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Filed Pursuant to Rule 424(b)(4)
Registration No. 333-197896

Prospectus

13,725,490 Shares of Common Stock

We are offering 13,725,490 shares of our common stock pursuant to this prospectus.

Our common stock is listed on The NASDAQ Capital Market under the symbol "ASTM." On September 10, 2014, the last reported price for our common stock was $2.93 per share.

Investing in our common stock involves a high degree of risk. See "Risk Factors" beginning on page 10.

	Per Share	Total
Public offering price	$ 2.55	$ 35,000,000
Underwriting discounts and commissions[(1)]	$ 0.153	$ 2,100,000
Proceeds, before expenses, to us	$ 2.397	$ 32,900,000

(1) The underwriters will receive compensation in addition to the underwriting discount. See "Underwriting" beginning on page 87 of this prospectus for a description of compensation payable to the underwriters.

We have granted a 30-day option to the underwriters to purchase up to an additional 2,058,823 shares of our common stock on the same terms and conditions set forth above.

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.

Delivery of the shares of common stock is expected to be made on or about September 16, 2014.

Sole Book-Running Manager

Ladenburg Thalmann

September 11, 2014

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You may rely only on the information provided or incorporated by reference in this prospectus and the documents incorporated herein and therein by reference, or in a prospectus supplement or amendment thereto. We and the underwriters have not authorized anyone to provide you with information different from that contained in or incorporated by reference into this prospectus. We and the underwriters are offering to sell, and seeking offers to buy, common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus, any free writing prospectus, or document incorporated by reference is accurate only as of its date, regardless of the time of delivery of this prospectus or of any sale of our common stock. Information contained on our website is not part of this prospectus. You should read this prospectus together with additional information described under the headings "Where You Can Find More Information" and "Incorporation by Reference" below. In various places in this prospectus, we refer you to sections for additional information by indicating the caption heading of the other sections. All cross-references in this prospectus are to captions contained in this prospectus, unless otherwise indicated. For investors outside the United States: We have not and the underwriters have not done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside the United States.

Carticel®, Epicel® and MACI™ and associated logo are trademarks of Aastrom Biosciences, Inc. Other trademarks and trade names that are the property of their respective owners are also contained in this prospectus.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus or incorporated by reference in this prospectus. This summary does not contain all o the information that you should consider in making your investment decision. You should read the entire prospectus carefully, especially the discussion regarding the risks of investing in our securities under the heading "Risk Factors" beginning on page 10 of this prospectus and our financial statements and related notes incorporated by reference in this prospectus, before investing in our securities. In this prospectus, "Aastrom," the "Company," "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.

Our Company

We are a fully integrated, commercial-stage biopharmaceutical company dedicated to the identification, development and commercialization of innovative therapies that enable the body to repair and regenerate damaged tissues and organs to restore normal structure and function. Our product portfolio is comprised of patient-specific (autologous) cell therapies utilizing proprietary manufacturing processes and systems. We have marketed products as well as developmental stage product candidates and our goal is to become the leading cell therapy and regenerative medicine company by developing, manufacturing and marketing best-in-class therapies for patients with significant unmet medical needs.

The following table summarizes our product portfolio and product candidate pipeline:

* Marketing in the EU has been temporarily suspended

** Investigator sponsored trial (University of Michigan)

Our approved and marketed products were acquired through the acquisition of the cell therapy and regenerative medicine (CTRM) business of Sanofi, a French *société anonyme* (Seller or Sanofi), in May 2014. We believe that our acquired CTRM business has been a pioneer in the development and commercialization of autologous cell therapies. The CTRM portfolio includes three marketed autologous cell therapy products, each of which are further described below: Carticel® (autologous cultured chondrocytes), a first-generation product for autologous chondrocyte implantation (ACI) currently marketed in the U.S.; MACI™ (matrix-applie characterized autologous cultured chondrocytes), a third-generation ACI product; and Epicel® (cultured epidermal autografts), a permanent skin replacement for full thickness burns greater than or equal to 30% of total body surface area. Our product candidate portfolio also includes ixmyelocel-T, a patient-specific multicellular therapy currently in development for the treatment of advanced heart failure due to ischemic dilated cardiomyopathy (DCM).

Carticel

Carticel, a first-generation ACI product for the treatment and repair of cartilage defects in the knee, is the first and currently the only FDA-approved autologous cartilage repair product. Carticel is indicated for the repair of symptomatic cartilage defects of the femoral condyle (medial, lateral or trochlea) caused by acute or repetitive trauma, in patients who have had an inadequate response to a prior arthroscopic or other surgical repair procedure such as debridement, or the removal of damaged or defective cartilage, microfracture, or the creation of tiny fractures in the bone to encourage new cartilage development, drilling/abrasion arthroplasty, or reshaping the joint, or osteochondral allograft/autograft, or transferring cartilage from one joint to another.

Carticel is implanted by orthopedic surgeons after obtaining a cartilage biopsy during an initial arthroscopic procedure. The patient's chondrocytes, which are the cells that produce cartilage, are isolated and expanded in a manufacturing process compliant with current Good Manufacturing Practices (cGMP). During a second surgical procedure, the cells are implanted in the cartilage defect under a sutured periosteal flap, where they produce new hyaline cartilage. The therapeutic advantage of this approach relative to other approaches, such as microfracture, is that the autologous chondrocytes produce the hyaline cartilage that is naturally present in the knee, rather than fibrous cartilage which lacks durability and the wear characteristics of hyaline cartilage.

In the U.S. annually, there are approximately 1 million arthroscopic procedures and more than 250,000 cartilage surgical procedures. In addition, approximately 50,000 patients under the age of 40 have full thickness defects greater than 2 cm^2. Patients seek retreatment for the repair of larger, symptomatic femoral condyle cartilage defects caused by acute or repetitive trauma. In 2013, approximately 1,100 Carticel implants were performed which generated net revenues of $35.2 million, and in the first quarter of 2014, Carticel implants generated net revenues of $7.9 million. We believe that by increasing engagement with, and education of, managed care payors and hospitals we can improve the coordination of reimbursement and care to improve the physician and patient Carticel experience. We also believe that a consistent positive experience using Carticel will increase utilization and market share.

Epicel

Epicel (cultured epidermal autografts) can be a permanent skin replacement for full thickness burns greater than or equal to 30% of total body surface area (TBSA). Epicel is currently the only FDA-approved autologous epidermal product available for large total surface area burns. Currently, approximately 100 patients are treated with Epicel in the U.S. each year. In 2013, net revenues were $7.1 million for Epicel.

Epicel was approved in the United States as a humanitarian use device (HUD) under a Humanitarian Device Exemption (HDE). Devices eligible for an HDE are intended for diseases or conditions that occur in a maximum of 4,000 individuals annually in the United States.

Epicel is produced by isolating and expanding keratinocytes, which are the predominant cell type in the epidermis or outer layer of the skin, obtained from a sma biopsy of a patient's healthy skin. Epicel is an important treatment option for patients with severe burns because these patients are generally understood to need a keratinocyte-based epithelium and there is very little skin, which is the only other source of keratinocyte-based epithelium, available for autografts for these patients.

Each year in the U.S., more than 40,000 people are hospitalized for burns. More than 2,000 of these patients are treated for burns covering more than 30% of the TBSA, the labeled indication for Epicel. Of these patients, fewer than 100 each year are treated with Epicel. Currently, the mortality rate for this group is approximately 34%, partially due to the lack of healthy tissue from which to harvest autografts. Relative to clinical need, we believe Epicel is underutilized due to lac of consistent promotional effort and burn center support. We expect Epicel's utility to grow as commercial and clinical efforts are appropriately dedicated to the product and providers.

MACI

MACI, is a third-generation ACI product for the treatment of focal chondral cartilage defects in the knee. MACI received marketing authorization in Europe in June 2013 by meeting the requirements of the Advanced Therapy and Medicinal Product (ATMP) guidelines. MACI has been commercially available in the Europear Union (EU) since 1998. Aside from a small number of currently pending procedures, marketing of MACI have been temporarily suspended as part of a restructuring of the business primarily due to an unfavorable pricing environment. We believe that MACI, which is a Phase 3 product candidate in the U.S., has strong revenue potential in the U.S., and we are planning to discuss approval requirements with the FDA. The timing and process to gain approval in the U.S. and a possible reintroduction in select EU countries have not yet been determined.

Similar to Carticel, during an initial surgical procedure, a surgeon obtains a biopsy of healthy cartilage and the chondrocytes are isolated, expanded and uniforml seeded onto a bioabsorbable Type I/IIIa collagen membrane to form the implant in a cGMP manufacturing process at a facility in Copenhagen, Denmark. Unlike Carticel, MACI is implanted during a mini-arthrotomy in which the implant is trimmed to the size of the defect and fixed in the defect with fibrin glue and without sutures.

The advantage of MACI relative to Carticel is that it provides the same efficacy with improvement in ease of use for the physician and reduced morbidity for the patient. The implant procedure for MACI is less invasive than for Carticel, entailing a mini-arthrotomy or even arthroscopic delivery, eliminating the need for a periosteum harvest and sutures.

MACI, if introduced in the U.S., should both replace Carticel and, we believe, expand the market since MACI shares all of the advantages of Carticel, including durability of response, while being less invasive, shortening procedure time, eliminating the need for a periosteal harvest, having a lower frequency of subsequent surgical interventions and an improved recovery period.

The pivotal clinical trial supporting MACI registration in Europe, Superiority of MACI Implant to Microfracture Treatment (SUMMIT), was completed in 2012. Analysis of this 144 patient superiority study demonstrated that there is a statistically significant and clinically meaningful improvement in the co-primary endpoint o pain and function for those patients treated with a MACI implant compared to microfracture which was the current standard of care. We expect that the FDA may require an additional clinical trial to support approval of a BLA in the United States.

Marrow Donation

Like many companies and academic institutions conducting research on cell therapy, we require consistent access to high quality bone marrow. As part of an effort to lower our costs we have begun collecting bone marrow for research use using our bone marrow collection center located in San Diego, CA and our wholly-owned subsidiary Marrow Donation, LLC. We initiated commercial sales of bone marrow in June 2014. Based on the strong interest that we believe exists across the biopharmaceutical industry in the use of bone marrow and bone marrow-derived cells as drug discovery tools, we believe that this represents an opportunity for our company.

Ixmyelocel-T

Our preapproval stage portfolio also includes ixmyelocel-T, a unique patient-specific multicellular therapy derived from an adult patient's own bone marrow which utilizes our proprietary, highly automated and scalable manufacturing system. 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 M2-like anti-inflammatory macrophages.

We are currently enrolling patients in a Phase 2b study (ixCELL-DCM), evaluating the efficacy and safety of ixmyelocel-T in patients with advanced heart failur due to ischemic DCM, an indication for which ixymyelocel-T has been granted a U.S. Orphan Drug designation. The randomized, double-blind, placebo-controlled study is designed to treat 108 patients at approximately 35 sites in the U.S. and Canada. We expect that patients will be followed for 12 months for the primary efficac endpoint of major acute coronary events (MACE). We expect to complete enrollment of the study by the end of 2014, and have top-line efficacy results approximately 12 months later.

Ixmyelocel-T has been granted a U.S. Orphan Drug designation by the FDA for the treatment of DCM, which allows for seven years of market exclusivity from product approval in the United States. We also have an ongoing ixmyelocel-T clinical study for the treatment of craniofacial reconstruction, for which we expect results by the first half of 2016, and have conducted clinical studies for the treatment of critical limb ischemia (CLI).

Our Strategy

Our objective is to become the leading cell therapy and regenerative medicine company by developing, manufacturing and marketing best-in-class therapies for patients with significant unmet medical needs that require the repair and regeneration of damaged tissues and organs.

To achieve this objective, we intend to:

- Fully integrate the acquired commercial stage CTRM business and restructure the combined businesses to reduce redundancies and related costs, as well as take advantage of complementary technology platforms;
- Achieve accretive impact from the U.S. Carticel and Epicel business beginning in 2015;
- Lower the manufacturing costs for Carticel through an improved ratio of Carticel unit sales to biopsies as well as other efficiencies;
- Assess and capitalize on opportunities to increase revenue from Carticel in the U.S.;
- Develop and execute on a regulatory strategy for the approval of MACI in the U.S.;

- Develop a commercial strategy for the profitable reintroduction of MACI in the EU;
- Expand Epicel usage in the severely burned patient segment by increasing the level of commercial and clinical efforts dedicated to the product and providers;
- 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;
- 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; and
- Explore partnerships to maximize the potential of our products and product candidates.

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 10 of this prospectus. These risks include, but are not limited to, the following:

- Our past losses and expected future losses cast doubt on our ability to continue as a going concern and operate profitably;
- We may not be able to raise the required capital to conduct our operations and/or develop and commercialize our product candidates;
- The failure to successfully integrate the acquired business, products and operations in the expected time frame, or at all, may adversely affect the combined company's future results;
- Our products and product development programs are based on novel technologies and are inherently risky;
- The failure to obtain and maintain required regulatory approvals would severely limit our ability to sell our products and product candidates;
- We have limited experience in manufacturing products for commercial purposes;
- We have limited manufacturing capacity and our commercial manufacturing operations in the U.S. depend on one facility;
- If our patents and proprietary rights do not provide substantial protection, then our business and competitive position will suffer; and
- If we fail to maintain the patents and patent applications covering our products or product candidates our competitive position would be adversely affected.

Company 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 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 below, the information on, or accessible through, our website is not part of this prospectus.

THE OFFERING

Common stock offered by us	13,725,490 shares
Common stock to be outstanding after this offering	21,726,830 shares of common stock (or 23,785,653 shares if the underwriters exercise in full their option to purchase additional shares)
Option to purchase additional shares	We have granted the underwriters a 30-day option to purchase up to 2,058,823 additional shares of our common stock.
Use of proceeds	We expect to use the net proceeds from this offering to support commercialization of our marketed products and fund the development costs associated with our Phase 2b ixCELL-DCM clinical trial of ixmyelocel-T for the treatment of advanced heart failure due to ischemic dilated cardiomyopathy and our preclinical studies, as well as for working capital and general corporate purposes including reimbursing Sanofi for the one-time cash payment, expected to be in an amount of €2.5 million (or approximately $3.3 million), to the former shareholders of Verigen AG in connection with the continued development of MACI in the U.S. We may also use a portion of the net proceeds to acquire or invest in complementary cell therapy and regenerative medicine businesses, technologies, products or assets. See "Use of Proceeds".
Risk factors	You should carefully read "Risk Factors" in this prospectus for a discussion of factors that you should consider before deciding to invest in our common stock.
NASDAQ Capital Market symbol	ASTM

The number of shares of our common stock that will be outstanding immediately after this offering is based on 8,001,340 shares of common stock outstanding as of August 27, 2014 (all share amounts disclosed prior to October 16, 2013 have been adjusted to reflect the reverse stock split on a retroactive basis) and excludes:

- 506,969 shares of our common stock issuable upon the exercise of stock options outstanding as of August 27, 2014 at a weighted average exercise pric of $22.69 per share;
- 966,654 shares of common stock issuable upon the exercise of warrants outstanding as of August 27, 2014 at exercise prices of $17.28 per share (January 2010—226,299 shares), $3.30 per share (December 2010—15,405 shares) and $4.80 per share (August 2013—724,950 shares) in each case, before any adjustment as a result of this offering; and
- 615,400 shares of common stock issuable upon the conversion of preferred stock outstanding as of August 27, 2014.

