients with DCM typically present with symptoms of congestive heart failure, including limitations in physical activity and shortness of breath. Ischemic DCM is associated with atherosclerotic cardiovascular disease and prior heart attacks and is the most common form of dilated cardiomyopathy, representing an estimated 60% of all DCM patients. 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 ischemic DCM patients that are refractory to further medical therapy such as prescription drugs, devices, and/or further revascularization procedures including bypass surgery and angioplasty, are limited to heart transplantation and placement of left ventricular assist devices

(LVADs). There are less than 2,500 heart transplantations in the United States each year. Many refractory DCM patients are not eligible for heart

transplantation and transplants are extremely expensive at an estimated cost of over $1 million. LVADs are also expensive at an estimated cost of over $175,000 and have a mortality rate of 50% at two years.

A majority of advanced heart failure patients that are refractory to medical therapy have DCM, and we believe that the refractory ischemic DCM market represents a substantial market opportunity for ixmyelocel-T. These refractory ischemic DCM patients are currently the target patient population for our clinical development of ixmyelocel-T, with approximately 175,000 patients in the United States alone. Ixmyelocel-T has been granted a U.S. Orphan Drug designation by the FDA for the treatment of DCM, which we believe provides an efficient and cost-effective path to approval for ixmyelocel-T in this heart failure indication.

We have conducted two phase 2a multicenter, randomized, open-label clinical studies in patients with ischemic DCM and nonischemic DCM investigating surgical (IMPACT-DCM) and catheter-based (Catheter-DCM) delivery of ixmyelocel-T. We reported 12-month data for the surgical IMPACT-DCM study at the Heart Failure Society of America meeting in September 2011 and final 12-month results from the Catheter-DCM study at the Society for Cardiovascular Angiography and Interventions (SCAI) 2012 Scientific Sessions. Results from these studies demonstrated that ixmyelocel-T was well-tolerated in patients with DCM. In the Catheter-DCM study and post-surgery in the IMPACT-DCM study, the incidence of adverse events was comparable between the ixmyelocel-T groups and the control groups. Cardiac failure was reported more frequently in the control group relative to ixmyelocel-T in both studies.

While these exploratory phase 2a studies were not powered for determining differences in efficacy between treatment groups, there were consistent trends of clinically meaningful improvement in clinical endpoints observed in the ischemic DCM groups in both studies. In the combined ischemic DCM groups across both studies, major adverse cardiovascular events (MACE) were experienced by a lower percentage of ixmyelocel T-treated patients compared to control patients, representing a 45% reduction in the number of patients having a MACE event. Likewise, patients in the combined ischemic DCM groups that were treated with ixmyelocel-T had a lower average number of MACE events at 12 months compared to those in the control group, representing a 61% reduction in the average number of MACE events per patient. MACE is the recommended endpoint (mortality and cardiovascular hospitalizations) in Phase 3 heart failure studies as stated in the FDA 2009 Somatic Cell Therapy for Cardiac Diseases Draft Guidance. Consistent positive trends also were observed in several secondary efficacy measures in the ischemic DCM groups. The majority of ixmyelocel T-treated patients, but not placebo-treated patients (both IDCM and NIDCM), had improvement in NYHA Class over the 12 months following treatment. Improvement in NYHA Class is considered clinically meaningful. There was also a trend toward improved function, with a higher percentage of ixmyelocel T-treated IDCM patients showing an improvement in ejection fraction and increased 6 minute walk performance compared to the IDCM control patients.

We are currently enrolling patients in the Phase 2b ixCELL-DCM clinical study, which is a multicenter, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of ixmyelocel-T in patients with advanced heart failure due to ischemic DCM. The study is designed to enroll 108 patients at approximately 30 sites in the U.S. and Canada. Patients will be followed for 12 months for the primary efficacy endpoint of MACE events, defined as all-cause deaths, all-cause hospitalizations, and unplanned outpatient or emergency department visits for IV treatment of acute worsening heart failure. Secondary endpoints include clinical, functional, structural, symptomatic, quality of life, and biomarker measures at 3, 6 and 9 months. Patients will be followed for an additional 12 months for safety. We expect to complete enrollment of the ixCELL-DCM study by the end of the first quarter of 2014, and have top-line efficacy results in the second quarter of 2015.

Critical Limb Ischemia

CLI is the most serious and advanced stage of PAD resulting from chronic inflammation and lipid accumulation. 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, dyslipidemia, diabetes, obesity and stroke. CLI is used to describe patients 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 unsuitable for revascularization as they have exhausted all other reasonable treatment options and will likely require amputation. The one-year and four-year mortality rates for CLI patients that are unsuitable for revascularization that progress to amputation are

approximately 25% and 70%, respectively. Currently, there are an estimated 250,000 CLI patients that are unsuitable for revascularization in the United States.

Ixmyelocel-T has shown significant promise in the treatment of CLI patients with existing tissue loss that are unsuitable for revascularization. Our U.S. Phase 2b RESTORE-CLI program was a multi-center, randomized, double-blind, placebo-controlled clinical trial designed to evaluate the safety and efficacy of ixmyelocel-T in the treatment of patients with CLI that are unsuitable for revascularization. It was the largest multi-center, randomized, double-blind, placebo-controlled cellular therapy study ever conducted in CLI patients. We completed enrollment of this trial in February 2010 with a total of 86 patients at 18 sites across the United States.

Final results of the Phase 2b RESTORE-CLI clinical trial were presented at the American Heart Association Scientific Sessions in November 2011 and published in the peer-reviewed journal Molecular Therapy in April 2012. 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 61% reduction in risk (21% ixmyelocel-T treated versus 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.

We initiated the Phase 3 REVIVE-CLI clinical study, a multicenter, randomized, double-blind, placebo controlled study to evaluate the efficacy and safety of ixmyelocel-T in patients with CLI, in 2012. We had previously received Fast Track Designation from the FDA for use of ixmyelocel-T for the treatment of CLI and reached agreement with the FDA on a Special Protocol Assessment. Patients were randomized 1:1 and were to be followed for 12 months for the

primary efficacy endpoint of amputation-free survival. On March 27, 2013 we announced that we were stopping enrollment in the study for strategic business reasons. This study has been amended and is ongoing for the 41 patients that are enrolled in the study, and we plan to continue following these patients for 12 months to evaluate safety and certain efficacy measures. We expect to have results from this study in the second quarter of 2014.

Risks Associated with Our Business

An investment in our common stock involves a high degree of risk. You should carefully consider the risks summarized below. The risks are discussed more fully in the "Risk Factors" section of this prospectus beginning on page S-10 of this prospectus. These risks include, but are not limited to, the following:

- *We currently depend heavily on the success of ixmyelocel-T, our sole product candidate. Any failure to commercialize ixmyelocel-T, or significant delays in doing so, will have a material adverse effect on our business, operating results and financial condition.*
- *Our product development programs are based on novel technologies and are inherently risky.*
- *We may not be able to raise the required capital to conduct our operations and develop and commercialize our 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.*
- *If our patents and proprietary rights do not provide substantial protection, then our business and competitive position will suffer.*
- *Our past losses and expected future losses cast doubt on our ability to continue as a going concern and operate profitably.*

Table of Contents

Corporate Information

We were incorporated under the laws of the State of Michigan on March 24, 1989. Our principal executive offices are located at 24 Frank Lloyd Wright Drive, Lobby K, Ann Arbor, Michigan 48105 and our telephone number is (734) 418-4400. Our website address is www.aastrom.com. The reference to our website is intended to be an inactive textual reference and, except for the documents incorporated by reference as noted above, the information on, or accessible through, our website is not part of this prospectus.

Table of Contents

THE OFFERING

Common stock offered by us pursuant to this prospectus supplement	Shares having an aggregate offering price of up to $6,153,000.
Common stock to be outstanding after this offering	Up to 6,391,483 shares, assuming sales of 1,916,822 shares at a price of $3.21 per share, which was the closing price on The NASDAQ Capital Market on November 26, 2013. Actual number of shares issued will vary depending on the sales price under this offering.
Manner of offering	"At the market offering" that may be made from time to time through our agent, MLV. See "Plan of Distribution" on page S-24.
Use of proceeds	We intend to use the net proceeds of approximately $5,971,000 from this offering primarily to support our operations and continued development of ixmyelocel-T for severe, chronic ischemic cardiovascular diseases. See "Use of Proceeds" on page S-22.
NASDAQ Capital Market symbol	"ASTM"
Risk factors	This investment involves a high degree of risk. See "Risk Factors" beginning on page S-10 of this prospectus supplement as well as the other information included in or incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of risks you should consider carefully before making an investment decision.

The number of shares of our common stock that will be outstanding immediately after this offering as shown above is based on 4,322,129 shares outstanding as of September 30, 2013 (all share amounts disclosed prior to October 16, 2013 have been adjusted to reflect the reverse stock split on a retroactive basis). The number of shares outstanding as of September 30, 2013, as used throughout this prospectus supplement, unless otherwise indicated, excludes:

- 322,001 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2013 at a weighted average exercise price of $39.80 per share;
- 1,375,054 shares of common stock issuable upon the exercise of warrants outstanding as of September 30, 2013 at exercise prices of $25.40 per share (January 2010 — 226,299 shares), $5.60 per share (December 2010 - 15,405 shares) and $7.50 per share (August 2013 — 1,133,350 shares) in each case, before any adjustment as a result of this offering, which warrants are exercisable to purchase common stock; and

· 615,400 shares of common stock issuable upon the conversion of preferred stock outstanding as of September 30, 2013.

Unless otherwise stated, all information contained in this prospectus supplement reflects an assumed public offering price of $3.21 per share, which was the last reported sale price of our common stock on November 26, 2013.

Table of Contents

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below and in the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, as well as other information we include or incorporate by reference into this prospectus supplement and the accompanying 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 supplement, the accompanying prospectus and the incorporated documents 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, 2012, (ii) our Quarterly Report on Form 10-Q for the quarter ended September 30, 2013 and (iii) 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 continue as a going concern and operate profitably.

As of September 30, 2013, we had $10,816,000 of cash and cash equivalents. This is not sufficient to sustain our operations for one year. In light of our financial position, we are evaluating strategic and financial opportunities in the short-term in order to maintain adequate liquidity through December 31, 2013 and beyond. In the year ended December 31, 2012, we raised approximately $279,000 from the sale of our common stock pursuant to our at-the-market offering facility and since December 31, 2012, we raised approximately $4,120,000 from the sale of our common stock pursuant to such facility. In addition, in August 2013, we raised gross proceeds of $9,000,000 from sale of common stock and warrants under a Form S-1 registration statement. However, on a longer term basis, we will need to raise additional funds in order to complete product development programs and complete clinical trials needed to market and commercialize our products. We cannot be certain that such funding will be available on favorable terms, if 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, regulatory and manufacturing requirements and uncertainties, technological developments by competitors, and other factors. If we cannot raise such funds, we will not be able to develop or enhance products, take advantage of future opportunities, or respond to competitive pressures or unanticipated requirements, which would have a material adverse impact on our business, financial condition and results of operations. As a result of the need to raise additional capital and a net capital deficiency, there is uncertainty regarding our ability to maintain liquidity sufficient to operate our business effectively over at least the next twelve months, which raises substantial doubt as to our ability to continue as a going concern. The consolidated financial statements incorporated by reference in this prospectus do not include any adjustments that might result from the outcome of this uncertainty.

We were incorporated in 1989 and have experienced substantial operating losses since inception. As of September 30, 2013, we had accumulated a deficit of approximately $284,797,000 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

Table of Contents

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 may receive from this offering, 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 2b clinical trial for DCM), 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;
- 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.

Notwithstanding the proceeds we may receive from this offering, 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 DCM program), 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;

Table of Contents

- the liquidity and market volatility of our equity securities; and
- regulatory and manufacturing requirements and uncertainties, and 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 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.

We currently depend heavily on the success of ixmyelocel-T, our sole product candidate. Any failure to commercialize ixmyelocel-T, or significant delays in doing so, will have a material adverse effect on our business, operating results and financial condition.

We have invested a significant portion of our efforts and financial resources in the development of ixmyelocel-T. Our ability to generate future product revenue depends heavily on the successful development and commercialization of ixmyelocel-T. The successful commercialization of ixmyelocel-T will depend on several factors, including the following:

- obtaining marketing approvals from the FDA and other foreign regulatory authorities;
- successful enrollment of patients in our ongoing clinical studies of ixmyelocel-T;
- successful completion of our ongoing clinical studies of ixmyelocel-T;
- the successful audit of our facilities by additional regulatory authorities;
- maintaining the cGMP and cGTP compliance of our manufacturing facility;
- maintaining current manufacturing arrangements with third parties and establishing new manufacturing arrangements;

- our development of a successful sales and marketing organization for ixmyelocel-T;

Table of Contents

- an acceptable safety and efficacy profile of our product candidates following approval;
- the availability of reimbursement to patients from healthcare payers for our drug products, if approved; and
- other risks described in this “Risk Factors” section.