SUMMARY FINANCIAL DATA

The following table summarizes our financial data. We have derived the following summary financial data for the years ended December 31, 2011, 2012 and 201 from our audited financial statements. The summary financial data for the six months ended June 30, 2014 and 2013 and the balance sheet data as of June 30, 2014 have been derived from our unaudited interim financial statements. The unaudited interim financial results have been prepared on the same basis as the audited financial statements and reflect all adjustments necessary to fairly reflect our financial position as of June 30, 2014 and results of operations for the six months ended June 30, 2014 and 2013. Our historical results are not necessarily indicative of the results that may be expected in the future. The following summary financial data should be read in conjunction with: (i) "Management's Discussion and Analysis of Financial Condition and Results of Operations," and our financial statements and related notes appearing in our Annual Report on Form 10-K for the year ended December 31, 2013 and incorporated by reference in this prospectus, (ii) our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2014 and June 30, 2014 and (iii) our financial statements and related notes appearing in our Current Report o Form 8-K filed on June 2, 2014, as amended on June 16, 2014 and August 29, 2014, and incorporated by reference in this prospectus. For more details on how you ca obtain the documents incorporated by reference in this prospectus, see "Where You Can Find More Information" and "Incorporation by Reference."

	Year Ended December 31,			Six Months Ended June 30,	
	2013	2012	2011	2014	2013
	(in thousands, except per share data)				
Statements of Operations Data:					
Revenues	$ 19	$ 21	$ 18	$ 4,432	$ 11
Cost of product sales	4	6	4	5,009	3
Gross profit (loss)	15	15	14	(577)	8
Operating expenses:					
Research and development	15,104	26,025	21,330	7,635	9,214
Selling, general and administrative	5,875	7,750	7,724	4,954	3,193
Total operating expenses	20,979	33,775	29,054	12,589	12,407
Loss from operations	(20,964)	(33,760)	(29,040)	(13,166)	(12,399)
Other income (expense):					
(Increase) decrease in fair value of warrants	5,337	4,248	9,329	(1,104)	1,964
Bargain purchase gain	—	—	—	3,634	—
Net interest income (expense)	5	38	43	3	2
Total other income	5,342	4,286	9,372	2,533	1,966
Net loss	$ (15,622)	$ (29,474)	$ (19,668)	$ (10,633)	$ (10,433)
Net loss per share attributable to common shareholders (basic and diluted)	$ 6.95	$ 16.25	$ (10.18)	$ (2.18)	$ (5.75)
Weighted average number of common shares outstanding (basic and diluted)	3,016	2,060	1,931	6,195	2,263

In addition to our activities occurring separately from the CTRM business, which we refer to in the table below as our legacy business, the results of operations for the six months ended June 30, 2014 include one month of operating results of the CTRM business, including restructuring charges of $3.0 million, expenses for th discontinued Denmark operations, which was operated by the CTRM business, of $0.2 million and a bargain purchase gain of approximately $3.6 million. Net revenues for

the six months ended June 30, 2014 were $4.4 million and reflect one month of results from commercial operations of the CTRM business. Revenues were comprised of approximately $3.4 million of net sales of Carticel implants and surgical kits, approximately $0.9 million of net sales of Epicel grafts and biopsy kits, and approximately $0.1 million of revenue from commercial sales of bone marrow.

The following table summarizes the effect of the acquisition on our results of operations for the six months ended June 30, 2014:

	For the Six Months Ended June 30, 2014		
	Legacy Business	CTRM Business	Consolidated Business
	(in thousands)		
CTRM Business Contribution:			
Total revenues	$ 59	$ 4,373	$ 4,432
Cost of product sales	87	4,922	5,009
Gross profit (loss)	(28)	(549)	(577)
Total operating expenses	10,495	2,094	12,589
Loss from operations	(10,523)	(2,643)	(13,166)
Other income (expense)	(1,101)	—	(1,101)
Bargain purchase gain	3,634	—	3,634
Total other income loss	2,533	—	2,533
Net loss	$ (7,990)	$ (2,643)	$ (10,633)

In addition to the results reported in accordance with generally accepted accounting principles in the United States (GAAP), we are providing information regarding a non-GAAP financial measure. We completed our acquisition of the CTRM business in the quarter ended June 30, 2014, and shortly thereafter incurred significant restructuring costs. These costs are included in the financial results for the six months ended June 30, 2014. We are providing this non-GAAP financial measure to help investors better understand the future impact of the acquired business on our financial performance after certain costs, such as severance payments an other costs associated with the restructuring activities, which is also how management uses such figures. The non-GAAP measure is intended only as a supplement to the comparable GAAP measurement and the Company compensated for the limitations inherent in the use of this non-GAAP measure by using a GAAP measure in conjunction with the non-GAAP measure. As a result, investors should consider this non-GAAP measure in addition to, and not in substitution for or, as superior to, the comparable measurement of financial performance prepared in accordance with GAAP.

	For the Six Months Ended June 30, 2014
	(in thousands)
Non-GAAP Financial Measures:	
Net loss—GAAP	$ (10,633)
Net loss—Legacy business	(7,990)
Subtotal—Net loss—CTRM business	(2,643)
CTRM restructuring costs	3,005
CTRM Denmark operating expenses	231
Net income—CTRM business—Non-GAAP	$ 593

The table set forth below presents summary balance sheet data. The unaudited balance sheet data as adjusted gives effect to our issuance and sale of 13,725,490 shares of our common stock in this offering at the public offering price of $2.55 per share, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

	As of June 30, 2014	
	Actual	As Adjusted
	(in thousands)	
Balance Sheet Data:		
Cash	$ 7,263	$ 39,963
Total assets	19,836	52,536
Accumulated deficit	(298,398)	(298,398)
Total shareholders' equity	2,785	35,485

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, as well as other information we include or incorporate by reference into this prospectus, before making an investment decision. Our business, financial condition or results of operations could be materially adversely affected by the materialization of any of these risks. The trading price of our securities could decline due to the materialization of any of these risks, and you may lose all or part of your investment. This prospectus and the documents incorporated herein by reference also contain forward-looking statements that involve risks and uncertainties. Actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks described below and in the documents incorporated herein by reference, including (i) our Annual Report on Form 10-K for the year ended December 31, 2013; (ii) our Quarterly Report on Form 10-Q for each of the quarters ended March 31, 2014 and June 30, 2014; 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.

While we are a commercial-stage biopharmaceutical company following our acquisition of the CTRM business, we have not yet generated significant revenues. We have incurred net losses each year since our inception in 1989, including net losses of $15.6 million and $29.5 million for the years ended December 31, 2013 and 2012, respectively, and $6.0 million and $10.6 million for the three and six months ended March 31, 2014 and June 30, 2014. As of June 30, 2014, we had $7.3 million 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 the coming year and beyond. While we have access to certain amounts of financing through an agreement with Lincoln Park Capital Fund, LLC (Lincoln Park), there are certain factors, such as volume of trading in our common stock, our stock price and the ability to terminate the agreement with notice, which limit the amount that can be raised in a short period of time through our agreement with Lincoln Park. Also, the integration of the recently acquired business with our existing business will require additional financing. We anticipate that we will incur certain non-recurring charges in connection with the integration; however, we cannot identify the timing, nature and amount of all such charges as of the date of this registration statement. These costs along with the transaction costs that we incurred in connection with the negotiation and completion of the acquisition of the acquired business could materially affect our results of operations in the period in which such charges are recorded. In the longer term, we will need to raise additional funds in order to continue commercializing the products we acquired in connection with the acquisition of the acquired business, complete product development programs and complete clinical trials needed to market and commercialize our current product candidates. In addition, we expect to continue to incur significant operating expenses in connection with the operation of the acquired business, as we seek to, among other things, continue to develop our distribution network of third party distributors and independent sales professionals for the distribution of our products and product candidates and expand and protect our intellectual property portfolio for 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:

- Our ability to successfully integrate the acquired business with our existing business and streamline its operations;
- The rate and degree of progress for our product development;

- Our ability to maintain our facility as an FDA compliant and validated product manufacturing facility;
- 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; and
- Technological developments by competitors.

If we cannot raise such funds, we will not be able to develop, manufacture 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 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 June 30, 2014, we had accumulated a deficit of approximately $298 million 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, the prosecution of patent applications, and more recently, acquisition-related costs. We expect to continue to incur significant operating losses over the next several years and at least until, and probably after, streamlining the manufacturing and commercialization of the products we recently acquired and 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 product candidates and continuing the commercialization of 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 commercializing our products, 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 received a report from our independent registered public accounting firm with an explanatory paragraph for the year ended December 31, 2013 with respect to our ability to continue as a going concern. The existence of such a report may adversely affect our stock price and our ability to raise capital. There is no assurance that we will not receive a similar report for our year ended December 31, 2014.

In their report dated March 13, 2014, our independent registered public accounting firm expressed substantial doubt about our ability to continue as a going concern as we have suffered recurring losses from operations and have insufficient liquidity to fund our future operations. Our ability to continue as a going concern is subject to our ability to obtain necessary funding from outside sources, including obtaining additional funding from the sale of our securities, obtaining loans and grants from various financial institutions where possible. Our continued net operating losses increase the difficulty in meeting such goals and there can be no assurances that such methods will prove successful.

The failure to successfully integrate the acquired business and operations in the expected time frame may adversely affect the combined company's future results.

We believe that the acquisition of the acquired business will result in certain benefits, including certain manufacturing, sales and distribution and operational efficiencies. However, to realize these anticipated benefits, Aastrom's existing business and the acquired business must be successfully combined. We may be unable to effectively integrate the acquired business into our organization, make the acquired business profitable, and may not succeed in managing the acquired business or the larger company that results from this acquisition. The process of integration of an acquired business may subject us to a number of risks, including:

- Failure to successfully manage relationships with clients, distributors and suppliers;
- Demands on management related to the increase in size of the company after the acquisition;
- Diversion of management attention;
- Potential difficulties integrating and harmonizing financial reporting systems;
- Difficulties in the assimilation and retention of employees;
- Inability to retain the management, key personnel and other employees of the acquired business;
- Inability to establish uniform standards, controls, systems, procedures and policies;
- Inability to retain the customers of the acquired business;
- Exposure to legal claims for activities of the acquired business prior to acquisition; and
- Incurrence of additional expenses in connection with the integration process.

If the acquired business is not successfully integrated into our company, our business, financial condition and results of operations could be materially adversely affected, as well as our professional reputation. Furthermore, if we are unable to successfully integrate the acquired business and operations, or if there are delays in combining the businesses, the anticipated benefits of the acquisition may not be realized fully or at all or may take longer to realize than expected. Successful integration of the acquired business will depend on our ability to manage these operations, to realize opportunities for revenue growth presented by our products and eliminate certain excess costs of the acquired business.

The acquisition will result in the expansion of our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

As a result of the acquisition, our employee base increased significantly from 38 employees as of March 31, 2014 to 190 full-time employees as of July 31, 2014. We expect that such growth will impose significant additional responsibilities on our management. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The effective management of the acquired business could require significant capital expenditures and may divert financial resources from other projects, such as the development of our existing or future product candidates. In connection with the operation of the acquired business we expect to expand our internal sales and marketing capabilities as we build an internal sales and marketing organization and hire additional manufacturing, quality control, pharmacovigilance, regulatory affairs, quality assurance, and management personnel as necessary to maintain or expand our processing operations. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenue could be reduced, and

we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our products and our other product candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage our current growth.

We may not be able to raise the required capital to conduct our operations and develop and commercialize our product candidates.

We will require substantial additional capital resources in order to complete our product development programs, complete our clinical trials needed to market and commercialize our product candidates (including the Phase 2b clinical trial of ixmyelocel-T for the treatment of advanced heart failure due to ischemic DCM). In order to grow and expand our business, to introduce our new product candidates into the marketplace, 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 therapy 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 scale up our production capabilities for larger quantities of our products;
- The effect of commercialization activities and facility expansions, if and as required; and
- Complementary business acquisition or development opportunities.

We may direct Lincoln Park to purchase up to $15 million worth of shares of our common stock over a 30-month period generally in amounts up to 50,000 shares of our common stock on certain business days under a Purchase Agreement (the Purchase Agreement) we entered into with Lincoln Park on January 21, 2014 (the Lincoln Park Equity Line). As of June 30, 2014, we had sold $3.2 million worth of shares to Lincoln Park. However, there are certain factors, such as volume of trading in our common stock, our stock price and the ability to terminate the agreement with notice, which limit the amount that can be raised in a short period of time through the Lincoln Park Equity Line. The extent to which we rely on the Lincoln Park Equity Line as sources of funding will depend on a number of factors, including the prevailing market price of our common stock and the extent to which we are able to secure working capital from other sources. If obtaining sufficient funding from Lincoln Park were to prove impracticable or prohibitively dilutive, we will need to secure other sources of funding in order to satisfy our working capital needs. Even if we sell the maximum amount we are eligible to sell to Lincoln Park under the purchase agreements with Lincoln Park, respectively, we will still need additional capital to fully implement our business, operating and development plans. Should the financing we require to sustain our working capital needs be unavailable or prohibitively expensive when we require it, the consequences would have a material adverse effect on our business, operating results, financial condition and prospects.

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:

- Our ability to successfully integrate the acquired business and further commercialize our products;
- 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, 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 and product candidates.

We must maintain our domestic and foreign regulatory approvals to continue to commercialize our products. In addition, we must obtain the approval of the FDA before commercial sales of our cell therapy product candidates may commence in the United States, which we believe will ultimately be the largest market for our products. We anticipate that we will also be required to obtain additional approvals from various foreign regulatory authorities to initiate sales activities of cell therapy product candidates in those jurisdictions. If we cannot demonstrate the safety, purity and potency of our product candidates, including our cell therapy product candidates, produced in our production system, the FDA or other regulatory authorities could delay or withhold regulatory approval of our product candidates.

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 product candidates or adversely affect the regulatory approvals of our products.

Any changes in the governmental regulatory classifications of our products and product candidates could prevent, limit or delay our ability to market or develop our products and product candidates.

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 cell therapy products, any change in the regulatory classification or designation would affect our ability to obtain FDA approval of our products and product candidates. As each of our cell therapy products is, under current regulations, regulated as a biologic, a Biologics License Application (BLA) is

required to be submitted and approved by the FDA prior to the marketing of any of our products candidates.

Our product candidate, ixmyelocel-T, is still in clinical development. If we do not successfully continue or complete the clinical development of ixmyelocel-T, our ability to finance our operations may be adversely affected.

Our near-term prospects depend in part upon our ability to successfully continue and complete clinical trials of our product candidate, ixmyelocel-T, and to demonstrate its safety and effectiveness, as well as its superiority over existing therapies and standards of care, if any. We are currently enrolling and treating patients with ischemic DCM for the Phase 2b ixCELL-DCM clinical trial. Our ability to finance our company and to generate revenues will depend in part 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 ischemic DCM indication 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 products and 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.