Any failure to commercialize ixmyelocel-T or significant delays in doing so will have a material adverse effect on our business, results of operations and financial condition.

Our sole product candidate, ixmyelocel-T, is still in clinical development. If we do not successfully continue or complete the clinical development of ixmyelocel-T, our likelihood of success as a company and our ability to finance our operations will be substantially harmed.

Our near-term prospects substantially depend upon our ability to successfully continue and complete clinical trials of our lead product candidate, ixmyelocel-T, and to demonstrate its safety and efficacy, as well as its superiority over existing therapies and standards of care, if any. We are currently enrolling patients with ischemic DCM for the ixCELL-DCM trial, a Phase 2b clinical trial, and have recently treated the first patients in the trial. All of our other potential product candidates are in preclinical research or early clinical development. Our ability to finance our company and to generate revenues will depend heavily on our ability to obtain favorable results in the ongoing and planned clinical trials of ixmyelocel-T, including the ongoing ixCELL-DCM Phase 2b clinical trial, and to successfully develop and commercialize ixmyelocel-T. Ixmyelocel-T could be unsuccessful if it:

- does not demonstrate acceptable safety and efficacy in clinical trials, or otherwise does not meet applicable regulatory standards for approval;
- does not offer sufficient, clinically meaningful therapeutic or other improvements over existing or future drugs used to treat the DCM indications for which it is being tested;
- is not capable of being produced in commercial quantities at acceptable costs; or
- is not accepted as safe, efficacious, cost-effective, less costly and preferable to current therapies in the medical community and by third-party payers.

If we are not successful in developing and commercializing ixmyelocel-T or are significantly delayed in doing so, our financial condition and future prospects may be adversely affected and we may experience difficulties in raising the substantial additional capital required to fund our business.

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.

Table of Contents

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.

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. On March 27, 2013, we announced that we were stopping enrollment in the Phase 3 REVIVE clinical trial due to the slow patient accrual rate for the study and to optimize the use of our financial resources. If we experience similar delays in patient enrollment for other clinical trials, we could experience increased costs and delays associated with these 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 may 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 may use clinical research organizations (CROs) 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

Table of Contents

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, (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.

Failure of third parties, including Vention Medical, 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 its 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.

Table of Contents

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 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 market for 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 that we use in, and which 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

Table of Contents

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 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 four previous occasions, most recently in the first quarter of 2013. 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, with the last to expire during the third quarter of 2014. 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.

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 United States 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 United States government has the right to require us to grant an exclusive license under any of such inventions to a third party if the United States government

Table of Contents

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: (x) products using the invention which are sold in the United States are to be manufactured substantially in the United States, unless a waiver is obtained; (y) 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 (z) the United States 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 on reasonable terms. Excessive insurance costs or uninsured claims would increase our operating loss and adversely affect our financial condition.

Risks Related to Our Common Stock

We may be unable to continue as a going concern in which case our securities will have little or no value.

We have incurred substantial losses since inception and have a net capital deficiency. This raises substantial doubt about our ability to continue as a going concern. In the event we are not able to continue operations you will likely suffer a complete loss of your investment in our securities.

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

The market price of shares of our common stock has been volatile, ranging in closing price between $5.40 and $28.20 during the six months ended September 30, 2013, which has been retroactively adjusted for our twenty-to-one reverse stock split on October 16, 2013. 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;

Table of Contents

- reports by securities analysts;
- status of the investment markets;
- concerns related to management transitions; and
- delisting from The NASDAQ Capital Market.

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 common 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. We are currently offering an aggregate amount of $6,153,000 of common stock under such registration statement and pursuant to this prospectus supplement. In August 2013, we offered 1,500,000 shares of common stock and warrants to purchase up to 1,500,000 shares of common stock under a Form S-1 registration

statement, which became effective on August 14, 2013. We are entitled under our amended and restated articles of incorporation to issue up to 15,000,000 shares of common stock, no par value per share, and 5,000,000 shares of preferred stock, no par value per share. As of the date of this prospectus supplement, we had issued and outstanding 4,474,661 shares of common stock, 1,693,831 shares of common stock reserved for issuance upon the exercise of current outstanding options and warrants, and 1,632,500 shares of common stock reserved for issuance upon conversion of our Series B preferred stock. Accordingly, we will be able to issue up to 5,243,153 additional shares of common stock and 5,000,000 shares of preferred stock after the completion of this offering (assuming the sale of 1,916,822 shares at an assumed public offering price of $3.21 per share in this offering). Sales of our common stock in this offering will result in dilution to our shareholders—see "Dilution" on page S-23 for additional information. 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.

Some of our outstanding warrants include anti-dilution protection for any issuance of securities lower than the exercise price of such warrants such as is contemplated by this offering if such lower issuance occurs prior to the exercise or during the exercise period of the warrants. This anti-dilution protection could result in dilution to the shareholders and may contribute to downward pressure on the trading price of our common stock.

We currently have outstanding Class A warrants to purchase 226,229 shares of common stock issued in January 2010 and warrants to purchase 15,405 shares of common stock issued December 2010, with current exercise prices of $25.40 per common share and $5.60 per common share before any adjustment related to this offering, respectively. These warrants contain anti-dilution provisions that reduce the exercise price of the warrants if we issue or sell, or are deemed to have issued or sold, any shares of its common stock or securities exercisable or convertible into shares of common stock for no consideration or for a consideration per share less than the applicable exercise price in effect immediately prior to the time of such issue or sale, as is contemplated by this offering. The exercise of the warrants at prices below the market price of our common stock could adversely affect the price of shares of our common stock. In addition, sales of the shares of our common stock issuable upon exercise of the warrants could have a depressive effect on the price of our common stock, particularly if there is not a coinciding increase in demand by purchasers of our common stock.

Table of Contents

Eastern Capital Limited holds a large percentage of our outstanding capital stock and has 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'.

Eastern Capital Limited (Eastern Capital) has not entered into a lock-up agreement in connection with this offering. All of the accumulated dividends in Series B-1 non-voting preferred stock and outstanding Series B-2 voting preferred stock, representing a significant amount of our outstanding capital stock on a fully-converted basis, are held by Eastern Capital. The accumulated dividends in our Series B-1 non-voting preferred stock are exchangeable for shares of Series B-2 voting preferred stock and, in March 2017, are convertible into shares of our common stock. Based solely on the number of shares of Series B-2 preferred stock that Eastern Capital held as of September 30, 2013, Eastern Capital has beneficial ownership of approximately twelve percent (12%) (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-2 preferred) of our voting securities based on the approximately 4,938,000 shares of common stock and Series B-2 preferred stock outstanding as of September 30, 2013. Furthermore, in connection with the March 2012 financing, we amended our Shareholder Rights Plan described below under "Description of Capital Stock" 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 the Company even if such a change of control would benefit our other shareholders. The significant concentration of stock ownership may adversely affect the trading price of our 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 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, in certain cases, if 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) $65,000 (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.

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

Our Board of Directors (Board) 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.

Table of Contents

DIVIDEND POLICY

We have never declared dividends on our common stock, and currently do not plan to declare dividends on shares of our common stock in the foreseeable future. We expect to retain our future earnings, if any, for use in the operation and expansion of our business. Subject to the foregoing, the payment of cash dividends in the future, if any, will be at the discretion of our Board and will depend upon such factors as earnings levels, capital requirements, our overall financial condition and any other factors deemed relevant by our Board.

USE OF PROCEEDS

We expect to receive net proceeds of approximately $5,971,000 from this offering after deducting sales agent commissions and estimated offering expenses payable by us of approximately $30,000. The principal purposes of this offering are to obtain additional capital to support our operations and continued development of ixmyelocel-T for severe, chronic ischemic cardiovascular diseases.

We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion to allocate the net proceeds from this offering. Pending application of the net proceeds as described above, we expect to invest the net proceeds in highly liquid investments.

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.”

Table of Contents

DILUTION

Our net tangible book value as of September 30, 2013 was approximately $5,000,000, or $1.15 per share of common stock. Net tangible book value per share is calculated by subtracting our total liabilities from our total tangible assets, which is total assets less intangible assets, and dividing this amount by the number of shares of common stock outstanding. After giving effect to the sale by us of the full $6,153,000 of common stock that may be offered in this offering at an assumed offering price of $3.21 per share, which was the closing price of our common stock on The NASDAQ Capital Market on November 26, 2013, and after deducting estimated offering commissions and expenses payable by us, our as-adjusted net tangible book value as of September 30, 2013 would have been approximately $10,891,000, or $1.75 per share of common stock. This represents an immediate increase in the net tangible book value of $0.60 per share to our existing stockholders and an immediate and substantial dilution in net tangible book value of $1.46 per share to new investors. The following table illustrates this hypothetical per share dilution:

Assumed offering price per share			$	3.21
Net tangible book value per share as of September 30, 2013	$	1.15		
Increase per share attributable to new investors	$	0.60		
As-adjusted net tangible book value per share after this offering			$	1.75
Net dilution per share to new investors			$	1.46

The table above assumes for illustrative purposes that an aggregate of 1,916,822 shares of our common stock are sold at a price of $3.21 per share, the last reported sale price of our common stock on The NASDAQ Capital Market on November 26, 2013, for aggregate gross proceeds of $6,153,000. The shares sold in this offering, if any, will be sold from time to time at various prices. An increase of $1.00 per share in the price at which the shares are sold from the assumed offering price of $3.21 per share shown in the table above, assuming all of our common stock in the aggregate amount of $6,153,000 is sold at that price, would increase our adjusted net tangible book value per share after the offering to $1.88 per share and would increase the dilution in net tangible book value per share to new investors in this offering to $2.33 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of $1.00 per share in the price at which the shares are sold from the assumed offering price of $3.21 per share shown in the table above, assuming all of our common stock in the aggregate amount of $6,153,000 is sold at that price, would decrease our adjusted net tangible book value per share after the offering to $1.53 per share and would decrease the dilution in net tangible book value per share to new investors in this offering to $0.68 per share, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only.

Table of Contents

PLAN OF DISTRIBUTION

We have entered into an At Market Issuance Sales Agreement with MLV & Co. LLC (formerly McNicoll Lewis & Vlak), or MLV, dated June 16, 2011, as amended by Amendment No. 1 on November 29, 2013. Under the Sales Agreement, we sold common stock for an aggregate of approximately $4,120,000 to date. Pursuant to Amendment No. 1 we may issue and sell our common stock having aggregate sales proceeds of up to $6,153,000 from time to time through MLV acting as agent and/or principal. The form of Amendment No. 1 will be filed as an exhibit to a report filed under the Exchange Act and incorporated by reference in this prospectus supplement. The form of the Sales Agreement was filed as an exhibit to a report filed under the Exchange Act, and is incorporated by reference in this prospectus supplement. The sales, if any, of shares made under the sales agreement will be made by any method that is deemed an “at the market offering” as defined in Rule 415 promulgated under the Securities Act, including sales made directly or through The NASDAQ Capital Market, the existing trading market for our common stock, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices, and /or any other method permitted by law. We may instruct MLV not to sell common stock if the sales cannot be effected at or above the price designated by us from time to time. We or MLV may suspend the offering of common stock upon notice and subject to other conditions. As an agent, MLV will not engage in any transactions that stabilize the price of our common stock.

Each time we wish to issue and sell common stock under the sales agreement, we will notify MLV of the number of shares to be issued, the dates on which such sales are anticipated to be made, any minimum price below which sales may not be made and other sales parameters as we deem appropriate.

Once we have so instructed MLV, unless MLV declines to accept the terms of the notice, MLV has agreed to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. The obligations of MLV under the sales agreement to sell our common stock are subject to a number of conditions that we must meet.

We will pay MLV commissions for its services in acting as agent in the sale of common stock. MLV will be entitled to a commission in an amount up to 3% of the gross proceeds from the sale of common stock offered herby. The following table shows the commissions and proceeds, before our estimated offering expenses, to us, assuming all $6,153,000 of common stock is sold at an assumed price of $3.21 per share, which was the last reported sales price of our common stock on The NASDAQ Capital Market on November 26, 2013:

	Per Share *	Total *
Public offering price	$ 3.21	$ 6,153,000
Sales agent commissions **	$ 0.09	$ 182,000
Proceeds, before expenses, to us	$ 3.12	$ 5,971,000

* This is an offering that will be made, if at all, from time to time at the then-prevailing market prices. Therefore, there can be no assurances that the per share or total public offering price, underwriting commissions, and proceeds, before expenses, will be as set forth above.

** Sales agent commissions for sales of our common stock shall be at a fixed commission rate of up to 3% of the gross sales price per share sold.