Further, when manufacturing autologous cell therapies, the number and the composition of the cell population varies from patient to patient, in part due to the age of the patient, since the therapy is dependent on patient specific physiology. Such variability in the number and composition of these cells could adversely affect our ability to manufacture autologous cell therapies in a cost-effective manner and meet acceptable product release specifications for use in a clinical trial or, if approved, for commercial sale. As a consequence, the development and regulatory approval process for autologous cell therapy products could be delayed or may never be completed

Our products represent new classes of therapy that the marketplace may not understand or accept. Furthermore, the success of our products is dependent on wider acceptance by the medical community.

While our acquired products have had some commercial success to date, the broader market may not understand or accept our products. Our products represent new treatments or therapies and compete with a number of more conventional products and therapies manufactured and marketed by others. The new nature of our products creates significant challenges in regards to product development and optimization, manufacturing, government regulation, and third-party reimbursement.

As a result, the commercialization of our current products and development pathway for our potential products may be subject to increased scrutiny, as compared to the pathway for more conventional products.

The degree of market acceptance of any of our marketed or potential products will depend on a number of factors, including:

- The clinical safety and effectiveness of our products and their perceived advantage over alternative treatment methods;
- Our ability to convince health care providers that the use of our products in a particular procedure is more beneficial than the standard of care or other available methods;
- Our ability to explain clearly and educate others on the autologous use of patient-specific human tissue, to avoid potential confusion with and differentiate ourselves from the ethical controversies associated with human fetal tissue and engineered human tissue;
- Adverse reactions involving our products or the products or product candidates of others that are human tissue based;
- Our ability to supply a sufficient amount of our product to meet regular and repeated demand in order to develop a core group of medical professionals familiar with and committed to the use of our products; and
- The cost of our products and the reimbursement policies of government and third-party payers.

If patients or the medical community do not accept our potential products as safe and effective for any of the foregoing reasons, or for any other reason, it could affect our sales, having a material adverse effect on our business, financial condition and results of operations. While acceptance by the medical community may be fostered by broad evaluation via peer-reviewed literature, we may not have the resources to facilitate sufficient publication.

Our inability to complete our product development activities successfully would materially limit our ability to operate or finance our 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 regulatory 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 effective 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 operations 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 and product candidates. Clinical trial failures can occur at any stage of the testing and we may experience numerous unforeseen events during, or as a result of, the clinical trial process that could delay or prevent the continued commercialization of our products or future therapeutic product candidates.

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 effectiveness 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.

With respect to any clinical trials affecting our products or product candidates, failures or delays can occur at any stage of the trials, and may be directly or indirectly caused by a variety of factors, including but not limited to:

- Delays in securing clinical investigators or trial sites for our clinical trials;
- Delays in obtaining Institutional Review Board (IRB) and other regulatory approvals to commence a clinical trial;
- Slower than anticipated rates of patient recruitment and enrollment in our clinical trials, or failing to reach the targeted number of patients due to competition for patients from other trials;
- Limited or no availability of coverage, reimbursement and adequate payment from health maintenance organizations and other third party payers for the use of biological products supplied for use in our clinical trials;
- Negative or inconclusive results from clinical trials;
- Unforeseen side effects interrupting, delaying, or halting clinical trials of any future therapeutic product candidates, and possibly resulting in the FDA or other regulatory authorities denying approval of any future therapeutic product candidates;
- Unforeseen safety issues;
- Approval and introduction of new therapies or changes in standards of practice or regulatory requirements that render our clinical trial endpoints or the targeting of our proposed indications obsolete;
- Inability to monitor patients adequately during or after treatment or problems with investigator or patient compliance with the trial protocols;
- Inability to replicate in large controlled studies safety and efficacy data obtained from a limited number of patients in uncontrolled trials;
- Inability or unwillingness of medical investigators to follow our clinical protocols; and
- Unavailability of clinical trial supplies.

Moreover, our ability to complete the clinical trials for our product candidates in a timely manner depends on additional factors such as 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 of ixmyelocel-T 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 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 ixmyelocel-T cell manufacturing process would impair our cell product development.

We rely on third parties, including Vention Medical, Inc. (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 marketed cell therapy products and our product candidates. Vention is our sole supplier of cell cassettes used in the ixmyelocel-T manufacturing process, and 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 and maintain 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

Failure by our third-party manufacturers, including Vention, to comply with the regulatory guidelines set forth by the FDA with respect to our products could delay or prevent the completion of clinical trials, the approval of any product candidates or the commercialization of our products.

Third-party manufacturers, such as Vention, must be inspected by the FDA for current Good Manufacturing Practice, or cGMP, compliance before they can produce commercial product. We may be in competition with other companies for access to these manufacturers' facilities and may be subject to delays in manufacture if the manufacturers give other clients higher priority than they give to us. If we are unable to secure and maintain third-party manufacturing capacity, the development and sales of our products and our financial performance may be materially affected.

Manufacturers are obligated to operate in accordance with FDA-mandated requirements. A failure of any of our third-party manufacturers to establish and follow cGMP requirements and to document their adherence to such practices may lead to significant delays in the availability of material for clinical trials, may delay or prevent filing or approval of marketing applications for our products, and may cause delays or interruptions in the availability of our products for commercial distribution following FDA approval. This could result in higher costs to us or deprive us of potential product revenues.

Complying with cGMP and non-U.S. regulatory requirements will require that we expend time, money, and effort in production, recordkeeping, and quality control to assure that the product meets applicable specifications and other requirements. We, or our contracted manufacturing facility, must also pass a pre-approval inspection prior to FDA approval. Failure to pass a pre-approval inspection may significantly delay FDA approval of our products. If we fail to comply with these requirements, we would be subject to possible regulatory action and may be limited in the jurisdictions in which we are permitted to sell our products. As a result, our business, financial condition, and results of operations may be materially harmed.

The manufacture of cell therapy products is characterized by inherent risks and challenges and has proven to be a costly endeavor relative to manufacturing other therapeutics products. We have limited experience in manufacturing products for commercial purposes and we cannot assure you that we will be able to successfully and efficiently manage the manufacturing of our products, either ourselves or through third-party contractors with whom we may enter into strategic relationships.

The manufacture of cell therapy products, such as our products and product candidates, is highly complex and is characterized by inherent risks and challenges such as autologous raw material inconsistencies, logistical challenges, significant quality control and assurance requirements, manufacturing complexity, and significant manual processing. Unlike products that rely on chemicals for efficacy, such as most pharmaceuticals, cell therapy products are difficult to characterize due to the inherent variability of biological input materials. Difficulty in characterizing biological materials or their interactions creates greater risk in the manufacturing process. We attempt to mitigate risk associated with the manufacture of biologics by continuing to improve the characterization of all of our input materials, utilizing multiple vendors for supply of qualified biological materials, and manufacturing some of these materials ourselves. However, there can be no assurance that we will be able to maintain adequate sources of biological materials or that biological materials that we maintain in inventory will yield finished products that satisfy applicable product release criteria. Our inability to obtain necessary biological materials or to successfully manufacture cell therapy products that incorporate such materials could have a material adverse effect on our results of operations.

Additionally, we have limited experience in manufacturing products for commercial purposes and could experience difficulties in the continued manufacturing of our products. Because our experience in manufacturing, sales, marketing and distribution is limited, we may encounter unforeseen difficulties in our efforts to efficiently manage the manufacturing, sale and distribution of our products or have to rely on third-party contractors over which we may not have direct control to manufacture our products. Moreover, there can be no assurance that we or any third-party contractors with whom we enter into strategic relationships will be successful in streamlining manufacturing operations and implementing efficient, low-cost manufacturing capabilities and processes that will enable us to meet the quality, price and production standards or production volumes to achieve profitability. Our failure to develop these manufacturing processes and capabilities in a timely manner could prevent us from achieving our growth and profitability objectives as projected or at all.

We intend to obtain assistance to market our products and 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.

We have limited manufacturing capacity and our commercial manufacturing operations in the U.S. depend on one facility. Similarly, manufacturing of our lead product candidate, ixmyelocel-T, is conducted at one facility. If either facility is destroyed or we experience any manufacturing difficulties, disruptions or delays, this could limit supply of our products or adversely affect our ability to conduct our clinical trials and our business would be adversely impacted.

We presently conduct all of our commercial manufacturing operations in the U.S. at one facility located in Cambridge, Massachusetts. As a result, all of the commercial manufacturing of our marketed products, Epicel and Carticel, for the U.S. market takes place at a single U.S. facility. In addition, clinical trials for certain product candidates would primarily depend upon the manufacturing of such product candidates in the same Cambridge facility. Similarly, manufacturing of our lead product candidate, ixmyelocel-T, takes place at one facility located in Ann Arbor, Michigan. If regulatory, manufacturing or other problems require us to discontinue production at either facility, we will not be able to supply our products to our patients or have supplies for any clinical trials, which would adversely impact our business. If either facility or the equipment in it is significantly damaged or destroyed by fire, flood, power loss or similar events, we may not be able to quickly or inexpensively replace our manufacturing capacity or replace our facility at all. In the event of a temporary or protracted loss of this facility or equipment, we might not be able to transfer manufacturing to a third party. Even if we could transfer manufacturing from one facility to the other or to a third party, the shift would likely be expensive and time-consuming, particularly since an alternative facility would need to comply with the applicable regulatory and quality standard requirements whereby validation and FDA approval would be required before any products manufactured at that facility could be made commercially available.

Currently, we maintain insurance coverage totaling $4.0 million in Denmark and $32.0 million in the U.S. against damage to our property and equipment (recently increased by an additional $4.0 million in the U.S. as a result of the Transaction), an additional $1.0 million to cover business interruption and extra expenses, and $1.0 million to cover R&D restoration expenses. If we have underestimated our insurance needs, we will not have sufficient insurance to cover losses above and beyond the limits on our policies.

We are subject to significant regulation with respect to the manufacturing of our products.

All of those involved in the preparation of a cellular therapy for clinical trials or commercial sale, including our existing supply contract manufacturers and clinical trial investigators, are subject to extensive and continuing government regulations by the FDA and comparable agencies in other jurisdictions. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Our facilities and quality systems and the facilities and quality systems of some or all of our third party contractors and suppliers must pass inspection for compliance with the applicable regulations as a condition of FDA approval of our products. The FDA also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our third party contractors. In addition, the FDA may, at any time, audit or inspect a manufacturing facility involved with the preparation of our products or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted.

Recently, our manufacturing facility in Cambridge, Massachusetts was inspected by the FDA, resulting in the issuance of an FDA 483 List of Inspectional Observations, an inspection citing observations made during an FDA inspection of the manufacturing facility. We are undertaking remedial measures to improve our manufacturing process and communicate those measures to the FDA, but the FDA may decide that our remedial measures should be revised or expanded, or the FDA may not find our corrective actions to be adequate. Generally, if any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulation occurs independent of such an inspection or audit, we or the FDA may require remedial measures that may be costly and/or time consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales, recalls, warning letters, market withdrawals, seizures or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

We could incur significant costs complying with environmental and health and safety requirements, or as a result of liability for contamination or other harm caused by hazardous materials that we use.

Our research and development and manufacturing processes involve the use of hazardous materials. We are subject to federal, state, local and foreign environmental requirements, including regulations governing the use, manufacture, handling, storage and disposal of hazardous materials, discharge to air and water, the cleanup of contamination and occupational health and safety matters. We cannot eliminate the risk of contamination or injury resulting from hazardous materials, and we may incur liability as a result of any contamination or injury. Under some environmental laws and regulations, we could also be held responsible for costs relating to any contamination at our past or present facilities and at third party waste disposal sites where we have sent wastes. These could include costs relating to contamination that did not result from any violation of law, and in some circumstances, contamination that we did not cause. We may incur significant expenses in the future relating to any failure to comply with environmental laws. Any such future expenses or liability could have a significant negative impact on our financial condition. The enactment of stricter laws or regulations, the stricter interpretation of existing laws and regulations or the requirement to undertake the investigation or remediation of currently unknown environmental contamination at our own or third party sites may require us to make additional expenditures, which could be material.

In order to market any of our product candidates, including MACI and ixmyelocel-T, in the United States, the FDA requires us to file a BLA.

The FDA approved Carticel as a biological product, for which we currently hold a biologics license. MACI and ixmyelocel-T are also subject to the FDA's biological product requirements, which will require us to submit a new BLA for each product prior to being granted marketing approval. To the extent the FDA regulates each of MACI and ixmyelocel-T as a biological product and requires us to file a BLA, we would be unable to sell MACI or ixmyelocel-T unless and until we receive BLA approval from the FDA, which requires that we conduct clinical trials in support of approval of a BLA, which would be expensive and time consuming, and uncertain as to outcome. For example, the FDA may require that we conduct one or more clinical trials in support of approval of a BLA, which would result in the expenditure of additional financial resources and extended timelines to commercialization. In addition, before we can apply for a BLA for MACI in the U.S., we anticipate that we will be obligated to pay certain developmental milestones relating to regulatory and commercialization of MACI in the United States.

Our business, financial condition, results of operation and cash flows could be significantly and negatively affected by substantial governmental regulations.

Our products are subject to rigorous regulation by the FDA and numerous other federal, state and foreign governmental authorities. Overall, there appears to be a trend toward more stringent regulation worldwide, and we do not anticipate this trend to dissipate in the near future.

In general, the development, testing, labeling, manufacturing and marketing of our products are subject to extensive regulation and review by numerous governmental authorities both in the United States and abroad. The regulatory process requires the expenditure of significant time, effort and expense to bring new products to market. For example, FDA approved Epicel as a Humanitarian Use Device, or HUD, which is a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year. HUD treatment is subject to additional FDA requirements, such as recordkeeping, reporting, labeling, as well as limited use of a HUD when approved by an Institutional Review Board, or IRB, that oversees medical treatment. Failure to meet FDA requirements pertaining to a HUD could result in the suspension or revocation of the HUD. While Epicel has been approved as a HUD, oversight is conducted by the Center for Biologics Evaluation and Research (CBER) the branch of the FDA that regulates biologic products, as Epicel is a cell-based product.

If HUD approval is suspended or revoked, marketing approval for Epicel would require the submission and approval of a premarket approval application (or PMA) in order to be made commercially available, or an approved BLA. The PMA and BLA processes are costly, lengthy and uncertain. A PMA must be supported by extensive data, including, but not limited to, technical, preclinical, clinical trial, manufacturing and labeling data, to demonstrate to the FDA's satisfaction the safety and efficacy of the device for its intended use. A BLA must be supported by substantial evidence of clinical safety and effectiveness for its intended use as proven through clinical trials in a statistically significant patient population. If the HUD approval for Epicel was withdrawn, and we were unable to obtain approval of a PMA or BLA, we could not market Epicel for sale in the U.S.

We are also required to implement and maintain stringent reporting, labeling and record keeping procedures. More specifically, in the United States, both before and after a product is commercially released, we have ongoing responsibilities under FDA regulations. Compliance with the FDA's requirements, including the FDA's cGMP recordkeeping regulations, labeling and promotional requirements and adverse event reporting regulations, is subject to continual review and is monitored rigorously through periodic inspections by the FDA. Our failure to comply with U.S. federal, state and foreign governmental regulations could lead to the issuance of warning letters or untitled letters, the

imposition of injunctions, suspensions or loss of regulatory clearance or approvals, product recalls, termination of distribution, product seizures or civil penalties. In the most extreme cases, criminal sanctions or closure of our manufacturing facility are possible.

In addition, the pharmaceutical, biologic and medical industries also are subject to many complex laws and regulations governing Medicare and Medicaid reimbursement and targeting healthcare fraud and abuse, with these laws and regulations being subject to interpretation. In many instances, the industry does not have the benefit of significant regulatory or judicial interpretation of these laws and regulations. In certain public statements, governmental authorities have taken positions on issues for which little official interpretation was previously available. Some of these positions appear to be inconsistent with common practices within the industry but have not previously been challenged.

Various federal and state agencies have become increasingly vigilant in recent years in their investigation of various business practices, such as the federal Anti-kickback Statute and the federal False Claims Act. Governmental and regulatory actions against us can result in various actions that could adversely impact our operations, including:

- The recall or seizure of products;
- The suspension or revocation of the authority necessary for the production or sale of a product;
- The suspension of shipments from particular manufacturing facilities;
- The imposition of fines and penalties;
- The delay of our ability to introduce new products into the market;
- Our exclusion or the exclusion of our products from being reimbursed by federal and state healthcare programs (such as Medicare, Medicaid, Veterans Administration, or VA, health programs and Civilian Health and Medical Program Uniformed Service, or CHAMPUS); and
- Other civil or criminal prosecution or sanctions against us or our employees, such as fines, penalties or imprisonment.

Any of these actions, in combination or alone, or even a public announcement that we are being investigated for possible violations of these laws, could have a material adverse effect on our business, financial condition, results of operations and cash flows.

In the United States, if the FDA were to conclude that we are not in compliance with applicable laws or regulations or that any of our products are ineffective or pose an unreasonable health risk, the FDA could ban such products, detain or seize adulterated or misbranded products, order a recall, repair, replacement, or refund of payment of certain products, refuse to grant pending approval applications, refuse to provide certificates to foreign governments for exports, and/or require us to notify healthcare professionals and others that the products present unreasonable risks of substantial harm to the public health. The FDA may also impose operating restrictions on a companywide basis, enjoin and restrain certain violations of applicable law pertaining to our products and assess civil or criminal penalties against our officers, employees or us. The FDA may also recommend prosecution to the United States Department of Justice (DOJ). Adverse regulatory action, depending on its magnitude, may restrict us from effectively marketing and selling our products.

In many of the foreign countries in which our products are marketed, we are subject to regulations affecting, among other things, clinical efficacy, product standards, packaging requirements, labeling requirements, import/ export restrictions, tariff regulations, duties and tax requirements. Many of the regulations applicable to our products in these countries, such as the Medicinal Products Directive and the ATMP guidelines, governing products in the EU, are similar to those of the FDA. In addition, in many countries the national health or social security organizations require our products to be qualified

before they can be marketed with the benefit of reimbursement eligibility. Failure to receive or delays in the receipt of relevant foreign qualifications also could have a material adverse effect on our business, financial condition, results of operations and cash flows.

As both the U.S. and foreign government regulators have become increasingly stringent, we may be subject to more rigorous regulation by governmental authorities in the future. Our products and our operations are also often subject to the rules of industrial standards bodies, such as the International Standards Organization, or ISO. If we fail to adequately address any of these regulations, our business will be harmed.

Changes to our products or product candidates may require new regulatory approvals or may require us to recall or cease marketing our products until approvals are obtained.

Modifications to our products or product candidates may require new regulatory approvals, including supplements to any of our Investigational New Drug applications (IND) requesting FDA authorization to administer our investigational biological product to humans or supplements to our BLA or Humanitarian Device Exemption (HDE) application, or require us to recall or cease marketing the modified products until these approvals are obtained. We may not be able to obtain those additional approvals for the changes or additional indications in a timely manner, or at all. Obtaining approvals can be a time consuming process, and delays in obtaining required future approvals would adversely affect our ability to introduce new or improved products in a timely manner, which in turn would harm our future growth.

If we or our suppliers fail to comply with ongoing FDA or other foreign regulatory authority requirements, or if we experience unanticipated problems with our products, these products could be subject to restrictions or withdrawal from the market.

The manufacturing processes, reporting requirements, post-approval clinical data and promotional activities for each of our products is subject to continued regulatory review, oversight and periodic inspections by the FDA and other domestic and foreign regulatory bodies. In particular, we and our suppliers are required to comply with cGMP and Good Tissue Practice (GTP) regulations for the manufacture of our products and other regulations which cover requirements such as the methods and documentation pertaining to production controls, labeling, packaging, storage and shipment of any product for which we obtain clearance or approval. Regulatory bodies, such as the FDA, enforce the cGMP, GTP and other regulations through periodic inspections. For example, the holder of an approved BLA is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. The holder of an approved BLA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP and adherence to commitments made in the BLA. If we or a regulatory agency discovers previously unknown problems with a product such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

The failure by us or one of our suppliers to comply with applicable statutes and regulations administered by the FDA and other regulatory bodies, or the failure to timely and adequately respond

to any adverse inspectional observations or product safety issues, could result in, among other things, any of the following enforcement actions:

- Untitled letters, warning letters, fines, injunctions, consent decrees and civil penalties;
- Unanticipated expenditures to address or defend such actions;
- Client notifications for repair, replacement, refunds;
- Recall, detention or seizure of our products;
- Operating restrictions or partial suspension or total shutdown of production;
- Refusing or delaying our requests for approval of new products or modified products;
- Operating restrictions;
- Withdrawing product approvals that have already been granted;
- Refusal to approve a pending marketing application, such as a BLA or supplements to a BLA submitted by us;
- Refusal to grant export approval for our products; or
- Criminal prosecution.

If any of these actions were to occur it would harm our reputation and cause our product sales and profitability to suffer and may prevent us from generating revenue. Furthermore, our key suppliers may not currently be or may not continue to be in compliance with all applicable regulatory requirements which could result in our failure to produce our products on a timely basis and in the required quantities, if at all. In addition, we may be required to conduct costly post-approval studies, and post-market surveillance to monitor the safety or effectiveness of our products. We also must comply with adverse event reporting requirements, which require that we report certain adverse events involving patient use or treatment with our products. Later discovery of previously unknown problems with our products, including unanticipated adverse events or adverse events of unanticipated severity or frequency, manufacturing problems, or failure to comply with regulatory requirements such as cGMP or GTP, may result in changes to labeling, restrictions on such products or manufacturing processes, withdrawal of the products from the market, voluntary or mandatory recalls, fines, suspension of regulatory approvals, product seizures, injunctions or the imposition of civil or criminal penalties which would adversely affect our business, operating results and prospects.

Our marketed products may be used by physicians for indications that are not approved by the FDA. If the FDA finds that we marketed our products in a manner that promoted off-label use, we may be subject to civil or criminal penalties.

Under the Federal Food, Drug and Cosmetic Act (FFDCA) and other laws, we are prohibited from promoting our products for off-label uses. This means, for example, that we may not make claims about the use of our marketed products, Carticel or Epicel, outside of their approved indications, and we may not proactively discuss or provide information on off-label uses of Carticel or Epicel, with very specific and limited exceptions. The FDA does not, however, restrict physicians from prescribing products for off-label uses in the practice of medicine. Should the FDA determine that our activities constitute the promotion of off-label use, the FDA could bring action to prevent us from distributing Carticel or Epicel for the off-label use and could impose fines and penalties on us and our executives. In addition, failure to follow FDA rules and guidelines relating to promotion and advertising can result in, among other things, the FDA's refusal to approve a product, the suspension or withdrawal of an

approved product from the market, product recalls, fines, disgorgement of money, operating restrictions, injunctions or criminal prosecutions.

If the Office of Inspector General within the Department of Health and Human Services, the DOJ, or another federal or state agency determines that we have promoted off-label use of our products, we may be subject to various penalties, including civil or criminal penalties, and the off-label use of our products may result in injuries that lead to product liability suits, which could be costly to our business.

In addition to the FDA restrictions on our marketed products, several other types of state and federal healthcare laws have been applied by DOJ and state attorneys general to restrict certain marketing practices in the pharmaceutical industry. While physicians may prescribe products for off-label uses and indications, if other federal or state regulatory authorities determine that we have engaged in off-label promotion through remuneration, kickbacks or other monetary benefits to prescribers, we may be subject to civil or criminal penalties and could be prohibited from participating in government healthcare programs such as Medicaid and Medicare. In addition, government agencies or departments could conclude that we have engaged in off-label promotion and, potentially, caused the submission of false claims. Even if we are successful in resolving such matters without incurring penalties, responding to investigations or prosecutions will likely result in substantial costs and could significantly and adversely impact our reputation and divert management's attention and resources, which could have a material adverse effect on our business, operating results, financial condition and ability to finance our operations. In addition, the off-label use of our products may increase the risk of injury to patients, and, in turn, the risk of product liability claims. Product liability claims are expensive to defend and could divert our management's attention and result in substantial damage awards against us.

The price and sale of any of our products may be limited by health insurance coverage and government regulation.

Maintaining and growing sales of our products will depend in large part on the availability of adequate coverage and the extent to which third-party payers, including health insurance companies, health maintenance organizations (HMOs), and government health administration authorities such as Medicare and Medicaid, private insurance plans and managed care programs will pay for the cost of the products and related treatment. Hospitals and other healthcare provider clients that purchase our products typically bill various third-party payers to cover all or a portion of the costs and fees associated with the procedures in which such products are used, including the cost of the purchase of these products. Third-party payers are also increasingly attempting to contain healthcare costs by demanding price discounts or rebates and limiting both coverage and the amounts that they will pay for certain products, and, as a result, they may not cover or continue to provide adequate payment for our products. We might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of our products and product candidates to such payers' satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources. Our products and future products might not ultimately be considered cost-effective. Adequate third-party reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in our products and future product development. If coverage and adequate reimbursement are not available, reimbursement is available only to limited levels, or if our costs of production increase faster than increases in reimbursement levels, we may not be able to successfully grow the sales of our products or commercialize any product candidates for which marketing approval is obtained.

Coverage decisions and payment amounts are established at the discretion of the individual third-party payer, and the regulations that govern pricing, coverage and reimbursement vary widely from country to country. Many private payers in the United States, however, use coverage decisions and

payment amounts determined by the Centers for Medicare & Medicaid Services (CMS), as guidelines in setting their coverage and reimbursement policies. As the portion of the U.S. population over the age of 65 and eligible for Medicare continues to grow, we may be more vulnerable to coverage and reimbursement limitations imposed by CMS. While certain procedures using our products are currently covered by Medicare and other third-party payers, future action by CMS or other government agencies may diminish payments to physicians, outpatient centers and/or hospitals for covered services. As a result, we cannot be certain that the procedures performed with our products will be reimbursed at a cost-effective level or reimbursed at all.

Furthermore, the healthcare industry in the United States has experienced a trend toward cost containment as government and private insurers seek to control healthcare costs by imposing lower payment rates and negotiating reduced contract rates with service providers. Therefore, we cannot be certain that the procedures performed with our products will be reimbursed at a cost-effective level. Nor can we be certain that third-party payers using a methodology that sets amounts based on the type of procedure performed, such as those utilized by Medicare and in many privately managed care systems, will view the cost of our products to be justified so as to incorporate such costs into the overall cost of the procedure. Moreover, we are unable to predict what changes will be made to the reimbursement methodologies used by third-party payers in the future.

We face intense competition in the markets targeted by our products. Many of our competitors have substantially greater resources than we do, and we expect that all of our products will face intense competition from existing or future products.

All of our products face intense competition from existing and future products marketed by large companies. These competitors may successfully market products that compete with our products, successfully identify product candidates or develop products earlier than we do, or develop products that are more effective or cost less than our products. These competitive factors could require us to conduct substantial new research and development activities to establish new product targets, which would be costly and time consuming. These activities would adversely affect our ability to effectively commercialize products and achieve revenue and profits.

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

The markets for our products are highly competitive, subject to rapid technological changes, and vary for different candidates and processes that directly compete with our products. Our competitors in the medical and biotechnology industries may have superior products, research and development, manufacturing, and marketing capabilities, and financial resources or marketing positions. Furthermore, 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 for ixmyelocel-T 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. To the extent that others develop new technologies that address the targeted application for our products, our business will suffer. Finally, if we are unable to continue to develop and market new products and technologies

in a timely manner, the demand for our products may decrease or our products could become obsolete, and our revenue may decline.

Ethical, legal, social and other concerns surrounding the use of human tissue in synthetic biologically engineered products may negatively affect public perception of us or our products, or may result in increased scrutiny of our products and any future product candidates from a regulatory perspective, thereby reducing demand for our products, restricting our ability to market our products, or adversely affecting the market price for our common stock.

The commercial success of our products depends in part on general public acceptance of the use of human tissue for the treatment of human diseases and other conditions. While not as controversial as the use of embryonic stem cells and fetal tissue, the use of adult tissue has been the subject of substantial debate regarding related ethical, legal and social issues. We do not use embryonic stem cells or fetal tissue, but the public may not be able to, or may fail to, differentiate our autologous use of adult tissue from the use by others of embryonic stem cells or fetal tissue. This could result in a negative perception of our company or our products.

Future adverse events in the field of cellular based therapy or changes in public policy could also result in greater governmental regulation of our products and potential regulatory uncertainty or delay relating to any required testing or approval.

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 herds, which we believe to be the safest. 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 regulations for controls over bovine material in animal feed. These regulations do not appear to affect our ability to purchase the manufacturing materials we currently use. However, the FDA may propose new 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.

Carticel, MACI or any other product candidate for which we seek approval as a biologic, may face competition sooner than anticipated.

With the enactment of the Biologics Price Competition and Innovation Act of 2009, or BPCI Act, as part of the Patient Protection and Affordable Care Act, an abbreviated pathway for the approval of biosimilar and interchangeable biological products was created. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an existing brand product. Under the BPCI Act, an application for a biosimilar product cannot be approved by the FDA until twelve years after the original branded product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement the BPCI Act may be fully adopted by the FDA, any such processes could have

a material adverse effect on the future commercial prospects for our biological products. While the BCPI Act provides for a twelve-year period of exclusivity, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider any of our future product candidates to be a reference product for competing products, potentially creating the opportunity for competition sooner than anticipated.

Moreover, the extent to which a biosimilar product, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

Health care reform measures and changes in policies, funding, staffing and leadership at the FDA and other agencies could hinder or prevent the commercial success of our products.

In the United States, there have been a number of legislative and regulatory changes to the healthcare system in ways that could affect our future results of operations and the future results of operations of our potential customers.