We estimate that the total expenses for the offering, excluding compensation payable to MLV under the terms of the sales agreement, will be approximately $30,000.

Settlement for sales of common stock will generally occur on the third business day following the date on which any sales are made, or on some other date that is agreed upon by us and MLV in connection with a particular transaction, in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sale of the common stock on our behalf, MLV may, and will with respect to sales effected in an “at the market offering,” be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of MLV may be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to MLV against certain civil liabilities, including liabilities under the Securities Act. We have also agreed to reimburse MLV for certain other specified expenses.

Table of Contents

The offering of our common stock pursuant to the sales agreement will terminate upon the earlier of (i) the sale of all of our common stock provided for in this prospectus supplement or (ii) termination of the sales agreement as provided therein.

MLV and its affiliates may in the future provide various investment banking and other financial services for us and our affiliates, for which services they may in the future receive customary fees. To the extent required by Regulation M, MLV will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus supplement.

LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus supplement will be passed upon for us by Dykema Gossett PLLC, Ann Arbor, Michigan, acting as special counsel to the Company. MLV is being represented in connection with this offering by LeClairRyan, A Professional Coproration, New York, New York.

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, 2012 have been so incorporated in reliance on the report (which contains an explanatory paragraph relating to the Company’s ability to continue as a going concern as described in Note 1 to the consolidated financial statements) 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).

This prospectus supplement is part of a registration statement we filed with the SEC relating to the securities we may offer. As permitted by SEC rules, this prospectus supplement does not contain all of the information we have included in the registration statement and the accompanying exhibits and schedules we filed with the SEC. You may refer to the registration statement, exhibits and schedules for more information about us and the securities. The registration statements, exhibits and schedules are available at the SEC’s public reference room or through its website.

The SEC allows us to “incorporate by reference” the information we have filed with it, which means that we can disclose important information by referring you to those documents. The information we incorporate by reference is an important part of this prospectus supplement and the accompanying prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference into this prospectus supplement and the accompanying prospectus any future documents filed with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act subsequent to the date of this prospectus supplement and prior to the termination of the offering.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus supplement, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference herein is deemed to be part of this prospectus supplement, except for any information superseded by information in this prospectus supplement or in our subsequently filed Exchange Act documents. This prospectus supplement incorporates by reference the documents set forth below that we have

Table of Contents

previously filed with the SEC. These documents contain important information about us, our business and our finances.

- our annual report on Form 10-K for the period ended December 31, 2012, filed with the SEC on March 18, 2013;
- our quarterly reports on Form 10-Q for the quarters ended March 31, 2013, filed with the SEC on May 8, 2013, June 30, 2013, filed with the SEC on August 7, 2013 and September 30, 2013, filed with the SEC on November 12, 2013;
- our current reports on Form 8-K, filed with the SEC on March 8, 2013, March 29, 2013, April 9, 2013, April 23, 2013 (including exhibit 99.1 thereto), May 3, 2013, May 13, 2013, May 24, 2013, August 12, 2013, August 14, 2013, August 26, 2013, September 27, 2013, and October 10 , 2013, respectively (excluding any information furnished in such reports under Item 2.02, Item 7.01 or Item 9.01);
- our definitive Proxy Statements on Schedule 14A for the Annual Meeting of Shareholders, filed with the SEC on March 22, 2013 and for the Special Meeting of Shareholders, filed with the SEC on September 5, 2013;
- the description of the rights to purchase shares of our Series A Junior Participating Cumulative Preferred Stock contained in the Registration Statement on Form 8-A, filed with the SEC on August 12, 2011, including any amendment or report for the purpose of updating such description; and
- the description of our common stock contained in the amendment to our registration statements on Form S-1, filed with the SEC on August 12, 2013, including any amendment or report filed for the purpose of updating such description.

Pursuant to Rule 412 under the Securities Act, any statement contained in a document incorporated or deemed to be incorporated by reference into this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus modifies or supersedes the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

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, Lobby K, Ann Arbor, Michigan 48105, Attention: Investor Relations, or by telephoning us at (800) 556-0311. These filings may also be obtained through our website located at http://www.aastrom.com. The reference to our website is intended to be an inactive textual reference and, except for the documents incorporated by reference as noted above, the information on, or accessible through, our website is not intended to be part of this prospectus.

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 and that have not been described in a Form 8-K filed under the Exchange Act.

Table of Contents

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 United States.
CLI — Critical Limb Ischemia	A vascular disease characterized by insufficient blood flow in the lower extremities that causes severe pain, tissue loss or both.
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.

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	Our U.S. Phase 2 dilated cardiomyopathy clinical trial.
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.
Mesenchymal stromal cells	Connective tissue cells that, in the case of bone marrow derived MSC, function to support blood forming cells and secrete anti-inflammatory factors.

Table of Contents

TERM	DEFINITION
M2 anti-inflammatory macrophages	Specialized blood cells that remove damaged tissue and bacteria and secrete anti-inflammatory factors.
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.
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 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.

Table of Contents

PROSPECTUS
$100,000,000
AASTROM BIOSCIENCES, INC.
Common Stock
Preferred Stock
Debt Securities
Warrants
Units

We may from time to time issue, in one or more series or classes, up to $100,000,000 in aggregate principal amount of our common stock, preferred stock, debt securities, warrants and/or units. We may offer these securities separately or together in units. We will specify in the accompanying prospectus supplement the terms of the securities being offered. We may sell these securities to or through underwriters and also to other purchasers or through agents. We will set forth the names of any underwriters or agents, and any fees, conversions, or discount arrangements, in the accompanying prospectus supplement. We may not sell any securities under this prospectus without delivery of the applicable prospectus supplement.

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

Our common stock is traded on the Nasdaq Capital Market under the symbol “ASTM.” On June 15, 2011, the closing price for our common stock was $2.52 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 10 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 July 18, 2011.

Table of Contents

TABLE OF CONTENTS

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.

Table of Contents

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 developing expanded patient specific mixed cellular therapies for use in the treatment of severe, chronic ischemic cardiovascular diseases. Ixmyelocel-T (the new generic name for our cell therapy approved in March 2011) is a disease modifying therapy with multi-functional properties including: tissue remodeling, immuno-modulation and the promotion of angiogenesis, which is targeted to address the multiple underlying causes of many severe, chronic cardiovascular diseases such as critical limb ischemia (CLI). Our proprietary cell-manufacturing technology enables the manufacture of cell therapies expanded from a patient’s own bone marrow and delivered directly to damaged tissues. Preclinical and interim 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 also shown safety as well as provided indications of efficacy. Nearly 200 patients have been treated in recent clinical trials using ixmyelocel-T (over 400 patients safely treated since our inception) with no treatment related serious adverse events.

Our technology is a patient specific, expanded multi-functional cell therapy developed using our proprietary, automated processing system to produce human cell products for clinical use. The Aastrom process enhances 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 expanded, patient specific cell therapies is done under current Good Manufacturing Practices (cGMP) and current Good Tissue Practices (cGTP) guidelines required by the U.S. Food and Drug Administration (FDA).

Our expanded, patient specific multi-functional cellular therapies have several features that we believe are critical for success in treating patients with severe, chronic cardiovascular diseases:

Safe — our bone marrow-derived, expanded, patient specific cellular therapy leverages decades of scientific and medical experience, as bone marrow and bone marrow-like therapies have been used safely and efficaciously in medicine for over three decades.

Autologous (patient specific) — we start with the patient's own cells, which are accepted by the patient's immune system allowing the cells to differentiate and integrate into existing functional tissues, and we believe provides long-term engraftment and repair.

Expanded — we begin with a small amount of bone marrow from a patient (approximately 50 ml) and significantly expand the number of certain cell types, primarily CD90+ mesenchymal cells, CD14+ monocytes and alternatively activated macrophages to far more than are present in the patient's own bone marrow (up to 300 times the number of these cells compared with the starting bone marrow aspirate).

A mixture of cell types — we believe our proprietary mixture of cell types, which are normally found in bone marrow, but in different quantities, possess multiple activities 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 our therapy can be performed in an out-patient setting in a one-time, approximately 20 minute procedure. We are also pursuing a minimally invasive approach to cell delivery in other severe, chronic ischemic cardiovascular diseases such as DCM.

Our cell therapies are 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 advancing therapies for unmet medical needs in severe, chronic ischemic cardiovascular diseases. We have completed our Phase 2b clinical trial in CLI and we expect it to advance to a Phase 3 development program in 2011. Our CLI development program has received Fast Track Designation from the FDA. Our DCM program is in early Phase 2 clinical development and is focused on achieving proof of concept in this indication. 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" contained in this prospectus beginning on page 10.

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 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), ulcers, tissue loss or gangrene in the limbs, often leading to amputation and death. CLI leads to more than 160,000 amputations per year. The one-year and four-year mortality rates for no-option CLI patients that progress to amputation are approximately 25% and 70%, respectively. Our disease modifying therapy with multi-functional properties has shown significant promise in the treatment of CLI.

Clinical Programs

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. It was the largest multi-center, randomized, double-blind, placebo-controlled cellular therapy study ever conducted in 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 being treated in March 2010. These patients were followed for a period of 12 months following treatment. In addition to assessing the safety of our product, efficacy endpoints include amputation-free survival, time to first occurrence of treatment failure (defined as major amputation, all-cause mortality, doubling in wound size and de novo gangrene), major amputation rates, level of amputation, complete wound healing, patient quality of life and pain scores.

Results to date include two planned interim analyses and a final top-line analysis. In June 2010, we reported results at the Society of Vascular Surgery Meeting. This interim analysis included the six month results for 46 patients enrolled in the trial. The results included the finding that amputation free survival, defined as time to major amputation or death, was statistically significant in favor of our therapy (p=0.038). Additionally, statistical analysis revealed a significant increase in time to treatment failure (e.g., major amputation, doubling in wound size de novo gangrene, or death) (log-rank test, p=0.0053). Other endpoints measured (e.g., major amputation rate, complete wound healing, change in Wagner wound scale) showed encouraging trends, but had not reached statistical significance at the interim analysis. The primary purpose of the interim analysis was to assess performance of our therapy and, if positive, to help plan the Phase 3 program. In June 2010 we held discussions with the FDA, which confirmed the appropriateness of using amputation free survival as a primary endpoint for our planned Phase 3 program.

In November 2010, we presented six-month data on all 86 patients enrolled in the trial at the VEITHsymposium™ non-CME satellite session. Results of this analysis showed that the study 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 show a clinically meaningful

reduction of 56% in treatment failure events. Analysis of the data for amputation-free survival, a secondary endpoint which the study was not powered to demonstrate, showed a clinically meaningful reduction in event rates of 24%, but did not show statistical significance (p=0.5541).

In June 2011, we announced final top-line results from all 86 patients enrolled in the trial. Results of this analysis showed that the trial met its primary safety and efficacy endpoints, demonstrating a statistically significant improvement in the time to first occurrence of treatment failure at 12 months. We plan to present the full data from the RESTORE-CLI trial at an appropriate medical meeting in the fourth quarter of 2011.

We continue to make progress towards the Phase 3 clinical development program in CLI. In October 2010, we announced that the FDA had granted Fast Track Designation for the use of our multi-functional cellular therapy for the CLI indication. The Fast Track program is designed to facilitate the development and expedite the review of new drugs and biologics, intended to treat serious or life-threatening conditions that demonstrate the potential to address unmet medical needs. During June 2010 discussions with the FDA, Aastrom was encouraged to use the Special Protocol Assessment (SPA) process for the Phase 3 program. In October 2010, we submitted two SPA requests to the FDA, one for a “no option” patient population and another for a “poor option” patient population. The no option SPA request focuses on patients that have exhausted all other treatment options with the exception of amputation. The poor option SPA request focuses on patients that have not yet exhausted all other treatment options; however the options available are associated with poor outcomes. We expect to have the no option and poor option agreements on the SPA’s completed in the third quarter of 2011.

Table of Contents

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. There are two types of DCM: ischemic and non-ischemic. Ischemic DCM, the most common form, is associated with atherosclerotic cardiovascular disease. Among other causes, non-ischemic DCM can be triggered by toxin exposure, virus or genetic diseases. Patient prognosis depends on the stage and cause of the disease but is typically characterized by a high mortality rate. Other than heart transplantation or ventricular assist devices, there are currently no effective treatment options for end-stage patients with this disease. According to the book, *Heart Failure: A Combined Medical and Surgical Approach* (2007), DCM affects 200,000-400,000 patients in the United States alone.

In February 2007, the FDA granted Orphan Drug Designation to our investigational therapy for the treatment of DCM. Our DCM development program is currently in Phase 2 and we have two ongoing U.S. Phase 2 trials investigating surgical and catheter-based delivery for our product in the treatment of DCM.