Furthermore, there have been and continue to be a number of initiatives at the federal and state levels that seek to reduce healthcare costs. In March 2010, President Obama signed into law the Patient Protection and Affordable Health Care Act of 2010, as amended by the Health Care and Education Affordability Reconciliation Act of 2010 (jointly, the PPACA), which includes measures to significantly change the way health care is financed by both governmental and private insurers. Among the provisions of the PPACA of importance to the pharmaceutical industry are the following:

- An annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- Expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing both the volume of sales and manufacturers' Medicaid rebate liability;
- Expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- New requirements to report certain financial arrangements with physicians and teaching hospitals, as defined in the PPACA and its implementing regulations, including reporting any "transfer of value" made or distributed to teaching hospitals, prescribers, and other healthcare providers and reporting any ownership and investment interests held by physicians and their immediate family members and applicable group purchasing organizations during the preceding calendar year, with data collection required and reporting to the Centers for Medicare & Medicaid Services (CMS) required by the 90th day of each calendar year;
- Expansion of health care fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- A licensure framework for follow-on biologic products;
- A new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;

- Creation of the Independent Payment Advisory Board which, beginning in 2014, has authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription products and those recommendations could have the effect of law even if Congress does not act on the recommendations; and

- Establishment of a Center for Medicare Innovation at the CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other health care funding, which could have a material adverse effect on our customers and accordingly, our financial operations.

Additionally, individual states have become increasingly aggressive in passing legislation and implementing regulations designed to control product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and marketing cost disclosure and transparency measures, and designed to encourage importation from other countries and bulk purchasing. Legally-mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects.

In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what products and which suppliers will be included in their healthcare programs. This can reduce demand for our products or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects.

Additionally, given recent federal and state government initiatives directed at lowering the total cost of healthcare, Congress and state legislatures will likely continue to focus on healthcare reform and the reform of the Medicare and Medicaid programs. While we cannot predict the full outcome of any such legislation, it may harm our ability to market our products and generate revenues.

Furthermore, regulatory authorities' assessment of the data and results required to demonstrate safety and effectiveness can change over time and can be affected by many factors, such as the emergence of new information, including on other products, changing policies and agency funding, staffing and leadership. We cannot be sure whether future changes to the regulatory environment will be favorable or unfavorable to our business prospects.

Tissue-based products are regulated differently in different countries. These requirements may be costly and result in delay or otherwise preclude the distribution of our products in some foreign countries, any of which would adversely affect our ability to generate operating revenues.

Tissue based products are regulated differently in different countries. Many foreign jurisdictions have a different and may have a more difficult regulatory pathway for human tissue based products, which may prohibit the distribution of these products until the applicable regulatory agencies grant marketing approval, or licensure. The process of obtaining regulatory approval is lengthy, expensive and uncertain, and we may never seek such approvals, or if we do, we may never gain those approvals. Any adverse events in our clinical trials for a future product under development could negatively impact our products.

Competitor companies or hospitals may be able to take advantage of the EU rules permitting sales of unlicensed medicines for individual patients to sell competing products without a marketing authorization.

The EU medicines rules allow individual member states to permit the supply of a medicinal product without a marketing authorization to fulfill special needs, where the product is supplied in response to a bona fide unsolicited order, formulated in accordance with the specifications of a healthcare professional and for use by an individual patient under his direct personal responsibility.

This may, in certain countries, also apply to products manufactured in a country outside the EU and imported to treat specific patients or small groups of patients. In addition, advanced therapy medicinal products do not need a marketing authorization if they are prepared on a non-routine basis and are used within the same EU member state in a hospital in accordance with a medical prescription for an individual patient (named patient basis).

These exemptions could allow our competitors to make sales in the EU without having obtained a marketing authorization and without undergoing the expense of clinical trials, especially if those competitors have cell processing facilities in the relevant EU member state. Similarly, certain hospitals may be able to compete with us on the basis of these rules. Because any such sales would be made without a marketing authorization, there would be no need for the competitor company or hospital to refer to the clinical data in our marketing authorization dossiers, and so any data exclusivity protection that we may obtain for our products would not prevent such competing sales.

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 are dependent on our key manufacturing, quality and other management personnel and the loss of any of these individuals could harm our business.

Our success depends in large part upon the efforts of our key management and manufacturing and quality staff. The loss of any of these individuals, or our inability to attract and retain highly qualified scientific and management personnel in a timely manner, could materially and adversely affect our business and our future prospects. In the future, we may need to seek additional manufacturing and quality staff members. There is a high demand for highly trained manufacturing and quality personnel in our industry. We face competition for such personnel from other companies, research and academic institutions and other entities. We do not know whether we will be able to attract, train and retain highly qualified manufacturing and quality personnel in the future, which could have a material adverse effect on our business, financial condition and results of operations. A loss of one or more of our key personnel could severely and negatively impact our operations. Our key personnel are employed "at-will," and any of them may elect to pursue other opportunities at any time. We have no present intention of obtaining key man life insurance on any of our key management, manufacturing, quality or other personnel.

Risks Related to Intellectual Property

We have no patent protection for Epicel.

We have no issued patents or pending patent applications relating to Epicel. While we attempt to protect our proprietary information as trade secrets through certain agreements with our employees, consultants, agents and other organizations to which we disclose our proprietary information, we cannot

give any assurance that these agreements will provide effective protection for our proprietary information in the event of unauthorized use or disclosure of such information. If other cultured epidermal autografts are approved and marketed, we will be unable to prevent them from competing with Epicel in the marketplace. We expect that the presence of one or more competing products would reduce our market share and could negatively impact price levels and third party reimbursement policies for Epicel, any of which would materially affect our business.

Our issued patents relating to Carticel and MACI will expire soon and may be insufficient to protect our business.

We have issued patents in the United States and in certain foreign countries that relate to the combinations of chondrocytes and collagen membranes used in Carticel and MACI. However, the issued patents relating to Carticel are scheduled to expire by August of 2016 in the U.S. and by 2022 in Europe. Furthermore, the issued patents relating to MACI are scheduled to expire by August of 2016 in the U.S. and by August of 2017 in Europe. When these patents expire we may be subject to increased competition and our opportunity to establish or maintain product revenue could be substantially reduced or eliminated.

The patents we own may not be of sufficient scope or strength to provide us with significant commercial protection or commercial advantage, and competitors may be able to design around our patents or develop products that provide outcomes that are similar to ours without infringing on our intellectual property rights. In addition, we cannot be certain that any of our pending patent applications will be issued or that the scope of the claims in our pending patent applications will not be significantly narrowed or determined to be invalid.

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.

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. For example, from time to time, the U.S. Supreme Court (Supreme Court), other federal courts, the U.S. Congress or the United States Patent and Trademark Office (USPTO) may change the standards of patentability and any such changes could have a negative impact on our business. There have been several cases involving "gene patents" and diagnostic claims that have been considered by the Supreme Court. A suit brought by multiple plaintiffs, including the American Civil Liberties Union (ACLU) against Myriad Genetics (Myriad) and the USPTO, could impact biotechnology and diagnostic patents. That case involves certain of Myriad's U.S. patents related to the breast cancer susceptibility genes BRCA1 and BRCA2. The Federal Circuit court issued a written decision on July 29, 2011 that reversed the decision of the

U.S. District Court for the Southern District of New York that Myriad's composition claims to "isolated" DNA molecules cover unpatentable subject matter. The Federal Circuit court instead held that the breast cancer genes are patentable subject matter. Subsequently, on March 20, 2012, the Supreme Court issued a decision in Mayo Collaborative v. Prometheus Laboratories (Prometheus) a case involving patent claims directed to optimizing the amount of drug administered to a specific patient. According to that decision, Prometheus' claims failed to add enough inventive content to the underlying correlations to allow the processes they describe to qualify as patent-eligible processes that apply natural laws. The Supreme Court subsequently granted certiorari in the Myriad case, vacated the judgment, and remanded the case back to the Federal Circuit court for further consideration in light of their decision in the Prometheus case. The Federal Circuit court heard oral arguments on July 20, 2012, and issued a decision on August 16, 2012. The Federal Circuit court reaffirmed its earlier decision and held that composition of matter claims directed to isolated nucleic acids are patent-eligible subject matter, but that method claims consisting of only abstract mental processes are not patent-eligible. On September 25, 2012, the ACLU filed a petition for a writ of certiorari asking the Supreme Court to review the Federal Circuit court's decision with respect to the composition of matter claims. On November 30, 2012, the Supreme Court granted the petition and agreed to review the case. On June 13, 2013, the Supreme Court issued a decision in the Myriad case. According to the decision, claims directed to genomic DNA cover unpatentable subject matter. However, claims directed to cDNA are patent eligible subject matter.

On March 4, 2014, the USPTO issued a memorandum entitled "2014 Procedure For Subject Matter Eligibility Analysis Of Claims Reciting Or Involving Laws Of Nature/Natural Principles, Natural Phenomena, And/Or Natural Products". This memorandum provides guidance to patent examiners for examining claims reciting laws of nature/natural principles, natural phenomena, and/or natural products for patent eligibility in view of the Supreme Court decisions in Prometheus and Myriad. The guidance indicates that claims reciting such natural subject matter, read as a whole, that do not significantly differ from such natural subject matter should be rejected as non-statutory subject matter. We cannot assure you that our patent portfolio or our efforts to seek patent protection for our technology and products will not be negatively impacted by the guidance issued by the USPTO, the decisions described above, rulings in other cases, or changes in guidance or procedures issued by the USPTO.

Congress directed the USPTO to study effective ways to provide independent, confirming genetic diagnostic test activity where gene patents and exclusive licensing for primary genetic diagnostic tests exist. This study will examine the impact that independent second opinion testing has on providing medical care to patients; the effect that providing independent second opinion genetic diagnostic testing would have on the existing patent and license holders of an exclusive genetic test; the impact of current practices on testing results and performance; and the role of insurance coverage on the provision of genetic diagnostic tests. The USPTO was directed to report the findings of the study to Congress and provide recommendations for establishing the availability of independent confirming genetic diagnostic test activity by June 16, 2012. On August 28, 2012, the Department of Commerce sent a letter to the House and Senate Judiciary Committee leadership updating them on the status of the genetic testing report. The letter stated in part: "Given the complexity and diversity of the opinions, comments, and suggestions provided by interested parties, and the important policy considerations involved, we believe that further review, discussion, and analysis are required before a final report can be submitted to Congress." The USPTO issued a Request for Comments and Notice of Public Hearing on Genetic Diagnostic Testing on January 25, 2012, and held additional public hearings in February and March 2013. It is unclear whether the results of this study will be acted upon by the USPTO or result in Congressional efforts to change the law or process in a manner that could negatively impact our present or future patent portfolio.

There can be no assurance that the Supreme Court's decision in either the Myriad or Prometheus case will not have a negative impact on biotechnology patents generally or the ability of biotechnology

companies to obtain or enforce their patents in the future. Such negative decisions by the Supreme Court could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

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.

Given our patent position in regard to our products, if we are unable to protect the confidentiality of our proprietary information and know-how related to these products, our competitive position would be impaired and our business, financial condition and results of operations could be adversely affected.

Some of our technology, including our knowledge regarding the processing our products, is unpatented and is maintained by us as trade secrets. In an effort to protect these trade secrets, we require our employees, consultants, collaborators and advisors to execute confidentiality agreements upon the commencement of their relationships with us. These agreements require that all confidential information developed by the individual or made known to the individual by us during the course of the individual's relationship with us be kept confidential and not disclosed to third parties. These agreements, however, may not provide us with adequate protection against improper use or disclosure of confidential information, and these agreements may be breached. A breach of confidentiality could affect our competitive position. In addition, in some situations, these agreements may conflict with, or be subject to, the rights of third parties with whom our employees, consultants, collaborators or advisors have previous employment or consulting relationships. Also, others may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets.

Adequate remedies may not exist in the event of unauthorized use or disclosure of our confidential information. The disclosure of our trade secrets would impair our competitive position and could have a material adverse effect on our business, financial condition and results of operations.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submissions, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our products or product candidates, our competitive position would be adversely affected.

With respect to MACI and ixmyelocel-T, if we are unable to obtain and enforce patents and to protect our trade secrets, others could use our technology to compete with us, which could limit opportunities for us to generate revenues by licensing our technology and selling products.

Our success will depend in part on our ability to obtain and enforce patents and maintain trade secrets in the United States and in other countries. If we are unsuccessful in obtaining and enforcing patents, our competitors could use our technology and create products that compete with our products, without paying license fees or royalties to us.

The preparation, filing, and prosecution of patent applications can be costly and time consuming. Our limited financial resources may not permit us to pursue patent protection of all of our technology and products throughout the world.

Even if we are able to obtain issued patents covering our technology or products, we may have to incur substantial legal fees and other expenses to enforce our patent rights in order to protect our technology and products from infringing uses. We may not have the financial resources to finance the litigation required to preserve our patent and trade secret rights.

A successful challenge to our trademarks could force us to rebrand Epicel, Carticel, or MACI.

We rely on our trademarks to distinguish our products from the products of our competitors, and have registered or applied to register a number of these trademarks. Third parties may challenge our use of the trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing these new brands.

Intellectual property litigation could harm our business. We may be subject to patent infringement claims that could be costly to defend, which may limit our ability to use disputed technologies, and which could prevent us from pursuing research and development or commercialization of some of our products, require us to pay licensing fees to have freedom to operate and/or result in monetary damages or other liability for us.

The success of our business will depend significantly on our ability to operate without infringing patents and other 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. If the technology that we use infringes a patent held by others, we could be sued for monetary damages by the patent holder or its licensee, or we could be prevented from continuing research, development, and commercialization of products that rely on that technology, unless we are able to obtain a license to use the patent. The cost and availability of a license to a patent cannot be predicted, and the likelihood of obtaining a license at an acceptable cost would be lower if the patent holder or any of its licensees is using the patent to develop or market a product with which any of our existing product candidates or our products would compete. If we could not obtain a necessary license, we would need to develop or obtain rights to alternative technologies, which could prove costly and could cause delays in product development, or we could be forced to discontinue the development or marketing of any products that were developed using the technology covered by the patent.

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 expect to 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 become involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time consuming and unsuccessful and have a material adverse effect on the success of our business.

Competitors may infringe our patents or misappropriate or otherwise violate our intellectual property rights. To counter infringement or unauthorized use, litigation may be necessary in the future to enforce or defend our intellectual property rights, to protect our trade secrets or to determine the validity and scope of our own intellectual property rights or the proprietary rights of others. Also, third parties may initiate legal proceedings against us to challenge the validity or scope of intellectual property rights we own or control. These proceedings can be expensive and time consuming. Many of our current and potential competitors have the ability to dedicate substantially greater resources to defend their intellectual property rights than we can. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating our intellectual property.

Litigation could result in substantial costs and diversion of management resources, which could harm our business and financial results. In addition, in an infringement proceeding, a court may decide that a patent owned by or licensed to us is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of shares of our common stock.

If we infringe the rights of third parties we could be prevented from selling products, forced to pay damages, and defend against litigation.

If our products, methods, processes and other technologies infringe the proprietary rights of other parties, we could incur substantial costs and we may have to: obtain licenses, which may not be available on commercially reasonable terms, if at all; abandon an infringing product; redesign our products or processes to avoid infringement; stop using the subject matter claimed in the patents held by others; pay damages; and/or defend litigation or administrative proceedings which may be costly whether we win or lose, and which could result in a substantial diversion of our financial and management resources.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- Others may be able to make products that are the same as or similar to our products or product candidates, but that are not covered by the claims of the patents that we own or have exclusively licensed;
- We or any strategic partners might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or have exclusively licensed;
- We might not have been the first to file patent applications covering certain of our inventions;
- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- It is possible that our pending patent applications will not lead to issued patents;
- Issued patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable as a result of legal challenges;
- Our competitors might conduct research and development activities in the U.S. and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- We may not develop additional proprietary technologies that are patentable; and
- The patents of others may have an adverse effect on our business.

Others may challenge our patent or other intellectual property rights or sue us for infringement.

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 has been or is 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 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.

The use of our products and product candidates may expose us to product liability claims, and we may not be able to obtain adequate insurance. As a result, such 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. Moreover, we derive the raw materials for our products from patients serving as their own donors, the production process is complex, and the handling requirements are specific, all of which increase the likelihood of quality failures and subsequent product liability claims. We may not be able to obtain or maintain product liability insurance on acceptable terms with adequate coverage or at all. If we are unable to obtain insurance, or if claims against us substantially exceed our coverage, then our business could be adversely impacted. Excessive insurance costs or uninsured claims would increase our operating loss and adversely affect our financial condition. Whether or not we are ultimately successful in any product liability litigation, such litigation could consume substantial amounts of our financial and managerial resources and could result in, among other things:

- Significant awards against us;
- Substantial litigation costs;
- Recall of the product;
- Injury to our reputation;
- Withdrawal of clinical trial participants; or
- Adverse regulatory action.

Any of these results could have a material adverse effect on our business, financial condition and results of operations.

Risks Related to an Investment in 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. 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.

We have identified a material weakness in our internal control over financial reporting. If we fail to remediate this material weakness and implement and maintain proper and effective internal control over financial reporting in the future, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, investors' views of us and, as a result, the value of our common stock.

We identified a material weakness in the operation of our internal controls over financial reporting as of June 30, 2014. A material weakness is a deficiency, or a 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 financial statements will not be prevented or detected on a timely basis. The material weakness relates to the evaluation of significant transactions and the financial close process. Specifically, we did not have a sufficient level of accounting and supervisory personnel nor did we have the appropriate level of technical accounting experience and training necessary for our financial reporting requirements during this period. This material weakness contributed to adjustments identified by our independent registered public accounting firm during the quarter ended June 30, 2014. We have commenced efforts to remediate this material weakness through process and internal control improvements. However, if we cannot correct the material weakness we have identified, or if we

experience other material weaknesses investor confidence and our stock price could be adversely affected. Further, if material weaknesses or deficiencies in our internal controls exist and go undetected, our financial statements could contain material misstatements that, when discovered in the future, could cause us to fail to meet our future reporting obligations and cause the price of our common stock to decline.

The market price of the common stock of the combined company may be affected by factors different from those affecting the market price for our common stock in recent history.

Our business in recent history differs from that of the CTRM business, and our current combined business differs from recent history, and accordingly, the results of operations for the combined company may be affected by factors different from those affecting our results of operation in recent history. As a result, the market price for our stock may be impacted differently in the future by those factors than it is currently.

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 $3.31 and $6.49 during the six months ended June 30, 2014. The price of our common stock may continue to fluctuate in response to a number of events and factors, such as:

- Clinical trial results;
- Our inability to successfully integrate the acquired business with our existing business;
- The amount of our cash resources and our ability to obtain additional funding;
- Announcements of research activities, business developments, technological innovations or new products by us or our competitors;
- Entering into or terminating strategic relationships;
- Regulatory developments in both the United States and abroad;
- Disputes concerning patents or proprietary rights;
- Changes in our revenues or expense levels;
- Public concern regarding the safety, efficacy or other aspects of the products or methodologies we are developing;
- News or reports from other stem cell, cell therapy or regenerative medicine companies;
- Reports by securities analysts;
- Status of the investment markets;
- Concerns related to management transitions; and
- Delisting from The NASDAQ Capital Market.

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.

Our failure to meet the continued listing requirements of The NASDAQ Capital Market could result in a de-listing of our common stock.

If we fail to satisfy the continued listing requirements of The NASDAQ Capital Market, such as the corporate governance requirements or the minimum closing bid price requirement, NASDAQ may take steps to de-list our common stock. Such a de-listing would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. In the event of a de-listing, we would take actions to restore our compliance with NASDAQ's listing requirements, but we can provide no assurance that any such action taken by us would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the NASDAQ minimum bid price requirement or prevent future non-compliance with NASDAQ's listing requirements.

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

In the six months ended June 30, 2014, we have sold (i) an aggregate of approximately $5,400,000 of shares of common stock pursuant to our At-the-Market Sales Agreement (ATM) with MLV & Co. LLC (MLV) (formerly McNicoll, Lewis & Vlak) through June 30, 2014, and (ii) an aggregate of approximately $3,200,000 of shares of our common stock to Lincoln Park pursuant to the Lincoln Park Equity Line. During 2013, we sold (i) an aggregate of approximately $5,200,000 of shares of common stock pursuant to our ATM through December 31, 2013, and (ii) in August 2013, we sold 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 and pursuant to a prospectus supplement first made available on August 14, 2013. The ATM, which as of June 30, 2014 had remaining capacity of approximately $9,600,000, allowed us to sell our common stock from time to time under a registration statement on Form S-3 filed in June 2011, pursuant to which we registered $100,000,000 of our securities for public sale. The Form S-3 registration statement filed in June 2011 expired in July 2014, and we intend to file a new registration statement on Form S-3 to continue the ATM program in the coming months. Additionally, pursuant to the Lincoln Park Equity Line we may direct Lincoln Park to purchase up to $15,000,000 worth of shares of our common stock over a 30-month period generally in amounts up to 50,000 shares of our common stock. As of June 30, 2014, we had remaining capacity of approximately $11,800,000 worth of shares under the Lincoln Park Equity Line. However, there are certain factors, such as volume of trading in our common stock, our stock price and the ability to terminate the agreement with notice, which limit the amount that can be raised in a short period of time through the Lincoln Park Equity Line.

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.

We do not anticipate paying dividends on our common stock and, accordingly, shareholders must rely on stock appreciation for any return on their investment.

We have never declared or paid cash dividends on our common stock and do not expect to do so in the foreseeable future. The declaration of dividends is subject to the discretion of our board of directors and will depend on various factors, including our operating results, financial condition, future prospects and any other factors deemed relevant by our board of directors. You should not rely on an investment in our company if you require dividend income from your investment in our company. The success of your investment will likely depend entirely upon any future appreciation of the market price

of our common stock, which is uncertain and unpredictable. There is no guarantee that our common stock will appreciate in value.

We expect that our quarterly results of operations will fluctuate, and this fluctuation could cause our stock price to decline.

Our quarterly operating results are likely to fluctuate in the future. These fluctuations could cause our stock price to decline. The nature of our business involves variable factors, such as the timing of the research, development and regulatory pathways of our product candidates, which could cause our operating results to fluctuate.

Due to the possibility of fluctuations in our revenues and expenses, we believe that quarter-to-quarter comparisons of our operating results are not a good indication of our future performance.

Efforts to comply with recently enacted changes in securities laws and regulations will increase our costs and require additional management resources, and we still may fail to comply.

As directed by Section 404 of the Sarbanes-Oxley Act of 2002, the Securities and Exchange Commission (SEC) adopted rules requiring public companies to include a report of management on their internal controls over financial reporting in their annual reports on Form 10-K. In addition, in the event we are no longer a smaller reporting company, the independent registered public accounting firm auditing our financial statements would be required to attest to the effectiveness of our internal controls over financial reporting. If we are unable to conclude that we have effective internal controls over financial reporting or if our independent registered public accounting firm is required to, but is unable to provide us with a report as to the effectiveness of our internal controls over financial reporting, investors could lose confidence in the reliability of our financial statements, which could result in a decrease in the value of our securities.

If our common stock becomes subject to the SEC's penny stock rules, broker-dealers may experience difficulty in completing customer transactions and trading activity in our securities may be adversely affected.

If at any time our securities are no longer listed on a national securities exchange, including The NASDAQ Stock Market, or we have net tangible assets of $5,000,000 or less and our common stock has a market price per share of less than $5.00, transactions in our common stock will be subject to the SEC's "penny stock" rules. If our common stock becomes subject to the "penny stock" rules promulgated under the Securities Exchange Act of 1934, as amended, broker-dealers may find it difficult to effectuate customer transactions and trading activity in our securities may be adversely affected. For any transaction involving a penny stock, unless exempt, the rules require:

- That a broker or dealer approve a person's account for transactions in penny stocks; and
- The broker or dealer receive from the investor a written agreement to the transaction, setting forth the identity and quantity of the penny stock to be purchased.

In order to approve a person's account for transactions in penny stocks, the broker or dealer must:

- Obtain financial information and investment experience objectives of the person; and
- Make a reasonable determination that the transactions in penny stocks are suitable for that person and the person has sufficient knowledge and experience in financial matters to be capable of evaluating the risks of transactions in penny stocks.

The broker or dealer must also deliver, prior to any transaction in a penny stock, a disclosure schedule prescribed by the SEC relating to the penny stock market, which, in highlight form:

- Sets forth the basis on which the broker or dealer made the suitability determination; and
- That the broker or dealer received a signed, written agreement from the investor prior to the transaction.

Generally, brokers may be less willing to execute transactions in securities subject to the "penny stock" rules. This may make it more difficult for investors to dispose of our common stock and cause a decline in the market value of our stock.

Disclosure also has to be made about the risks of investing in penny stocks in both public offerings and in secondary trading and about the commissions payable to both the broker-dealer and the registered representative, current quotations for the securities and the rights and remedies available to an investor in cases of fraud in penny stock transactions. Finally, monthly statements have to be sent disclosing recent price information for the penny stock held in the account and information on the limited market in penny stocks.

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.

As of June 30, 2014, we had outstanding Class A warrants to purchase 226,299 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 $18.09 per common share and $3.30 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.

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.

On March 9, 2012, the Company entered into a Securities Purchase Agreement with Eastern Capital Limited, a Cayman exempted company (Eastern), to sell 12,308 shares of Series B-1 non-voting preferred stock (Series B-1 preferred stock) in a private placement to Eastern, at a price of $3,250 per share. The Series B-1 preferred stock were exchanged on a one-for-one basis for shares of the Series B-2 voting preferred stock (Series B-2 preferred stock) of the Company in May 2012. Eastern currently holds all of our outstanding Series B-2 preferred stock as well as the accumulated dividends in Series B-1 preferred stock and outstanding Series B-2 voting preferred stock, representing a significant amount of our outstanding capital stock on a fully-converted basis. The accumulated dividends in our Series B-1 preferred stock are exchangeable for shares of Series B-2 preferred stock, subject to certain limitations, and, in March 2017, are convertible into shares of our common stock at our option or Eastern's option, subject to certain limitations.

Based solely on the number of shares of common stock and Series B-2 preferred stock that Eastern Capital held as of June 30, 2014, Eastern Capital has beneficial ownership of approximately 13.5% (calculated on an as converted to common stock basis and excluding warrants and any shares that accrue as a dividend on the shares of Series B-2 preferred) of our voting securities based on the approximately 7,019,488 shares of common stock and Series B-2 preferred stock outstanding as of June 30, 2014. 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 not exchanged for shares of Series B-2 preferred stock and/or converted into shares of our common stock, after March 2017, we may be required to redeem the then outstanding shares of Series B-1 preferred stock and any dividend shares accrued thereon at a price equal to the greater of (A) $3,250 (subject to adjustments for stock splits and similar events) plus all accrued dividends and (B) the then fair market value of a share of common stock multiplied by the number of shares of common stock into which such share of Series B-1 preferred stock is then convertible. Such redemption would be completed in three annual installments beginning not more than 120 days after we receive a request for redemption. The requirement for us to redeem Eastern Capital's shares of Series B-1 preferred stock in cash could diminish our working capital, the consequences of which could have a material adverse effect on our business, operating results, financial condition and prospects.

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.

Risks Related to this Offering

Our management will have broad discretion in allocating the net proceeds of this offering, and may use the proceeds in ways with which you disagree.

Our management has significant flexibility in applying the net proceeds we expect to receive in this offering. Because the net proceeds are not required to be allocated to any specific investment or transaction, and therefore you cannot determine at this time the value or propriety of our application of those proceeds, you and other shareholders may not agree with our decisions. In addition, our use of the proceeds from this offering may not yield a significant return or any return at all for our shareholders. The failure by our management to apply these funds effectively could have a material adverse effect on our business, results of operations or financial condition. See "Use of Proceeds" for a further description of how management intends to apply the proceeds from this offering.

You will experience immediate dilution in the book value per share of the common stock you purchase.

Because the public offering price per share is substantially higher than the book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. After giving effect to the sale by us of 13,725,490 shares of common stock in this offering at the public offering price of $2.55 per share, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, investors in this offering will suffer immediate and substantial dilution of approximately $1.00 per share in the net tangible book value of the common stock acquired. See "Dilution" below for a more detailed discussion of the dilution you will incur if you purchase shares in this offering.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plan, could result in additional dilution of the percentage ownership of our shareholders and could cause our stock price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our shareholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities. If we sell common stock, convertible securities or other equity securities, your investment in our common stock will be diluted. These sales may also result in material dilution to our existing shareholders, and new investors could gain rights superior to our existing shareholders.

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 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, except as required by law, 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;
- Integration of our acquired business and assets;
- Commercialization plans; or
- Revenue expectations and operating results.

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

The net proceeds from the sale of common stock offered pursuant to this prospectus will be approximately $32.7 million after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us (or net proceeds of approximately $37.6 million if the underwriters' over-allotment option is exercised in full), in each case based upon the public offering price of $2.55 per share.

The principal purposes of this offering are to obtain additional capital to support commercialization of our marketed products and fund the development costs associated with our Phase 2b ixCELL-DCM clinical trial of ixmyelocel-T for the treatment of advanced heart failure due to ischemic dilated cardiomyopathy and our preclinical studies, as well as for working capital and general corporate purposes, including reimbursing Sanofi for the one-time cash payment, expected to be in an amount of €2.5 million (or approximately $3.3 million), to the former shareholders of Verigen AG in connection with the continued development of MACI in the U.S. We may also use a portion of the net proceeds to acquire or invest in complementary cell therapy and regenerative medicine businesses, technologies, products or assets.

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."

PRICE RANGE OF OUR COMMON STOCK

Our common stock is traded on The NASDAQ Capital Market under the symbol "ASTM." Our common stock has, from time to time, traded on a limited, sporadic and volatile basis. The table below shows the high and low closing prices for our common stock for the periods indicated, as reported by NASDAQ. Prices per share of our common stock have been adjusted for the twenty-for-one reverse stock split on October 16, 2013 on a retroactive basis.