Surgical Trial Program — DCM

In May 2008, the FDA activated our investigational new drug application (IND) for surgical delivery of our therapy. The 40-patient U.S. IMPACT-DCM clinical trial began with the treatment of the first patient in November 2008. This multi-center, randomized, controlled, prospective, open-label, Phase 2 study was designed to include 20 patients with ischemic DCM and 20 patients with non-ischemic DCM. We completed enrollment of the 40 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 is 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 post-treatment.

Table of Contents

Six-month data from the IMPACT-DCM interim analysis were presented at The Sixth International Conference on Cell Therapy for Cardiovascular Disease on January 20, 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 quality of life and functional and structural parameters in the treatment group as compared with the control group. We expect to report 12-month data from the IMPACT-DCM clinical study in the third quarter of 2011.

Catheter Trial Program — DCM

In November 2009, the FDA activated our second IND to allow for the evaluation of our therapy delivered by a percutaneous direct catheter injection as opposed to surgically. The Catheter-DCM clinical trial is designed to explore catheter-based 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. We expect to report six-month results from the Catheter-DCM Phase 2 trial in the third quarter of 2011.

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.

About this Prospectus

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, utilizing a shelf registration process. Under the shelf registration process, we may offer shares of our common stock and preferred stock, various series of debt securities, warrants to purchase any of such securities, and units comprised of any such securities with a total value of up to $100,000,000 from time to time under this prospectus at prices and on terms to be determined by market conditions at the time of offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

Table of Contents

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity;
- original issue discount, if any;
- rates and times of payment of interest, dividends or other payments, if any;
- redemption, conversion, exchange, settlement or sinking fund terms, if any;
- conversion, exchange or settlement prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion, exchange or settlement prices or rates and in the securities or other property receivable upon conversion, exchange or settlement;
- ranking;
- restrictive covenants, if any;
- voting or other rights, if any; and
- important federal income tax considerations.

A prospectus supplement may include a discussion of risks or other special considerations applicable to us or the offered securities. A prospectus supplement may also add, update or change information in this prospectus. If there is any inconsistency between the information in this prospectus and any applicable prospectus supplement, you must rely on the information in the prospectus supplement. Please carefully read both this prospectus and any applicable prospectus supplement together with the additional information described under the heading “Where You Can Find More Information.”

The registration statement containing this prospectus, including exhibits to the registration statement, provides additional information about us and the securities offered under this prospectus. The registration statement can be read at the SEC’s website (www.sec.gov) or at the SEC’s Public Reference Room mentioned under the heading “Where You Can Find More Information.”

We have not authorized any broker-dealer, salesperson or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus and an accompanying supplement to this prospectus. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or an accompanying prospectus supplement. This prospectus and an accompanying supplement to this prospectus do not constitute an offer to sell or the solicitation of an offer to buy securities, nor do this prospectus and an accompanying supplement to this prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation. The information contained in this prospectus and an accompanying prospectus supplement speaks only as of the date set forth on the applicable cover page and may not reflect subsequent changes in our business, financial condition, results of operations and prospects even though this prospectus and any accompanying prospectus supplement is delivered or securities are sold on a later date.

Table of Contents

We may sell the securities directly to or through underwriters, dealers or agents. We, and our underwriters or agents, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through underwriters, dealers or agents, we will include in any applicable prospectus supplement:

- the names of those underwriters, dealers or agents;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options, if any; and
- the net proceeds to us.

Common Stock

As discussed below under the heading "The Securities We May Offer," we may issue shares of our common stock from time to time. 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, 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 of directors, or 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 Restated Articles of Incorporation, as amended, or the Charter, which may be amended by the holders of a majority of the outstanding shares of common stock.

Preferred Stock

As discussed below under the heading "The Securities We May Offer," we may issue shares of our preferred stock from time to time, in one or more series. Under our Charter, our Board has the authority, without further action by shareholders, to designate up to 5,000,000 shares of preferred stock in one or more series and to fix the designations, powers, preferences and the relative, participating, optional or other special rights of the shares of each series and any qualification, limitations and restrictions thereon, any or all of which may be greater than the rights of our common stock.

If we issue preferred stock, we will fix the designations, powers, preferences and the relative, participating, optional or other special rights, and any qualification, limitations and restrictions of the shares of each series that we sell under this prospectus and applicable prospectus supplements in the certificate of designations relating to that series. If we issue preferred stock, we will incorporate by reference into the registration statement of which this prospectus is a part the form of any certificate of designations that describes the terms of such series of preferred stock before the issuance thereof. We urge you to read any prospectus supplement related to any series of preferred stock we may offer, as well as the complete certificate of designations that contains the terms of the applicable series of preferred stock.

Table of Contents

Debt Securities

As discussed below under the heading "The Securities We May Offer," we may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. Unless we give you different information in the applicable prospectus supplement, (i) the debt securities will be unsecured, (ii) the senior debt securities will be unsubordinated obligations and will rank equally with all of our other unsecured and unsubordinated indebtedness, and (iii) the subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all or some portion of our indebtedness. Any convertible debt securities that we issue will be convertible into or exchangeable for our common stock or other securities of ours. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

If we issue debt securities, they will be issued under one or more documents called indentures, which are contracts between us and a trustee for the holders of the debt securities. We urge you to read any prospectus supplement related to the series of debt securities being offered, as well as the complete indenture that contains the terms of the debt securities. If we issue debt securities, indentures and forms of debt securities containing the terms of such debt securities will be incorporated by reference into the registration statement of which this prospectus is a part from other filings we would make with the SEC.

Warrants

As discussed below under the heading "The Securities We May Offer," we may issue warrants for the purchase of common stock, preferred stock, debt securities and/or units (as described below) in one or more series, from time to time. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from those securities.

If we issue warrants, they will be evidenced by warrant agreements or warrant certificates issued under one or more warrant agreements, which are contracts between us and an agent for the holders of the warrants. We urge you to read any prospectus supplement related to any series of warrants we may offer, as well as the complete warrant agreement and warrant certificate that contain the terms of the warrants. If we issue warrants, forms of warrant agreements and warrant certificates relating to such warrants will be incorporated by reference into the registration statement of which this prospectus is a part from other filings we would make with the SEC.

Units

As discussed below under the heading "The Securities We May Offer," we may issue units comprised of shares of common stock, shares of preferred stock, debt securities and warrants in any combination. We may issue units in such amounts and in as many distinct series as we wish.

Table of Contents

If we issue units, they will be issued under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. We urge you to read any prospectus supplement related to any series of units we may offer, as well as the complete unit agreement and unit certificate that contain the terms of the units. If we issue units, forms of unit agreements and unit certificates relating to such units will be incorporated by reference into the registration statement of which this prospectus is a part from other filings we would make with the SEC.

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 Transition Report on Form 10-KT for the transition period from July 1, 2010 to December 31, 2010, (ii) our Quarterly Report on Form 10-Q for the quarter ended March 31, 2011 and (iii) 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 March 31, 2011, we have incurred a cumulative net loss totaling approximately $226,200,000, 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.

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;
- 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 in June 2009. As a result, we no longer have access to the potential funding from Fusion Capital under that agreement. However, we believe that with our existing cash and cash equivalents we will have adequate liquidity to finance our operations, including development of our products and product candidates, through at least December 31, 2011. Absent receipt of proceeds from an equity offering or otherwise, we believe we will have adequate liquidity to finance our operations through at least December 31, 2011. While our budgeted cash usage and operating plan through December 31, 2011 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 (without jeopardizing our pursuit of a Phase 3 clinical trial for CLI) such that we believe that we will have sufficient cash on hand through at least December 31, 2011.

We will need to raise 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

Table of Contents

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 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.

Table of Contents

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.

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.

Table of Contents

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 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.

Failure of third parties, including 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 ATEK Medical, LLC, or ATEK, 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. ATEK is our sole supplier of cell cassettes

Table of Contents

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 payors will pay for our products and related treatments.

Table of Contents

Reimbursement by third party payors depends on a number of factors, including the payor's determination that use of the product is safe and effective, not experimental or investigational, medically necessary, appropriate for the specific patient and cost-effective. Reimbursement in the United States or foreign countries may not be available or maintained for any of our product candidates. If we do not obtain approvals for adequate third party reimbursements, we may not be able to establish or maintain price levels sufficient to realize an appropriate return on our investment in product development. Any limits on reimbursement from third party payors may reduce the demand for, or negatively affect the price of, our products. For example, in the past, published studies suggested that stem cell transplantation for breast cancer, which constituted a significant portion of the overall stem cell therapy market at the time, may have limited clinical benefit. The lack of reimbursement for these procedures by insurance payors has negatively affected the marketability of our products in this indication in the past.

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 payors 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 payors 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.

Table of Contents

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 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.

We have identified a material weakness in our internal control over financial reporting that resulted in the restatement of prior periods' consolidated financial statements. We cannot guarantee that additional material weaknesses will not arise in the future, which could affect our ability to report our results of operations and financial condition accurately and in a timely manner.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes in accordance with U.S. generally accepted accounting principles, or GAAP. Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2010 and identified a material weakness related to our prior interpretation of ASC 815 and our initial classification and subsequent accounting of warrants as either liabilities or equity instruments. As a result of this material weakness, our management concluded that our internal control over financial reporting was not effective as of December 31, 2010. This material weakness resulted in a material misstatement of our liabilities, non-cash expense relating to the changes in fair value of common stock warrants and accumulated deficit accounts and related financial disclosures and the restatement of our consolidated financial statements for the years ended June 30, 2008, 2009 and 2010 and each of the quarterly periods from September 30, 2008 through September 30, 2010. See Part II — Item 9A, "Controls and Procedures" in our Transition Report on Form 10-KT for the six month period ended December 31, 2010.

A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our annual or interim consolidated financial statements will not be prevented or detected on a timely basis. The effectiveness of any controls or procedures is subject to certain limitations, and as a result, internal control over financial reporting may not prevent or detect misstatements. A control can provide only reasonable, not absolute, assurance that the objectives of the control system will be attained. Although we believe that we have taken actions to remediate this material weakness, we can give no assurance that additional material weaknesses or restatements of financial results will not arise in the future due to a failure to implement and maintain adequate internal control over financial reporting or circumvention of these controls. Additionally, even our improved controls and procedures may not be adequate to prevent or identify errors or irregularities or ensure that our financial statements are prepared in accordance with GAAP. If we cannot maintain and execute adequate internal control over financial reporting or implement required new or improved controls that provide reasonable assurance of the reliability of the financial reporting and preparation of our financial statements for external use, we could suffer harm to our reputation, fail to meet our public reporting requirements on a timely basis, cause investors to lose confidence in our reported financial information or be unable to properly report on our business and the results of our operations, and the trading price of our common stock could be materially adversely affected.

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.

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 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 affect on the market price of our shares.

The market price of shares of our common stock has been volatile, ranging in closing price between $1.34 and $4.20 during the twelve-month period ended March 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 the United States or 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;

Table of Contents

- 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.

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 current or future equity offerings may cause dilution and could cause the price of our common stock to decline.

In addition to the equity being registered in connection with this prospectus, 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. In addition, we are offering an aggregate amount of $20,300,000 of common stock under such registration statement and pursuant to a prospectus supplement first made available on June 16, 2011. We are entitled under our Charter to issue up to 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. As of June 15, 2011, we had issued and outstanding 38,625,225 shares of common stock, 23,209,491 shares of common stock reserved for issuance upon the exercise of current outstanding options and warrants, and 591,226 shares of common stock reserved for issuance of additional grants under our 2009 Omnibus Incentive Plan. Accordingly, we will be able to issue up to 87,574,058 additional shares of common stock and 5,000,000 shares of preferred stock. Sales of our common stock offered through current or future equity offerings, including sales of our securities under this prospectus, may result in substantial dilution to our shareholders. 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.

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

Our Board 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.

Table of Contents

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.

Table of Contents

HOW WE INTEND TO USE THE PROCEEDS

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

Unless otherwise provided in a supplement or amendment to this prospectus, we intend to use any net proceeds from this offering, together with other available funds, for operating costs, 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

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

- through underwriters for resale to the public or investors;
- transactions on the Nasdaq Stock Market or on any national securities exchange or U.S. inter-dealer system of a registered national securities association on which our common stock may be listed or quoted at the time of sale;
- in the over-the-counter market;
- in private transactions and transactions otherwise than on these exchanges or systems or in the over-the-counter market;
- in “at the market” offerings, within the meaning of Rule 415(a)(4) of the Securities Act of 1933, as amended, or the Securities Act, to or through a market maker or into an existing trading market, on an exchange or otherwise;
- in connection with short sales of the shares;

Table of Contents

- by pledge to secure debt and other obligations;
- through the writing of options, whether the options are listed on an options exchange or otherwise;
- in connection with the writing of non-traded and exchange-traded call options, in hedge transactions and in settlement of other transactions in standardized or over-the-counter options;

- through a combination of any of the above transactions; or
- any other method permitted by law.

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

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

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

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

In compliance with the guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8.0% of the aggregate amount of the securities offered to this prospectus.

Table of Contents

We may agree to indemnify underwriters, dealers and agents who participate in the distribution of our securities against various liabilities, including liabilities under the Securities Act. We may also agree to contribute to payments that the underwriters, dealers or agents may be required to make in respect of these liabilities. We may authorize dealers or other persons who act as our agents to solicit offers by various institutions to purchase our securities from us under contracts that provide for payment and delivery on a future date. We may enter into these contracts with commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and others. If we enter into these agreements concerning any series of our securities, we will indicate that in the prospectus supplement or amendment.

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

CERTAIN PROVISIONS OF MICHIGAN LAW AND OF OUR CHARTER AND BYLAWS; 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.

Table of Contents

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.

Transfer Agent and Registrar

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

THE SECURITIES WE MAY OFFER

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

Description of Capital Stock

The following description of our capital stock and certain provisions of our 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; 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, 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

Table of Contents

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.

Preferred Stock

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

The purpose of authorizing our Board to issue preferred stock in one or more series and determine the number of shares in the series and its rights and preferences is to eliminate delays associated with a shareholder vote on specific issuances. Examples of rights and preferences that the Board may fix are:

- dividend rights,
- dividend rates,
- conversion rights,
- voting rights,
- terms of redemption, and
- liquidation preferences.

The issuance of preferred stock, while providing desirable flexibility in connection with possible acquisitions and other corporate purposes, could make it more difficult for a third party to acquire, or could discourage a third party from acquiring, a majority of our outstanding voting stock. The rights of holders of our common stock described above, will be subject to, and may be adversely affected by, the rights of any preferred stock that we may designate and issue in the future.

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

- the title and stated value;
- the number of shares authorized;

- the liquidation preference per share;
- the purchase price;
- the dividend rate, period and payment date, and method of calculation for dividends;

Table of Contents

- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;
- voting rights, if any, of the preferred stock;
- preemptive rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of any material United States federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

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

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

Description of Debt Securities

The paragraphs below describe the general terms and provisions of the debt securities we may issue. When we offer to sell a particular series of debt securities, we will describe the specific terms of the securities in a supplement to this prospectus, including any additional covenants or changes to existing covenants relating to such series. The prospectus supplement also will indicate whether the general terms and provisions described in this prospectus apply to a particular series of debt securities. You should read the actual indenture if you do not fully understand a term or the way we use it in this prospectus.

Table of Contents

We may offer senior or subordinated debt securities. Each series of debt securities may have different terms. The senior debt securities will be issued under one or more senior indentures, dated as of a date prior to such issuance, between us and the trustee identified in the applicable prospectus supplement, as amended or supplemented from time to time. We will refer to any such indenture throughout this prospectus as the “senior indenture.” Any subordinated debt securities will be issued under one or more separate indentures, dated as of a date prior to such issuance, between us and the trustee identified in the applicable prospectus supplement, as amended or supplemented from time to time. We will refer to any such indenture throughout this prospectus as the “subordinated indenture” and to the trustee under the senior or subordinated indenture as the “trustee.” The senior indenture and the subordinated indenture are sometimes collectively referred to in this prospectus as the “indentures.” The indentures will be subject to and governed by the Trust Indenture Act of 1939, as amended. We included copies of the forms of the indentures as exhibits to our registration statement and they are incorporated into this prospectus by reference.

If we issue debt securities at a discount from their principal amount, then, for purposes of calculating the aggregate initial offering price of the offered securities issued under this prospectus, we will include only the initial offering price of the debt securities and not the principal amount of the debt securities.

We have summarized below the material provisions of the indentures and the debt securities, or indicated which material provisions will be described in the related prospectus supplement. The prospectus supplement relating to any particular securities offered will describe the specific terms of the securities, which may be in addition to or different from the general terms summarized in this prospectus. Because the summary in this prospectus and in any prospectus supplement does not contain all of the information that you may find useful, you should read the documents relating to the securities that are described in this prospectus or in any applicable prospectus supplement. Please read "Where You Can Find More Information" to find out how you can obtain a copy of those documents. Except as otherwise indicated, the terms of the indentures are identical. As used under this caption, the term "debt securities" includes the debt securities being offered by this prospectus and all other debt securities issued by us under the indentures.

General

The indentures:

- do not limit the amount of debt securities that we may issue;
- allow us to issue debt securities in one or more series;
- do not require us to issue all of the debt securities of a series at the same time;
- allow us to reopen a series to issue additional debt securities without the consent of the holders of the debt securities of such series; and
- provide that the debt securities will be unsecured, except as may be set forth in the applicable prospectus supplement.

Table of Contents

Unless we give you different information in the applicable prospectus supplement, the senior debt securities will be unsubordinated obligations and will rank equally with all of our other unsecured and unsubordinated indebtedness. Payments on the subordinated debt securities will be subordinated to the prior payment in full of all of our senior indebtedness, as described under "Description of Debt Securities—Subordination" and in the applicable prospectus supplement.

Each indenture provides that we may, but need not, designate more than one trustee under an indenture. Any trustee under an indenture may resign or be removed and a successor trustee may be appointed to act with respect to the series of debt securities administered by the resigning or removed trustee. If two or more persons are acting as trustee with respect to different series of debt securities, each trustee shall be a trustee of a trust under the applicable indenture separate and apart from the trust administered by any other trustee. Except as otherwise indicated in this prospectus, any action described in this prospectus to be taken by each trustee may be taken by each trustee with respect to, and only with respect to, the one or more series of debt securities for which it is trustee under the applicable indenture.

The prospectus supplement for each offering will provide the following terms, where applicable:

- the title of the debt securities and whether they are senior or subordinated;
- the aggregate principal amount of the debt securities being offered, the aggregate principal amount of the debt securities outstanding as of the most recent practicable date and any limit on their aggregate principal amount, including the aggregate principal amount of debt securities authorized;
- the price at which the debt securities will be issued, expressed as a percentage of the principal and, if other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof or, if applicable, the portion of the principal amount of such debt securities that is convertible into common stock or other securities of Aastrom or the method by which any such portion shall be determined;
- if convertible, the terms on which such debt securities are convertible, including the initial conversion price or rate and the conversion period and any applicable limitations on the ownership or transferability of common stock or other securities of Aastrom received on conversion;
- the date or dates, or the method for determining the date or dates, on which the principal of the debt securities will be payable;
- the fixed or variable interest rate or rates of the debt securities, or the method by which the interest rate or rates is determined;
- the date or dates, or the method for determining the date or dates, from which interest will accrue;

Table of Contents

- the dates on which interest will be payable;
- the record dates for interest payment dates, or the method by which such dates will be determine;
- the persons to whom interest will be payable;
- the basis upon which interest will be calculated if other than that of a 360-day year of twelve 30-day months;

- any make-whole amount, which is the amount in addition to principal and interest that is required to be paid to the holder of a debt security as a result of any optional redemption or accelerated payment of such debt security, or the method for determining the make-whole amount;
- the place or places where the principal of, and any premium or make-whole amount, and interest on, the debt securities will be payable;
- where the debt securities may be surrendered for registration of transfer or conversion or exchange;
- where notices or demands to or upon us in respect of the debt securities and the applicable indenture may be served;
- the times, prices and other terms and conditions upon which we may redeem the debt securities;
- any obligation we have to redeem, repay or purchase the debt securities pursuant to any sinking fund or analogous provision or at the option of holders of the debt securities, and the times and prices at which we must redeem, repay or purchase the debt securities as a result of such obligation;
- the currency or currencies in which the debt securities are denominated and payable if other than United States dollars, which may be a foreign currency or units of two or more foreign currencies or a composite currency or currencies and the terms and conditions relating thereto, and the manner of determining the equivalent of such foreign currency in United States dollars;
- whether the principal of, and any premium or make-whole amount, or interest on, the debt securities of the series are to be payable, at our election or at the election of a holder, in a currency or currencies other than that in which the debt securities are denominated or stated to be payable, and other related terms and conditions;
- whether the amount of payments of principal of, and any premium or make-whole amount, or interest on, the debt securities may be determined according to an index, formula or other method and how such amounts will be determined;
- whether the debt securities will be in registered form, bearer form or both and (i) if in registered form, the person to whom any interest shall be payable, if other than the person in whose name the security is registered at the close of business on the regular record date for such interest, or (ii) if in bearer form, the manner in which, or the person to whom, any interest on the security shall be payable if otherwise than upon presentation and surrender upon maturity;

Table of Contents

- any restrictions applicable to the offer, sale or delivery of securities in bearer form and the terms upon which securities in bearer form of the series may be exchanged for securities in registered form of the series and vice versa, if permitted by applicable laws and regulations;
- whether any debt securities of the series are to be issuable initially in temporary global form and whether any debt securities of the series are to be issuable in permanent global form with or without coupons and, if so, whether beneficial owners of interests in any such permanent global security may, or shall be required to, exchange their interests for other debt securities of the series, and the manner in which interest shall be paid;
- the identity of the depositary for securities in registered form, if such series are to be issuable as a global security;
- the date as of which any debt securities in bearer form or in temporary global form shall be dated if other than the original issuance date of the first security of the series to be issued;
- the applicability, if any, of the defeasance and covenant defeasance provisions described in this prospectus or in the applicable indenture;
- whether and under what circumstances we will pay any additional amounts on the debt securities in respect of any tax, assessment or governmental charge and, if so, whether we will have the option to redeem the debt securities in lieu of making such a payment;
- whether and under what circumstances the debt securities being offered are convertible into common stock or other securities of Aastrom, as the case may be, including the conversion price or rate and the manner or calculation thereof;
- the circumstances, if any, specified in the applicable prospectus supplement, under which beneficial owners of interests in the global security may obtain definitive debt securities and the manner in which payments on a permanent global debt security will be made if any debt securities are issuable in temporary or permanent global form;
- any provisions granting special rights to holders of securities upon the occurrence of such events as specified in the applicable prospectus supplement;
- if the debt securities of such series are to be issuable in definitive form only upon receipt of certain certificates or other documents or satisfaction of other conditions, then the form and/or terms of such certificates, documents or conditions;
- the name of the applicable trustee and the nature of any material relationship with us or any of our affiliates, and the percentage of debt securities of the class necessary to require the trustee to take action;
- any deletions from, modifications of or additions to our events of default or covenants with regard to such debt securities and any change in the right of any trustee or any of the holders to declare the principal amount of any of such debt securities due and payable;
- applicable CUSIP numbers; and
- any other terms of such debt securities not inconsistent with the provisions of the applicable indenture.

We may issue debt securities that provide for less than the entire principal amount thereof to be payable upon declaration of acceleration of the maturity of the debt securities. We refer to any such debt securities throughout this prospectus as "original issue discount securities." The applicable prospectus supplement will describe the United States federal income tax consequences and other relevant considerations applicable to original issue discount securities.

We also may issue indexed debt securities. Payments of principal of, and premium and interest on, indexed debt securities are determined with reference to the rate of exchange between the currency or currency unit in which the debt security is denominated and any other currency or currency unit specified by us, to the relationship between two or more currencies or currency units or by other similar methods or formulas specified in the prospectus supplement.

Except as described under "—Merger, Consolidation or Sale of Assets" or as may be set forth in any prospectus supplement, the debt securities will not contain any provisions that (i) would limit our ability to incur indebtedness or (ii) would afford holders of debt securities protection in the event of (a) a highly leveraged or similar transaction involving us, or (b) a change of control or reorganization, restructuring, merger or similar transaction involving us that may adversely affect the holders of the debt securities. In the future, we may enter into transactions, such as the sale of all or substantially all of our assets or a merger or consolidation, that may have an adverse effect on our ability to service our indebtedness, including the debt securities, by, among other things, substantially reducing or eliminating our assets.

Neither the MBCA nor our governing instruments define the term "substantially all" as it relates to the sale of assets. Additionally, Michigan cases interpreting the term "substantially all" rely upon the facts and circumstances of each particular case. Consequently, to determine whether a sale of "substantially all" of our assets has occurred, a holder of debt securities must review the financial and other information that we have disclosed to the public.

We will provide you with more information in the applicable prospectus supplement regarding any deletions, modifications, or additions to the events of default or covenants that are described below, including any addition of a covenant or other provision providing event risk or similar protection.

Payment

Unless we give you different information in the applicable prospectus supplement, the principal of, and any premium or make-whole amount, and interest on, any series of the debt securities will be payable at the corporate trust office of the trustee. We will provide you with the address of the trustee in the applicable prospectus supplement. We may also pay interest by mailing a check to the address of the person entitled to it as it appears in the applicable register for the debt securities or by wire transfer of funds to that person at an account maintained within the United States.