	Price Ranges	
	High	Low
2014		
First Quarter	$ 6.49	$ 3.31
Second Quarter	5.05	3.51
Third Quarter (through September 10, 2014)	4.08	2.86
2013		
First Quarter	$ 28.20	$ 14.00
Second Quarter	16.00	8.02
Third Quarter	15.48	5.40
Fourth Quarter	5.70	3.21
2012		
First Quarter	$ 44.00	$ 35.60
Second Quarter	52.80	38.80
Third Quarter	43.60	31.40
Fourth Quarter	32.60	23.00

CAPITALIZATION

The following table sets forth our capitalization as of June 30, 2014:

- On an actual basis; and
- On an as adjusted basis to give further effect to our issuance and sale of 13,725,490 shares of our common stock in this offering at the public offering price of $2.55 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

	As of June 30, 2014	
	Actual	As adjusted
	(in thousands, except share amounts)	
Cash	$ 7,263	$ 39,963
Shareholders' equity:		
Series B-2 voting convertible preferred stock, no par value: shares authorized and reserved—38,500; shares issued and outstanding—12,308	$ 38,389	$ 38,389
Common stock, no par value: shares authorized—75,000,000; shares issued and outstanding, actual—7,019,488; shares issued and outstanding, as adjusted—20,744,978	262,789	295,489
Other comprehensive income	5	5
Accumulated deficit	(298,398)	(298,398)
Total shareholders' equity	$ 2,785	$ 35,485

The foregoing discussion is based on 7,019,488 shares of our common stock outstanding as of June 30, 2014 and excludes:

- 506,969 shares of our common stock issuable upon the exercise of stock options outstanding as of June 30, 2014 at a weighted average exercise price of $22.69 per share;
- 1,329,154 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2014 at exercise prices of $18.09 per share (January 2010—226,299 shares), $3.30 per share (December 2010—15,405 shares) and $4.80 per share (August 2013—1,087,450 shares) in each case, before any adjustment as a result of this offering; and
- 615,400 shares of common stock issuable upon the conversion of preferred stock outstanding as of June 30, 2014.

DILUTION

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

The net tangible book value (deficit) of our common stock as of June 30, 2014 was approximately ($552,000), or ($0.08) per share. Net tangible book value (deficit) per share represents our total tangible assets less our total tangible liabilities, divided by the number of shares of common stock.

Net tangible book value (deficit) dilution per share to new investors represents the difference between the amount per share paid by purchasers in this offering and the as adjusted net tangible book value (deficit) per share of our common stock immediately after the completion of this offering. After giving effect to our issuance and sale of 13,725,490 shares of common stock in this offering at the public offering price of $2.55 per share, and after deducting estimated underwriting discounts and commissions and estimated offering expenses, our as adjusted net tangible book value as of June 30, 2014 would have been $1.55 per share. This represents an immediate increase in net tangible book value of $1.63 per share to existing shareholders and an immediate dilution in net tangible book value of $1.00 per share to new investors purchasing shares of our common stock in this offering at the public offering price, as illustrated in the following table:

Offering price per share		$ 2.55
Net tangible book value per share as of June 30, 2014	$ (0.08)	
Increase in net tangible book value per share attributable to new investors	$ 1.63	
As adjusted net tangible book value per share after giving effect to the offering		$ 1.55
Dilution per share to new investors		$ 1.00

If the underwriters exercise in full their option to purchase up to 2,058,823 additional shares of common stock at the public offering price of $2.55 per share, the as adjusted net tangible book value after this offering would be $1.63 per share, representing an increase in net tangible book value of $1.71 per share to existing shareholders and immediate dilution in net tangible book value of $0.92 per share to investors purchasing our common stock in this offering at the public offering price.

The foregoing discussion is based on 7,019,488 shares of our common stock outstanding as of June 30, 2014 and excludes:

- 506,969 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2014 at a weighted average exercise price of $22.69 per share;
- 1,329,154 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2014, at exercise prices of $18.09 per share (January 2010—226,299 shares), $3.30 per share (December 2010—15,405 shares) and $4.80 per share (August 2013—1,087,450 shares) in each case, before any adjustment as a result of this offering; and
- 615,400 shares of common stock issuable upon the conversion of preferred stock outstanding as of June 30, 2014.

BUSINESS

Business Overview

We are a fully integrated, commercial-stage biopharmaceutical company dedicated to the identification, development and commercialization of innovative therapies that enable the body to repair and regenerate damaged tissues and organs to restore normal structure and function. Our product portfolio is comprised of patient-specific (autologous) cell therapies utilizing proprietary manufacturing processes and systems. We have marketed products as well as developmental stage product candidates and our goal is to become the leading cell therapy and regenerative medicine company by developing, manufacturing and marketing best-in-class therapies for patients with significant unmet medical needs.

The following table summarizes our product portfolio and product candidate pipeline:

* Marketing in the EU has been temporarily suspended

** Investigator-sponsored trial (University of Michigan)

Acquisition of Sanofi's CTRM Business

On May 30, 2014, we completed the acquisition of the CTRM business, certain assets, including all of the outstanding equity interests of Genzyme Biosurgery ApS, a wholly-owned subsidiary of Sanofi and over 250 patents and patent applications of Seller and certain of its subsidiaries and assumed certain liabilities for purposes of acquiring a portion of the CTRM business, which researches, develops, manufactures, markets and sells Carticel, MACI and Epicel (the Transaction). In consideration for the acquisition of the CTRM business, we paid a total purchase price of approximately $6.5 million, as follows: (a) $4 million was paid in cash on the closing date of the Transaction, and (b) a $2.5 million promissory note was paid on July 30, 2014.

Concurrent with the closing of the Transaction, we and Sanofi entered into (i) certain IP assignment and license agreements to effect the transfer and license of the intellectual property related to the CTRM Business assigned and/or licensed to us, (ii) certain assignment and assumption of lease agreements for each of the real property leases being assigned to us, and (iii) transition services and transition supply agreements.

Our Strategy

Our objective is to become the leading cell therapy and regenerative medicine company by developing, manufacturing and marketing best-in-class therapies for patients with significant unmet medical needs that require the repair and regeneration of damaged tissues and organs.

To achieve this objective, we intend to:

- Fully integrate the acquired commercial stage CTRM business and restructure the combined businesses to reduce redundancies and related costs, as well as take advantage of complementary technology platforms;
- Achieve accretive impact from the U.S. Carticel and Epicel business beginning in 2015;
- Lower the manufacturing costs for Carticel through an improved ratio of Carticel unit sales to biopsies as well as other efficiencies;
- Assess and capitalize on opportunities to increase revenue from Carticel in the U.S.;
- Develop and execute on a regulatory strategy for the approval of MACI in the U.S.;
- Develop a commercial strategy for the profitable reintroduction of MACI in the EU;
- Expand Epicel usage in the severely burned patient segment by increasing the level of commercial and clinical efforts dedicated to the product and providers;
- 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; and
- 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.

Our Marketed Products

Our approved and marketed products were acquired through the acquisition of the CTRM business of Sanofi, in May 2014. We believe that our acquired CTRM business has been a pioneer in the development and commercialization of autologous cell therapies. The CTRM portfolio includes three marketed autologous cell therapy products, each of which are further described below: Carticel (autologous cultured chondrocytes), a first-generation product for autologous chondrocyte implantation (ACI) currently marketed in the U.S., MACI (matrix-applied characterized autologous cultured

chondrocytes), a third-generation ACI product, and Epicel (cultured epidermal autografts), a permanent skin replacement for full thickness burns greater than or equal to 30% of total body surface area. Our product candidate portfolio also includes ixmyelocel-T, a patient-specific multicellular therapy currently in development for the treatment of advanced heart failure due to ischemic dilated cardiomyopathy (DCM).

Background of Cartilage Defects

Damage to cartilage in the knee can occur from acute trauma or repetitive trauma from playing sports, exercising, working or performing everyday activities. When damaged, cartilage in the knee does not usually heal on its own. If left untreated, cartilage defects can progress and lead to degenerative joint disease, osteoarthritis and potentially require total knee replacement, a poor option for younger and more active patients.

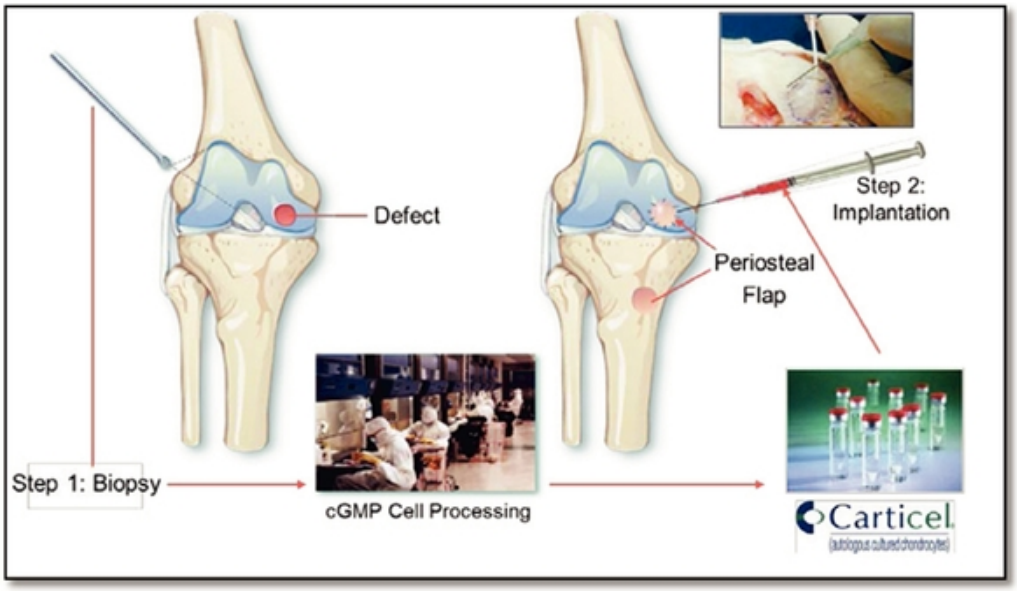
For patients diagnosed with cartilage defects, there are several treatment options, including arthroscopic debridement/chondroplasty, marrow stimulation techniques such as microfracture, a minimally invasive procedure that can be performed during the initial arthroscopic procedure, osteochondral autografts for smaller cartilage injuries, allografts, and autologous chondrocyte implants for larger, more complex injuries.

Carticel

Carticel, a first-generation ACI product for the treatment and repair of cartilage defects in the knee, is the first and currently the only FDA-approved autologous cartilage repair product. Carticel is indicated for the repair of symptomatic cartilage defects of the femoral condyle (medial, lateral or trochlea) caused by acute or repetitive trauma, in patients who have had an inadequate response to a prior arthroscopic or other surgical repair procedure such as debridement, or the removal of damaged or defective cartilage, microfracture, or the creation of tiny fractures in the bone to encourage new cartilage development, drilling/abrasion arthroplasty, or reshaping the joint, or osteochondral allograft/autograft, or transferring cartilage from one joint to another. Carticel received a Biologics License Application (BLA) approval in 1997 and is currently marketed in the U.S. It is generally used on patients with larger lesions (greater than 3 cm2). In the year ended December 31, 2013, net revenues were $35.2 million for Carticel, and in the three months ended March 31, 2014, net revenues were $7.9 million for Carticel.

Carticel is implanted by orthopedic surgeons after obtaining a cartilage biopsy during an initial arthroscopic procedure. The patient's chondrocytes, which are the cells that produce cartilage, are isolated and expanded in a manufacturing process compliant with current Good Manufacturing Practices (cGMP). During a second surgical procedure, the cells are implanted in the cartilage defect under a sutured periosteal flap, where they produce new hyaline cartilage. The therapeutic advantage of this approach relative to other approaches, such as microfracture, is that the autologous

chondrocytes produce the hyaline cartilage that is naturally present in the knee, rather than fibrous cartilage which lacks durability and the wear characteristics of hyaline cartilage.



The Study of the Treatment of Articular Repair (STAR) was designed to determine the safety and efficacy of Carticel in patients who had an inadequate response to a prior cartilage repair procedure. Completed in 2005, this FDA post-approval commitment was a four-year, prospective, multicenter study of 154 patients at 29 participating sites. In a clinically challenging population comprised of patients who suffered moderate-to-large chondral defects and who failed at least one prior surgical cartilage repair treatment, Carticel demonstrated long-term durability up to four years and statistically significant and clinically meaningful reductions in pain and improvement in function. Efficacy data demonstrating durability of repair is now out to 20 years for Carticel.

Market Opportunity for Carticel

In the U.S. annually, there are approximately 1 million arthroscopic procedures and more than 250,000 cartilage surgical procedures. In addition, approximately 50,000 patients under the age of 40 have full thickness defects greater than 2 cm^2. Patients seek retreatment for the repair of larger, symptomatic femoral condyle cartilage defects caused by acute or repetitive trauma. In our experience, patients are often frustrated by recurring symptoms, as they tend to be young, active and motivated to return to a high level of activity.

Typical initial cartilage surgical procedures include chondroplasty (debridement) and/or microfracture. These two procedures account for 98% of all cartilage surgical procedures. Although initial microfracture results demonstrate pain score improvement, generally, only patients with the Class 1, or the smallest defects, do not experience deterioration after 18 months.

Patients seeking retreatment account for about 2.5% of the cartilage surgical repair market and often receive either allograft, autograft or ACI.

Treatment with Carticel provides an opportunity to replace the damaged cartilage with native hyaline cartilage. The documented duration of response from Carticel is unsurpassed by any other treatment, with some patients experiencing a duration of response up to 20 years. In 2013, out of the 50,000 patients seeking retreatment, approximately 1,100 Carticel implants were performed which generated net revenues of $35.2 million, and in the first quarter of 2014, Carticel implants generated net revenues of $7.9 million. We believe that by increasing engagement with, and education of,

managed care payors and hospitals we can improve the coordination of reimbursement and care to improve the physician and patient Carticel experience. We also believe that a consistent positive experience using Carticel will increase utilization and market share.

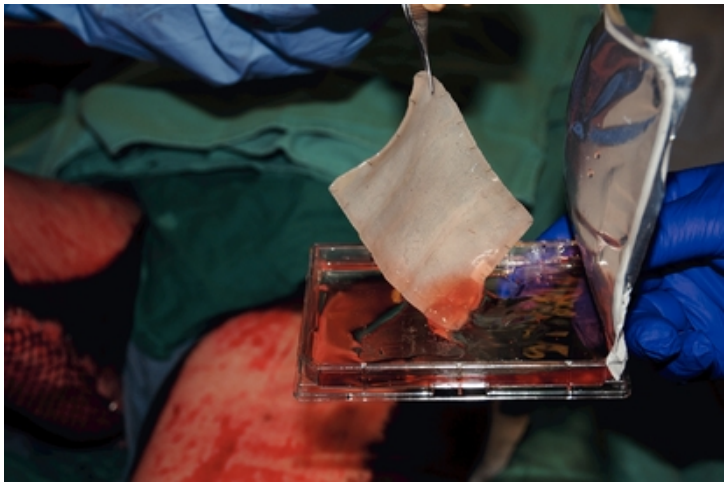
In the U.S., the orthopedic physician target audience is very concentrated, with 60% of the current Carticel business originating from approximately 110 physicians. We believe that our target audience is a group of physicians who self-identify as sports medicine physicians. We believe this target audience is approximately 450 physicians. Most private payers have a medical policy that allows treatment with Carticel. The 15 largest payers have a formal medical policy for Carticel, representing 132 million covered lives.

Epicel

Epicel (cultured epidermal autografts) can be a permanent skin replacement for full thickness burns greater than or equal to 30% of total body surface area (TBSA). Epicel is currently the only FDA-approved autologous epidermal product available for large total surface area burns. Currently, approximately 100 patients are treated with Epicel in the U.S. each year. In the year ended December 31, 2013, net revenues were $7.1 million for Epicel.