All monies that we pay to a paying agent or a trustee for the payment of the principal of, and any premium or make-whole amount, or interest on, any debt security will be repaid to us if unclaimed at the end of two years after the obligation underlying payment becomes due and payable. After funds have been returned to us, the holder of the debt security may look only to us for payment, without payment of interest for the period which we hold the funds.

Denomination, Interest, Registration and Transfer

Unless otherwise described in the applicable prospectus supplement, the debt securities of any series will be issuable in denominations of $1,000 and integral multiples of $1,000.

Subject to the limitations imposed upon debt securities that are evidenced by a computerized entry in the records of a depository company rather than by physical delivery of a note, a holder of debt securities of any series may:

- exchange them for any authorized denomination of other debt securities of the same series and of a like aggregate principal amount and kind upon surrender of such debt securities at the corporate trust office of the applicable trustee or at the office of any transfer agent that we designate for such purpose; and

- surrender them for registration of transfer or exchange at the corporate trust office of the applicable trustee or at the office of any transfer agent that we designate for such purpose.

Every debt security surrendered for registration of transfer or exchange must be duly endorsed or accompanied by a written instrument of transfer satisfactory to the applicable trustee or transfer agent. Payment of a service charge will not be required for any registration of transfer or exchange of any debt securities, but we or the trustee may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection therewith. If in addition to the applicable trustee, the applicable prospectus supplement refers to any transfer agent initially designated by us for any series of debt securities, we may at any time rescind the designation of any such transfer agent or approve a change in the location through which any such transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for such series. We may at any time designate additional transfer agents for any series of debt securities.

Neither we, nor any trustee, will be required to:

- issue, register the transfer of or exchange debt securities of any series during a period beginning at the opening of business 15 days before the day that the notice of redemption of any debt securities selected for redemption is mailed and ending at the close of business on the day of such mailing;

- register the transfer of or exchange any debt security, or portion thereof, so selected for redemption, in whole or in part, except the unredeemed portion of any debt security being redeemed in part; and

- issue, register the transfer of or exchange any debt security that has been surrendered for repayment at the option of the holder, except the portion, if any, of such debt security not to be so repaid.

Table of Contents

Merger, Consolidation or Sale of Assets

The indentures provide that we may, without the consent of the holders of any outstanding debt securities, (i) consolidate with, (ii) sell, lease or convey all or substantially all of our assets to, or (iii) merge with or into, any other entity provided that:

- either we are the continuing entity, or the successor entity, if other than us, assumes the obligations (a) to pay the principal of, and any premium or make-whole amount, and interest on, all of the debt securities and (b) to duly perform and observe all of the covenants and conditions contained in each indenture;
- after giving effect to the transaction, there is no event of default under the indentures and no event which, after notice or the lapse of time, or both, would become such an event of default, occurs and continues; and
- an officers' certificate and legal opinion covering such conditions are delivered to each applicable trustee.

Covenants

Existence. Except as described under "—Merger, Consolidation or Sale of Assets," the indentures require us to do or cause to be done all things necessary to preserve and keep in full force and effect our existence, rights and franchises. However, the indentures do not require us to preserve any right or franchise if we determine that any right or franchise is no longer desirable in the conduct of our business.

Payment of taxes and other claims. The indentures require us to pay, discharge or cause to be paid or discharged, before they become delinquent (i) all taxes, assessments and governmental charges levied or imposed on us, our subsidiaries or our or our subsidiaries' income, profits or property, and (ii) all lawful claims for labor, materials and supplies which, if unpaid, might by law become a lien upon our property or the property of our subsidiaries. However, we will not be required to pay, discharge or cause to be paid or discharged any such tax, assessment, charge or claim whose amount, applicability or validity is being contested in good faith by appropriate proceedings.

Provision of financial information. The indentures require us to (i) within 15 days of each of the respective dates by which we are required to file our annual reports, quarterly reports and other documents with the SEC, file with the trustee copies of the annual report, quarterly report and other documents that we file with the SEC under Section 13 or 15(d) of the Exchange Act, (ii) file with the trustee and the SEC any additional information, documents and reports regarding compliance by us with the conditions and covenants of the indentures, as required, (iii) within 30 days after the filing with the trustee, mail to all holders of debt securities, as their names and addresses appear in the applicable register for such debt securities, without cost to such holders, summaries of any documents and reports required to be filed by us pursuant to (i) and (ii) above, and (iv) supply, promptly upon written request and payment of the reasonable cost of duplication and delivery, copies of such documents to any prospective holder.

Additional covenants. The applicable prospectus supplement will set forth any additional covenants of Aastrom relating to any series of debt securities.

Table of Contents

Events of Default, Notice and Waiver

Unless the applicable prospectus supplement states otherwise, when we refer to "events of default" as defined in the indentures with respect to any series of debt securities, we mean:

- default in the payment of any installment of interest on any debt security of such series continuing for 30 days;
- default in the payment of principal of, or any premium or make-whole amount on, any debt security of such series for five business days at its stated maturity;
- default in making any sinking fund payment as required for any debt security of such series for five business days;
- default in the performance or breach of any covenant or warranty in the debt securities or in the indenture by Aastrom continuing for 60 days after written notice as provided in the applicable indenture, but not of a covenant added to the indenture solely for the benefit of a series of debt securities issued thereunder other than such series;
- a default under any bond, debenture, note, mortgage, indenture or instrument:

  (i) having an aggregate principal amount of at least $30,000,000; or

  (ii) under which there may be issued, secured or evidenced any existing or later created indebtedness for money borrowed by us or our subsidiaries, if we are directly responsible or liable as obligor or guarantor,

if the default results in the indebtedness becoming or being declared due and payable prior to the date it otherwise would have, without such indebtedness having been discharged, or such acceleration having been rescinded or annulled, within 30 days after notice to the issuing company specifying such default. Such notice shall be given to us by the trustee, or to us and the trustee by the holders of at least 10% in principal amount of the outstanding debt securities of that series. The written notice shall specify such default and require us to cause such indebtedness to be discharged or cause such acceleration to be rescinded or annulled and shall state that such notice is a "Notice of Default" under such indenture;

- bankruptcy, insolvency or reorganization, or court appointment of a receiver, liquidator or trustee of Aastrom or any significant subsidiary of Aastrom; and

- any other event of default provided with respect to a particular series of debt securities.

When we use the term “significant subsidiary,” we refer to the meaning ascribed to such term in Rule 1-02 of Regulation S-X promulgated under the Securities Act.

If an event of default occurs and is continuing with respect to debt securities of any series outstanding, then the applicable trustee or the holders of 25% or more in principal amount of the debt securities of that series will have the right to declare the principal amount of all the debt securities of that series to be due and payable. If the debt securities of that series are original issue discount securities or indexed securities, then the applicable trustee or the holders of 25% or more in principal amount of the debt securities of that series will have the right to declare the portion of the principal amount as may be specified in the terms thereof to be due and payable. However, at any time after such a declaration of acceleration has been made, but before a judgment or decree for payment of the money due has been obtained by the applicable trustee,

Table of Contents

the holders of at least a majority in principal amount of outstanding debt securities of such series or of all debt securities then outstanding under the applicable indenture may rescind and annul such declaration and its consequences if:

- we have deposited with the applicable trustee all required payments of the principal, any premium or make-whole amount, interest and, to the extent permitted by law, interest on overdue installment of interest, plus applicable fees, expenses, disbursements and advances of the applicable trustee; and

- all events of default, other than the non-payment of accelerated principal, or a specified portion thereof, and any premium or make-whole amount, have been cured or waived.

The indentures also provide that the holders of at least a majority in principal amount of the outstanding debt securities of any series or of all debt securities then outstanding under the applicable indenture may, on behalf of all holders, waive any past default with respect to such series and its consequences, except a default:

- in the payment of the principal, any premium or make-whole amount, or interest;

- in respect of a covenant or provision contained in the applicable indenture that cannot be modified or amended without the consent of the holders of the outstanding debt security that is affected by the default; or

- in respect of a covenant or provision for the benefit or protection of the trustee, without its express written consent.

The indentures require each trustee to give notice to the holders of debt securities within 90 days of a default unless such default has been cured or waived. However, the trustee may withhold notice if specified persons of such trustee consider such withholding to be in the interest of the holders of debt securities. The trustee may not withhold notice of a default in the payment of principal, any premium or interest on any debt security of such series or in the payment of any sinking fund installment in respect of any debt security of such series.

The indentures provide that holders of debt securities of any series may not institute any proceedings, judicial or otherwise, with respect to such indenture or for any remedy under the indenture, unless the trustee fails to act for a period of 60 days after the trustee has received a written request to institute proceedings in respect of an event of default from the holders of 25% or more in principal amount of the outstanding debt securities of such series, as well as an offer of indemnity reasonably satisfactory to the trustee. However, this provision will not prevent any holder of debt securities from instituting suit for the enforcement of payment of the principal of, and any premium or make-whole amount, and interest on, such debt securities at the respective due dates thereof.

The indentures provide that, subject to provisions in each indenture relating to its duties in the case of a default, a trustee has no obligation to exercise any of its rights or powers at the request or direction of any holders of any series of debt securities then outstanding under the indenture, unless the holders have offered to the trustee reasonable security or indemnity. The holders of at least a majority in principal amount of the outstanding debt securities of any series or of all debt securities then outstanding under an indenture shall have the right to direct the time, method and place of conducting any proceeding for any remedy available to the applicable

Table of Contents

trustee, or of exercising any trust or power conferred upon such trustee. However, a trustee may refuse to follow any direction which:

- is in conflict with any law or the applicable indenture;

- may involve the trustee in personal liability; or

- may be unduly prejudicial to the holders of debt securities of the series not joining the proceeding.

Within 120 days after the close of each fiscal year, we will be required to deliver to each trustee a certificate, signed by one of our several specified officers, stating whether or not that officer has knowledge of any default under the applicable indenture. If the officer has knowledge of any default, the notice must specify the nature and status of the default.

Modification of the Indentures

The indentures provide that modifications and amendments may be made only with the consent of the affected holders of at least a majority in principal amount of all outstanding debt securities issued under that indenture. However, no such modification or amendment may, without the consent of the holders of the debt securities affected by the modification or amendment:

- change the stated maturity of the principal of, or any premium or make-whole amount on, or any installment of principal of or interest on, any such debt security;
- reduce the principal amount of, the rate or amount of interest on, or any premium or make-whole amount payable on redemption of, any such debt security;
- reduce the amount of principal of an original issue discount security that would be due and payable upon declaration of acceleration of the maturity thereof or would be provable in bankruptcy, or adversely affect any right of repayment of the holder of any such debt security;
- change the place of payment or the coin or currency for payment of principal of, or any premium or make-whole amount, or interest on, any such debt security;
- impair the right to institute suit for the enforcement of any payment on or with respect to any such debt security;
- reduce the percentage in principal amount of any outstanding debt securities necessary to modify or amend the applicable indenture with respect to such debt securities, to waive compliance with particular provisions thereof or defaults and consequences thereunder or to reduce the quorum or voting requirements set forth in the applicable indenture; and
- modify any of the foregoing provisions or any of the provisions relating to the waiver of particular past defaults or covenants, except to increase the required percentage to effect such action or to provide that some of the other provisions may not be modified or waived without the consent of the holder of such debt security.

The holders of a majority in aggregate principal amount of the outstanding debt securities of each series may, on behalf of all holders of debt securities of that series, waive, insofar as that series is concerned, our compliance with material restrictive covenants of the applicable indenture.

Table of Contents

We and our respective trustee may make modifications and amendments of an indenture without the consent of any holder of debt securities for any of the following purposes:

- to evidence the succession of another person to us as obligor under such indenture;
- to add to our covenants for the benefit of the holders of all or any series of debt securities or to surrender any right or power conferred upon us in such indenture;
- to add events of default for the benefit of the holders of all or any series of debt securities;
- to add or change any provisions of an indenture (i) to change or eliminate restrictions on the payment of principal of, or premium or make-whole amount, or interest on, debt securities in bearer form, or (ii) to permit or facilitate the issuance of debt securities in uncertificated form, provided that such action shall not adversely affect the interests of the holders of the debt securities of any series in any material respect;
- to change or eliminate any provisions of an indenture, provided that any such change or elimination shall become effective only when there are no debt securities outstanding of any series created prior thereto which are entitled to the benefit of such provision;
- to secure the debt securities;
- to establish the form or terms of debt securities of any series;
- to provide for the acceptance of appointment by a successor trustee or facilitate the administration of the trusts under an indenture by more than one trustee;
- to cure any ambiguity, defect or inconsistency in an indenture, provided that such action shall not adversely affect the interests of holders of debt securities of any series issued under such indenture; and
- to supplement any of the provisions of an indenture to the extent necessary to permit or facilitate defeasance and discharge of any series of such debt securities, provided that such action shall not adversely affect the interests of the holders of the outstanding debt securities of any series.

Voting

The indentures provide that in determining whether the holders of the requisite principal amount of outstanding debt securities of a series have given any request, demand, authorization, direction, notice, consent or waiver under the indentures or whether a quorum is present at a meeting of holders of debt securities:

- the principal amount of an original issue discount security that shall be deemed to be outstanding shall be the amount of the principal thereof that would be due and payable as of the date of such determination upon declaration of acceleration of the maturity thereof;
- the principal amount of any debt security denominated in a foreign currency that shall be deemed outstanding shall be the United States dollar equivalent, determined on the issue date for such debt security, of the principal amount or, in the case of an original issue discount security, the United States dollar equivalent on the issue date of such debt security of the amount determined as provided in the preceding bullet point;

Table of Contents

- the principal amount of an indexed security that shall be deemed outstanding shall be the principal face amount of such indexed security at original issuance, unless otherwise provided for such indexed security under such indenture; and

- debt securities owned by us or any other obligor upon the debt securities or by any affiliate of ours or of such other obligor shall be disregarded.

The indentures contain provisions for convening meetings of the holders of debt securities of a series. A meeting will be permitted to be called at any time by the applicable trustee, and also, upon request, by us or the holders of at least 25% in principal amount of the outstanding debt securities of such series, in any such case upon notice given as provided in such indenture. Except for any consent that must be given by the holder of each debt security affected by the modifications and amendments of an indenture described above, any resolution presented at a meeting or adjourned meeting duly reconvened at which a quorum is present may be adopted by the affirmative vote of the holders of a majority of the aggregate principal amount of the outstanding debt securities of that series represented at such meeting.

Notwithstanding the preceding paragraph, except as referred to above, any resolution relating to a request, demand, authorization, direction, notice, consent, waiver or other action that may be made, given or taken by the holders of a specified percentage, which is less than a majority of the aggregate principal amount of the outstanding debt securities of a series, may be adopted at a meeting or adjourned meeting duly reconvened at which a quorum is present by the affirmative vote of such specified percentage.

Any resolution passed or decision taken at any properly held meeting of holders of debt securities of any series will be binding on all holders of such series. The quorum at any meeting called to adopt a resolution, and at any reconvened meeting, will be persons holding or representing a majority in principal amount of the outstanding debt securities of a series. However, if any action is to be taken relating to a consent or waiver which may be given by the holders of at least a specified percentage in principal amount of the outstanding debt securities of a series, the persons holding such percentage will constitute a quorum.

Notwithstanding the foregoing provisions, the indentures provide that if any action is to be taken at a meeting with respect to any request, demand, authorization, direction, notice, consent, waiver or other action that such indenture expressly provides may be made, given or taken by the holders of a specified percentage in principal amount of all outstanding debt securities affected by such action, or of the holders of such series and one or more additional series:

- there shall be no minimum quorum requirement for such meeting; and

- the principal amount of the outstanding debt securities of such series that vote in favor of such request, demand, authorization, direction, notice, consent, waiver or other action shall be taken account in determining whether such request, demand, authorization, direction, notice, consent, waiver or other action has been made, given or taken under such indenture.

Table of Contents

Subordination

Unless otherwise provided in the applicable prospectus supplement, subordinated debt securities will be subject to the following subordination provisions.

Upon any distribution to our creditors in a liquidation, dissolution or reorganization, the payment of the principal of and interest on any subordinated debt securities will be subordinated to the extent provided in the applicable indenture in right of payment to the prior payment in full of all senior debt. However, our obligation to make payments of the principal of and interest on such subordinated debt securities otherwise will not be affected. No payment of principal or interest will be permitted to be made on subordinated debt securities at any time if a default on senior debt exists that permits the holders of such senior debt to accelerate its maturity and the default is the subject of judicial proceedings or we receive notice of the default. After all senior debt is paid in full and until the subordinated debt securities are paid in full, holders of subordinated debt securities will be subrogated to the rights of holders of senior debt to the extent that distributions otherwise payable to holders of subordinated debt securities have been applied to the payment of senior debt. The subordinated indenture will not restrict the amount of senior debt or other indebtedness of Aastrom and its subsidiaries. As a result of these subordination provisions, in the event of a distribution of assets upon insolvency, holders of subordinated debt securities may recover less, ratably, than our general creditors.

The term “senior debt” will be defined in the applicable indenture as the principal of and interest on, or substantially similar payments to be made by us in respect of, other outstanding indebtedness, whether outstanding at the date of execution of the applicable indenture or subsequently incurred, created or assumed. The prospectus supplement may include a description of additional terms implementing the subordination feature.

No restrictions will be included in any indenture relating to subordinated debt securities upon the creation of additional senior debt.

If this prospectus is being delivered in connection with the offering of a series of subordinated debt securities, the accompanying prospectus supplement or the information incorporated in this prospectus by reference will set forth the approximate amount of senior debt outstanding as of the end of our most recent fiscal quarter.

Discharge, Defeasance and Covenant Defeasance

Unless otherwise indicated in the applicable prospectus supplement, the indentures allow us to discharge our obligations to holders of any series of debt securities issued under any indenture when:

- either (i) all securities of such series have already been delivered to the applicable trustee for cancellation; or (ii) all securities of such series have not already been delivered to the applicable trustee for cancellation but (a) have become due and payable, (b) will become due and payable within one

year, or (c) if redeemable at our option, are to be redeemed within one year, and we have irrevocably deposited with the applicable trustee, in trust, funds in such currency or currencies, currency unit or units

Table of Contents

or composite currency or currencies in which such debt securities are payable, an amount sufficient to pay the entire indebtedness on such debt securities in respect of principal and any premium or make-whole amount, and interest to the date of such deposit if such debt securities have become due and payable or, if they have not, to the stated maturity or redemption date;

- we have paid or caused to be paid all other sums payable; and

- an officers' certificate and an opinion of counsel stating the conditions to discharging the debt securities have been satisfied has been delivered to the trustee.

Unless otherwise indicated in the applicable prospectus supplement, the indentures provide that, upon our irrevocable deposit with the applicable trustee, in trust, of an amount, in such currency or currencies, currency unit or units or composite currency or currencies in which such debt securities are payable at stated maturity, or government obligations, or both, applicable to such debt securities, which through the scheduled payment of principal and interest in accordance with their terms will provide money in an amount sufficient to pay the principal of, and any premium or make-whole amount, and interest on, such debt securities, and any mandatory sinking fund or analogous payments thereon, on the scheduled due dates therefor, the issuing company may elect either:

- to defease and be discharged from any and all obligations with respect to such debt securities; or

- to be released from its obligations with respect to such debt securities under the applicable indenture or, if provided in the applicable prospectus supplement, its obligations with respect to any other covenant, and any omission to comply with such obligations shall not constitute an event of default with respect to such debt securities.

Notwithstanding the above, we may not elect to defease and be discharged from the obligation to pay any additional amounts upon the occurrence of particular events of tax, assessment or governmental charge with respect to payments on such debt securities and the obligations to register the transfer or exchange of such debt securities, to replace temporary or mutilated, destroyed, lost or stolen debt securities, to maintain an office or agency in respect of such debt securities, or to hold monies for payment in trust.

The indentures only permit us to establish the trust described in the paragraph above if, among other things, we have delivered to the applicable trustee an opinion of counsel to the effect that the holders of such debt securities will not recognize income, gain or loss for United States federal income tax purposes as a result of such defeasance or covenant defeasance and will be subject to United States federal income tax on the same amounts, in the same manner and at the same times as would have been the case if such defeasance or covenant defeasance had not occurred. Such opinion of counsel, in the case of defeasance, will be required to refer to and be based upon a ruling received from or published by the Internal Revenue Service or a change in applicable United States federal income tax law occurring after the date of the indenture. In the event of such defeasance, the holders of such debt securities would be able to look only to such trust fund for payment of principal, any premium or make-whole amount, and interest.

Table of Contents

When we use the term "government obligations," we mean securities that are:

- direct obligations of the United States or the government that issued the foreign currency in which the debt securities of a particular series are payable, for the payment of which its full faith and credit is pledged; or

- obligations of a person controlled or supervised by and acting as an agency or instrumentality of the United States or other government that issued the foreign currency in which the debt securities of such series are payable, the payment of which is unconditionally guaranteed as a full faith and credit obligation by the United States or such other government, which are not callable or redeemable at the option of the issuer thereof and shall also include a depository receipt issued by a bank or trust company as custodian with respect to any such government obligation or a specific payment of interest on or principal of any such government obligation held by such custodian for the account of the holder of a depository receipt. However, except as required by law, such custodian is not authorized to make any deduction from the amount payable to the holder of such depository receipt from any amount received by the custodian in respect of the government obligation or the specific payment of interest on or principal of the government obligation evidenced by such depository receipt.

Unless otherwise provided in the applicable prospectus supplement, if after we have deposited funds and/or government obligations to effect defeasance or covenant defeasance with respect to debt securities of any series, (i) the holder of a debt security of such series is entitled to, and does, elect under the terms of the applicable indenture or the terms of such debt security to receive payment in a currency, currency unit or composite currency other than that in which such deposit has been made in respect of such debt security, or (ii) a conversion event occurs in respect of the currency, currency unit or composite currency in which such deposit has been made, the indebtedness represented by such debt security will be deemed to have been, and will be, fully discharged and satisfied through the payment of the principal of, and premium or make-whole amount, and interest on, such debt security as they become due out of the proceeds yielded by converting the amount so deposited in respect of such debt security into the currency, currency unit or composite currency in which such debt security becomes payable as a result of such election or such cessation of usage based on the applicable market exchange rate.

When we use the term "conversion event," we mean the cessation of use of:

- a currency, currency unit or composite currency both by the government of the country that issued such currency and for the settlement of transactions by a central bank or other public institutions of or within the international banking community;

- the European Currency Unit both within the European Monetary System and for the settlement of transactions by public institutions of or within the European Communities; or

- any currency unit or composite currency other than the European Currency Unit for the purposes for which it was established.

Unless otherwise provided in the applicable prospectus supplement, all payments of principal of, and any premium or make-whole amount, and interest on, any debt security that is payable in a foreign currency that ceases to be used by its government of issuance shall be made in United States dollars.

Table of Contents

In the event that (i) we effect covenant defeasance with respect to any debt securities and (ii) those debt securities are declared due and payable because of the occurrence of any event of default, the amount in the currency, currency unit or composite currency in which such debt securities are payable, and government obligations on deposit with the applicable trustee, will be sufficient to pay amounts due on such debt securities at the time of their stated maturity but may not be sufficient to pay amounts due on such debt securities at the time of the acceleration resulting from such event of default. However, the issuing company would remain liable to make payments of any amounts due at the time of acceleration.

The applicable prospectus supplement may further describe the provisions, if any, permitting such defeasance or covenant defeasance, including any modifications to the provisions described above, with respect to the debt securities of or within a particular series.

Conversion Rights

The terms and conditions, if any, upon which the debt securities are convertible into common stock or other securities of Aastrom will be set forth in the applicable prospectus supplement. The terms will include whether the debt securities are convertible into shares of common stock or other securities of Aastrom, the conversion price, or manner of calculation thereof, the conversion period, provisions as to whether conversion will be at the issuing company's option or the option of the holders, the events requiring an adjustment of the conversion price and provisions affecting conversion in the event of the redemption of the debt securities and any restrictions on conversion.

Global Securities

The debt securities of a series may be issued in whole or in part in the form of one or more global securities that will be deposited with, or on behalf of, a depository identified in the applicable prospectus supplement relating to such series. Global securities, if any, issued in the United States are expected to be deposited with The Depository Trust Company, or DTC, as depository. We may issue global securities in either registered or bearer form and in either temporary or permanent form. We will describe the specific terms of the depository arrangement with respect to a series of debt securities in the applicable prospectus supplement relating to such series. We expect that unless the applicable prospectus supplement provides otherwise, the following provisions will apply to depository arrangements.

Once a global security is issued, the depository for such global security or its nominee will credit on its book-entry registration and transfer system the respective principal amounts of the individual debt securities represented by such global security to the accounts of participants that have accounts with such depository. Such accounts shall be designated by the underwriters, dealers or agents with respect to such debt securities or by us if we offer such debt securities directly. Ownership of beneficial interests in such global security will be limited to participants with the depository or persons that may hold interests through those participants.

Table of Contents

We expect that, under procedures established by DTC, ownership of beneficial interests in any global security for which DTC is the depository will be shown on, and the transfer of that ownership will be effected only through, records maintained by DTC or its nominee, with respect to beneficial interests of participants with the depository, and records of participants, with respect to beneficial interests of persons who hold through participants with the depository. Neither we nor the trustee will have any responsibility or liability for any aspect of the records of DTC or for maintaining, supervising or reviewing any records of DTC or any of its participants relating to beneficial ownership interests in the debt securities. The laws of some states require that certain purchasers of securities take physical delivery of such securities in definitive form. Such limits and laws may impair the ability to own, pledge or transfer beneficial interest in a global security.

So long as the depository for a global security or its nominee is the registered owner of such global security, such depository or such nominee, as the case may be, will be considered the sole owner or holder of the debt securities represented by the global security for all purposes under the applicable indenture. Except as described below or in the applicable prospectus supplement, owners of beneficial interest in a global security will not be entitled to have any of the individual debt securities represented by such global security registered in their names, will not receive or be entitled to receive physical delivery of any such debt securities in definitive form and will not be considered the owners or holders thereof under the applicable indenture. Beneficial owners of debt securities evidenced by a global security will not be considered the owners or holders thereof under the applicable indenture for any purpose, including with respect to the giving of any direction, instructions or approvals to the trustee under the indenture. Accordingly, each person owning a beneficial interest in a global security with respect to which DTC is the depository must rely on the procedures of DTC and, if such person is not a participant with the depository, on the procedures of the participant through which such person owns its interests, to exercise any rights of a holder under the applicable indenture. We understand that, under existing industry practice, if DTC requests any action of holders or if an owner of a beneficial interest in a global security desires to give or take any action which a holder is entitled to give or take under the applicable indenture, DTC would authorize the participants holding the relevant beneficial interest to give or take such action, and such participants would authorize beneficial owners through such participants to give or take such actions or would otherwise act upon the instructions of beneficial owners holding through them.

Payments of principal of, and any premium or make-whole amount, and interest on, individual debt securities represented by a global security registered in the name of a depository or its nominee will be made to or at the direction of the depository or its nominee, as the case may be, as the registered owner of the global security under the applicable indenture. Under the terms of the applicable indenture, we and the trustee may treat the persons in whose name debt securities, including a global security, are registered as the owners thereof for the purpose of receiving such payments. Consequently, neither we nor the

trustee have or will have any responsibility or liability for the payment of such amounts to beneficial owners of debt securities including principal, any premium or make-whole amount, or interest. We believe, however, that it is currently the policy of DTC to immediately credit the accounts of relevant participants with such payments, in amounts proportionate to their respective holdings of beneficial interests in the relevant global security as shown on the records of DTC or its nominee. We also expect that payments by participants to owners of beneficial interests in such global security held through such participants will be governed by standing instructions and customary practices, as is the case with securities held for the account of customers in bearer form or registered in street name, and will be the responsibility of such participants. Redemption notices with respect to any debt securities represented by a global security will be sent to the depository or its nominee. If less

Table of Contents

than all of the debt securities of any series are to be redeemed, we expect the depository to determine the amount of the interest of each participant in such debt securities to be redeemed to be determined by lot. Neither we, the trustee, any paying agent nor the security registrar for such debt securities will have any responsibility or liability for any aspect of the records relating to or payments made on account of beneficial ownership interests in the global security for such debt securities or for maintaining any records with respect thereto.

Neither we nor the trustee will be liable for any delay by the holders of a global security or the depository in identifying the beneficial owners of debt securities, and we and the trustee may conclusively rely on, and will be protected in relying on, instructions from the holder of a global security or the depository for all purposes. The rules applicable to DTC and its participants are on file with the SEC.

If a depository for any debt securities is at any time unwilling, unable or ineligible to continue as depository and we do not appoint a successor depository within 90 days, we will issue individual debt securities in exchange for the global security representing such debt securities. In addition, we may at any time and our sole discretion, subject to any limitations described in the applicable prospectus supplement relating to such debt securities, determine not to have any of such debt securities represented by one or more global securities and in such event will issue individual debt securities in exchange for the global security or securities representing such debt securities. Individual debt securities so issued will be issued in denominations of $1,000 and integral multiples of $1,000.

The debt securities of a series may also be issued in whole or in part in the form of one or more bearer global securities that will be deposited with a depository, or with a nominee for such depository, identified in the applicable prospectus supplement. Any such bearer global securities may be issued in temporary or permanent form. The specific terms and procedures, including the specific terms of the depositary arrangement, with respect to any portion of a series of debt securities to be represented by one or more bearer global securities will be described in the applicable prospectus supplement.

No Recourse

There is no recourse under any obligation, covenant or agreement in the applicable indenture or with respect to any security against any of our or our successor’s past, present or future shareholders, employees, officers or directors.

Description of Warrants

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

Table of Contents

General

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

We will evidence each series of warrants by warrant certificates that we will issue under a separate warrant agreement. We will enter into the warrant agreement with a warrant agent. We will indicate the name and address of the warrant agent in the applicable prospectus supplement relating to a particular series of warrants.

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

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;

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

Table of Contents

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

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

Exercise of Warrants

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

Holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent upon exercise.

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

Enforceability of Rights By Holders of Warrants

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

Table of Contents

Description of Units

We may issue units comprised of shares of common stock, shares of preferred stock, debt securities and warrants in any combination. We may issue units in such amounts and in as many distinct series as we wish. This section outlines certain provisions of the units that we may issue. If we issue units, they will be issued under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. The information described in this section may not be complete in all respects and is qualified entirely by reference to the unit agreement with respect to the units of any particular series. The specific terms of any series of units offered will be described in the applicable prospectus supplement. If so described in a particular supplement, the specific terms of any series of units may differ from the general description of terms presented below. We urge you to read any prospectus supplement related to any series of units we may offer, as well as the complete unit agreement and unit certificate that contain the terms of the units. If we issue units, forms of unit agreements and unit certificates relating to such units will be incorporated by reference as exhibits to the registration statement, which includes this prospectus.

Each unit that we may issue will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities

included in the unit may not be held or transferred separately, at any time or at any time before a specified date. The applicable prospectus supplement may describe:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement;
- the price or prices at which such units will be issued;
- the applicable United States federal income tax considerations relating to the units;
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and
- any other terms of the units and of the securities comprising the units.

The provisions described in this section, as well as those described under “Description of Capital Stock,” “Description of Debt Securities” and “Description of Warrants” will apply to the securities included in each unit, to the extent relevant and as may be updated in any prospectus supplements.

Issuance in Series

We may issue units in such amounts and in as many distinct series as we wish. This section summarizes terms of the units that apply generally to all series. Most of the financial and other specific terms of your series will be described in the applicable prospectus supplement.

Table of Contents

Unit Agreements

We will issue the units under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. We may add, replace or terminate unit agents from time to time. We will identify the unit agreement under which each series of units will be issued and the unit agent under that agreement in the applicable prospectus supplement.

The following provisions will generally apply to all unit agreements unless otherwise stated in the applicable prospectus supplement.

Modification without Consent

We and the applicable unit agent may amend any unit or unit agreement without the consent of any holder:

- to cure any ambiguity; any provisions of the governing unit agreement that differ from those described below;
- to correct or supplement any defective or inconsistent provision; or
- to make any other change that we believe is necessary or desirable and will not adversely affect the interests of the affected holders in any material respect.

We do not need any approval to make changes that affect only units to be issued after the changes take effect. We may also make changes that do not adversely affect a particular unit in any material respect, even if they adversely affect other units in a material respect. In those cases, we do not need to obtain the approval of the holder of the unaffected unit; we need only obtain any required approvals from the holders of the affected units.

Modification with Consent

We may not amend any particular unit or a unit agreement with respect to any particular unit unless we obtain the consent of the holder of that unit, if the amendment would:

- impair any right of the holder to exercise or enforce any right under a security included in the unit if the terms of that security require the consent of the holder to any changes that would impair the exercise or enforcement of that right; or
- reduce the percentage of outstanding units or any series or class the consent of whose holders is required to amend that series or class, or the applicable unit agreement with respect to that series or class, as described below.

Any other change to a particular unit agreement and the units issued under that agreement would require the following approval:

- If the change affects only the units of a particular series issued under that agreement, the change must be approved by the holders of a majority of the outstanding units of that series; or
- If the change affects the units of more than one series issued under that agreement, it must be approved by the holders of a majority of all outstanding units of all series affected by the change, with the units of all the affected series voting together as one class for this purpose.

Table of Contents

These provisions regarding changes with majority approval also apply to changes affecting any securities issued under a unit agreement, as the governing document.

In each case, the required approval must be given by written consent.

Unit Agreements Will Not Be Qualified under Trust Indenture Act

No unit agreement will be qualified as an indenture, and no unit agent will be required to qualify as a trustee, under the Trust Indenture Act. Therefore, holders of units issued under unit agreements will not have the protections of the Trust Indenture Act with respect to their units.

Mergers and Similar Transactions Permitted; No Restrictive Covenants or Events of Default

The unit agreements will not restrict our ability to merge or consolidate with, or sell our assets to, another corporation or other entity or to engage in any other transactions. If at any time we merge or consolidate with, or sell our assets substantially as an entirety to, another corporation or other entity, the successor entity will succeed to and assume our obligations under the unit agreements. We will then be relieved of any further obligation under these agreements.

The unit agreements will not include any restrictions on our ability to put liens on our assets, including our interests in our subsidiaries, nor will they restrict our ability to sell our assets. The unit agreements also will not provide for any events of default or remedies upon the occurrence of any events of default.

Governing Law

The unit agreements and the units will be governed by Michigan law.

Form, Exchange and Transfer

We will issue each unit in global—i.e., book-entry—form only. Units in book-entry form will be represented by a global security registered in the name of a depositary, which will be the holder of all the units represented by the global security. Those who own beneficial interests in a unit will do so through participants in the depositary's system, and the rights of these indirect owners will be governed solely by the applicable procedures of the depositary and its participants. We will describe book-entry securities, and other terms regarding the issuance and registration of the units in the applicable prospectus supplement.

Each unit and all securities comprising the unit will be issued in the same form.

If we issue any units in registered, non-global form, the following will apply to them.

The units will be issued in the denominations stated in the applicable prospectus supplement. Holders may exchange their units for units of smaller denominations or combined into fewer units of larger denominations, as long as the total amount is not changed.

- Holders may exchange or transfer their units at the office of the unit agent. Holders may also replace lost, stolen, destroyed or mutilated units at that office. We may appoint another entity to perform these functions or perform them ourselves.

Table of Contents

- Holders will not be required to pay a service charge to transfer or exchange their units, but they may be required to pay for any tax or other governmental charge associated with the transfer or exchange. The transfer or exchange, and any replacement, will be made only if our transfer agent is satisfied with the holder's proof of legal ownership. The transfer agent may also require an indemnity before replacing any units.

- If we have the right to redeem, accelerate or settle any units before their maturity, and we exercise our right as to less than all those units or other securities, we may block the exchange or transfer of those units during the period beginning 15 days before the day we mail the notice of exercise and ending on the day of that mailing, in order to freeze the list of holders to prepare the mailing. We may also refuse to register transfers of or exchange any unit selected for early settlement, except that we will continue to permit transfers and exchanges of the unsettled portion of any unit being partially settled. We may also block the transfer or exchange of any unit in this manner if the unit includes securities that are or may be selected for early settlement.

Only the depositary will be entitled to transfer or exchange a unit in global form, since it will be the sole holder of the unit.

Payments and Notices

In making payments and giving notices with respect to our units, we will follow the procedures as described in the applicable prospectus supplement.

Table of Contents

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 incorporated in this Prospectus by reference to the Transition Report on Form 10-KT for the six month period ended December 31, 2010 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 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 transition report on Form 10-KT for the transition period from July 1, 2010 to December 31, 2010, filed with the SEC on April 14, 2011;

Table of Contents

- portions of our definitive Proxy Statement for the Annual Meeting of Shareholders held on June 7, 2011 that have been incorporated by reference into the Form 10-KT;
- our quarterly report on Form 10-Q, filed with the SEC on May 16, 2011;
- our current reports on Form 8-K filed with the SEC on January 19, 2011, February 14, 2011, March 25, 2011, June 1, 2011 and June 9, 2011; 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 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.

Table of Contents

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.

Table of Contents

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	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.
Catheter-DCM	Aastrom’s U.S. Phase 2 clinical trial investigating catheter-based delivery of our product in the treatment of dilated cardiomyopathy.
CLI — Critical Limb Ischemia	A vascular disease characterized by insufficient blood flow in the lower extremities that causes severe pain, tissue loss or both.
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.
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.
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.

Table of Contents

TERM	DEFINITION
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.
SPP — Single-Pass Perfusion	SPP is Aastrom’s proprietary technology that controls gas and cell culture media exchange to enable the replication of early-stage stem and progenitor cells while preventing their differentiation into mature cells.
Stem Cell	Unspecialized (undifferentiated) cells that retain the ability to divide throughout a 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.

Table of Contents

$6,153,000

Common Stock
no par value per share
PROSPECTUS SUPPLEMENT

November 29, 2013