Epicel was approved in the United States as a HUD under a Humanitarian Device Exemption (HDE). Devices eligible for an HDE are intended for diseases or conditions that occur in a maximum of 4,000 individuals annually in the United States.

Epicel is produced by isolating and expanding keratinocytes, which are the predominant cell type in the epidermis or outer layer of the skin, obtained from a small biopsy of a patient's healthy skin. Epicel is an important treatment option for patients with severe burns because these patients are generally understood to need a keratinocyte-based epithelium and there is very little skin, which is the only other source of keratinocyte-based epithelium available for autografts for these patients.



Under the original HDE approval and pursuant to the Pediatric Medical Device Safety and Improvement Act of 2007 (FDASIA), Epicel could not be sold for an amount that exceeds the costs of research and development, fabrication, and distribution. In 2012, the FDASIA was modified so that under an HDE program, a manufacturer would be allowed to sell for a profit devices intended for a condition or disease that does not occur (or only rarely occurs) in pediatric patients, so long as it meets certain other specified conditions. Prior to July 1, 2014, Epicel was being sold below standard costs and those costs allowed under the modified FDASIA regulations. As of July 1, 2014, we have increased the price of Epicel to reflect the full costs allowed under those regulations. While devices eligible for an HDE are intended for diseases or conditions that occur in a maximum of 4,000 individuals annually in

the United States, the modified FDASIA does not cap the number of devices for which the manufacturer may obtain a profit per year at 4,000 devices, but rather assigns an "annual distribution number." A manufacturer may not distribute more than the annual distribution number assigned by FDA at the time the exemption is granted. We are currently investigating the potential impact of this change on our ability to sell Epicel for a profit.

Market Opportunity for Epicel

Each year in the U.S., more than 40,000 people are hospitalized for burns. More than 2,000 of these patients are treated for burns covering more than 30% of their TBSA, the labeled indication for Epicel. Of these patients, fewer than 100 each year are treated with Epicel. Currently, the mortality rate for this group is approximately 34%, partially due to the lack of healthy tissue from which to harvest autografts. Although age can vary, the typical Epicel patient is young and has suffered full thickness burns due to occupational, household or auto accidents, trash burning with gasoline, inappropriate use of space heaters or carelessness with flammable materials. Many of the most severely burned patients are medivac transported to one of the 127 specialized burn centers across the U.S. While the average acute care hospital has less than 3 admissions for burn annually, these specialized burn centers average over 200.

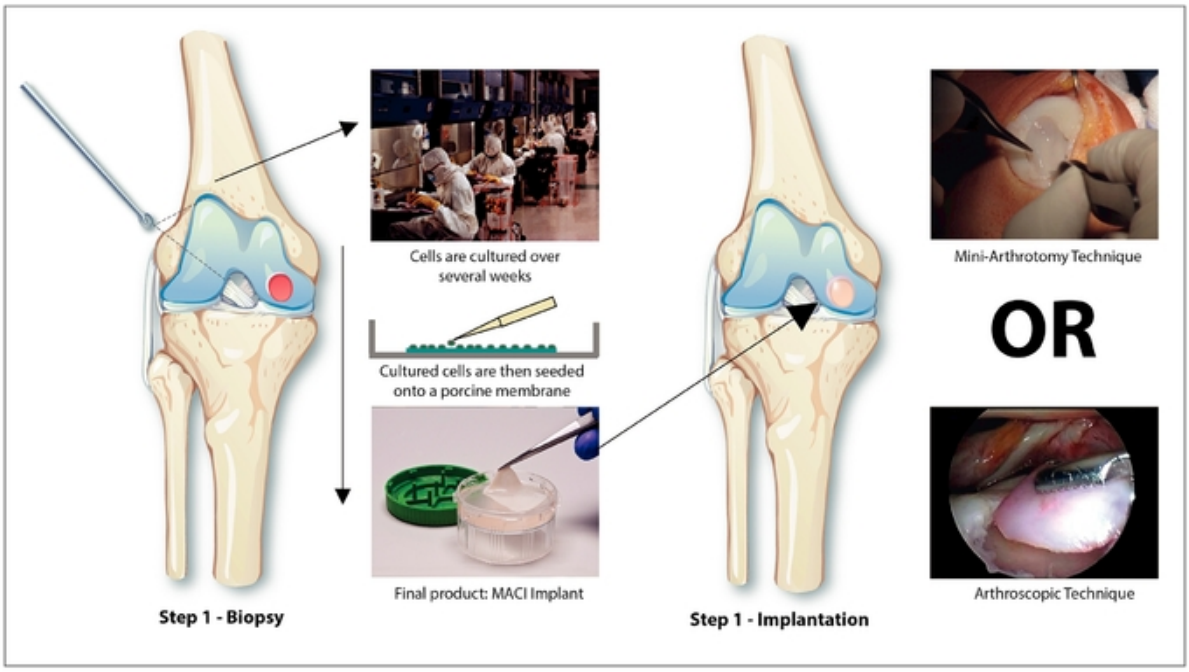
Relative to clinical need, we believe Epicel is underutilized due to lack of consistent promotional effort and burn center support. We expect Epicel's utility to grow as commercial and clinical efforts are appropriately dedicated to the product and providers. Currently more than 40% of our Epicel business comes from a single 70 bed burn center. The 127 specialized burn care facilities in the U.S. have a total of approximately 1,700 burn beds as of 2012. Up until July, 2014, we only used one sales representative for selling Epicel and two partially dedicated Medical Scientific Liaisons supporting Epicel inquiries. We have recently expanded the Epicel sales force to three representatives and intend to increase the number of burn centers called upon.

MACI

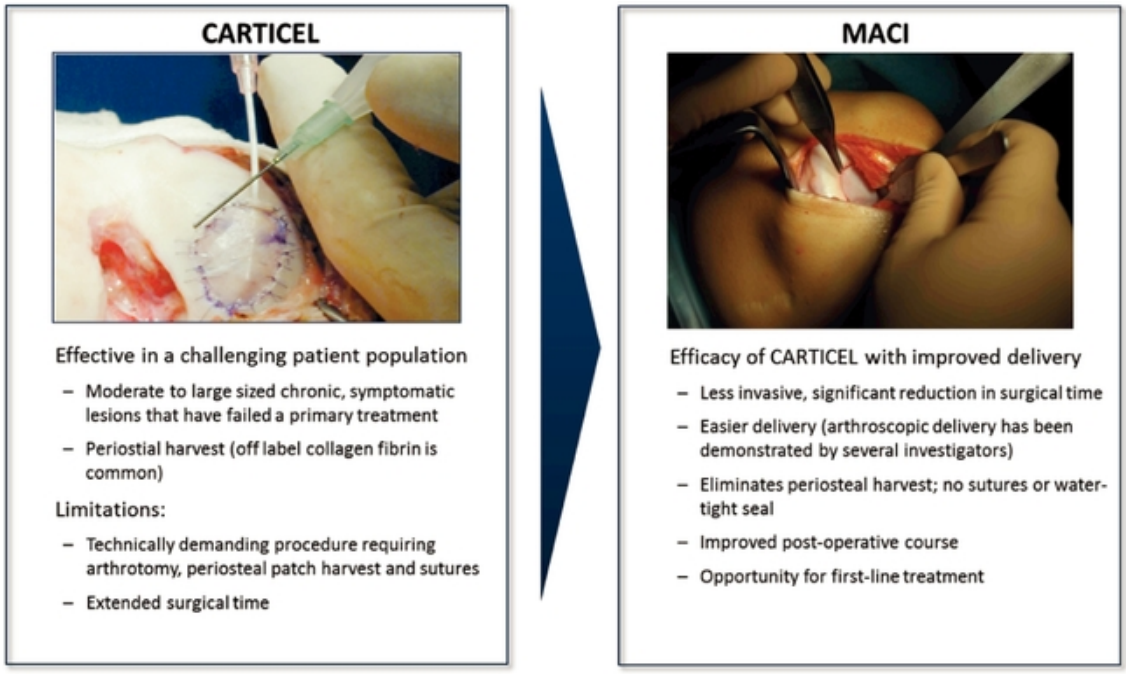
MACI, is a third-generation ACI product for the treatment of focal chondral cartilage defects in the knee. MACI received marketing authorization in Europe in June 2013 by meeting the requirements of the ATMP guidelines based on the results of the SUMMIT trial in which MACI was manufactured at, and supplied from, the Cambridge, Massachusetts site. MACI has been commercially available in the EU since 1998. Aside from a small number of currently pending procedures, marketing of MACI has been temporarily suspended as part of a restructuring of the business as of August 2014 primarily due to low utilization and an unfavorable pricing environment. We believe that MACI, which is a Phase 3 product candidate in the U.S., has strong revenue potential in the U.S. and we are planning to discuss approval requirements with the FDA. The timing and process to gain approval in the U.S. and a possible reintroduction in select EU countries have not yet been determined.

Similar to Carticel, during an initial surgical procedure, a surgeon obtains a biopsy of healthy cartilage and the chondrocytes are isolated, expanded and uniformly seeded onto a bioabsorbable Type I/IIIa collagen membrane to form the implant in a cGMP manufacturing process at a facility in

Copenhagen, Denmark. Unlike Carticel, MACI is implanted during a mini-arthrotomy in which the implant is trimmed to the size of the defect and fixed in the defect with fibrin glue and without sutures



The advantage of MACI relative to Carticel is that it provides the same efficacy with improvement in ease of use for the physician and reduced morbidity for the patient. The implant procedure for MACI is less invasive than for Carticel, entailing a mini-arthrotomy or even arthroscopic delivery, eliminating the need for a periosteum harvest and sutures.



The pivotal clinical trial supporting MACI registration in Europe, Superiority of MACI Implant to Microfracture Treatment (SUMMIT), was completed in 2012. Analysis of this 144 patient superiority study demonstrated that there is a statistically significant and clinically meaningful improvement in the co-primary endpoint of pain and function for those patients treated with a MACI implant compared to microfracture which was the current standard of care. We expect that the FDA may require an additional clinical trial to support approval of a BLA in the United States.

As part of its acquisition of Verigen AG (Verigen), Genzyme Corporation, a subsidiary of Sanofi, agreed to make cash payments to Verigen upon the achievement of developmental milestones relating to regulatory and commercialization of MACI in the United States. In connection with our acquisition of the CTRM business, we agreed that if we further develop MACI in the U.S., we will be obligated to pay these milestone payments. However, we understand that Sanofi intends to enter into a settlement agreement with the former shareholders of Verigen whereby these shareholders have agreed to discharge all obligations related to these MACI milestone payments in exchange for a one-time cash payment, expected to be in an amount of €2.5 million (approximately $3.3 million) due within two months from the date when all parties sign the settlement agreement. We are a third-party beneficiary of the settlement agreement and, as we agreed in connection with our acquisition of the CTRM business, we are responsible to reimburse Sanofi for this €2.5 million payment. As described more fully under the caption "Use of Proceeds" we intend to use a portion of the proceeds from this offering for the reimbursement.

Market Opportunity for MACI

MACI, if introduced in the U.S., should both replace Carticel and expand the market since MACI shares all of the advantages of Carticel, including durability of response, while being less invasive, shortening procedure time, eliminating the need for a periosteal harvest, having a lower frequency of subsequent surgical interventions and an improved recovery period.

Marrow Donation

Like many companies and academic institutions conducting research on cell therapy, we require consistent access to high quality bone marrow. As part of an effort to lower our costs we have begun collecting bone marrow for research use using our bone marrow collection center located in San Diego, CA and our wholly-owned subsidiary Marrow Donation, LLC. We initiated commercial sales of bone marrow in June 2014. Based on the strong interest that we believe exists across the biopharmaceutical industry in the use of bone marrow and bone marrow-derived cells as drug discovery tools, we believe that this represents an opportunity for our company.

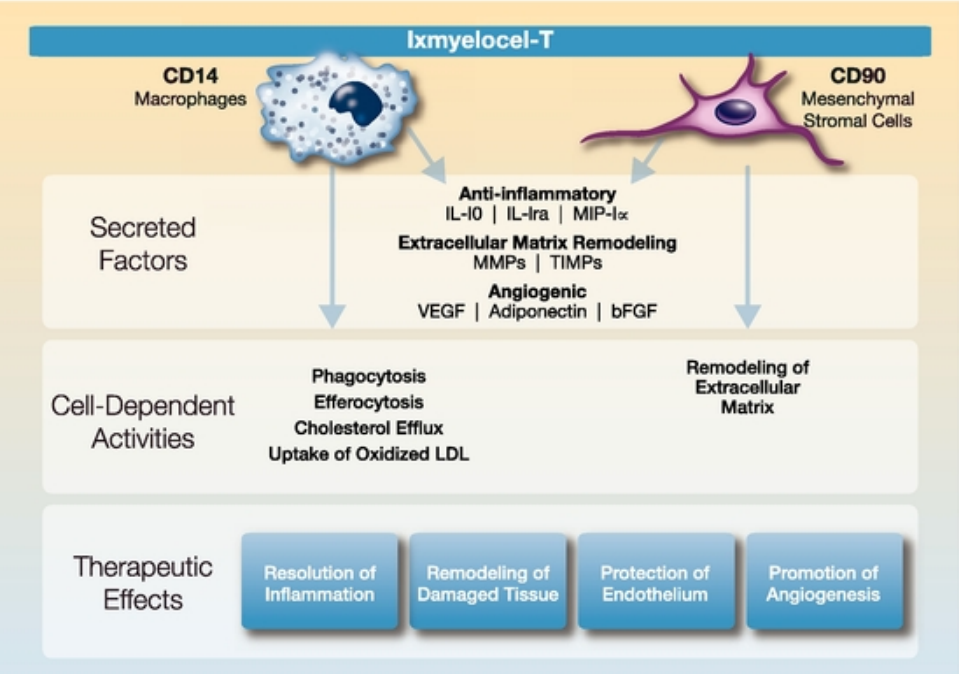
Ixmyelocel-T Technology Platform

Our preapproval stage portfolio also includes ixmyelocel-T, a unique patient-specific multicellular therapy derived from an adult patient's own bone marrow which utilizes our proprietary, highly automated and scalable manufacturing system. 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. We believe the novelty and advantage of using ixmyelocel-T is the expansion of a unique combination of cell populations, including MSCS and M2-like macrophages, which secrete a distinct combination of angiogenic and regenerative factors, and possess the ability to remain anti-inflammatory in the face of inflammatory challenge.

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.

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



Studies examining the impact of ixmyelocel-T on human umbilical vein endothelial cells *in vitro* demonstrate: the secretion of pro-angiogenic factors; enhanced migration of endothelial cells following injury; increased endothelial cell proliferation; and branch formation. Treatment with ixmyelocel-T in a rat model of hind limb ischemia *in vivo* resulted in significantly increased blood flow perfusion and capillary density, gene expression and plasma levels of the anti-inflammatory cytokine. Our studies demonstrate that ixmyelocel-T brings to bear a dynamic concert or angiogenic and anti-inflammatory effects, which facilitate ischemic tissue repair.

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 CLI:

- *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.

- *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.

Ixmyelocel-T 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. We expect to complete enrollment of the ixCELL-DCM study by the end of 2014, and have top-line efficacy results approximately 12 months later.

Ixmyelocel-T has been granted a U.S. Orphan Drug designation by the FDA for the treatment of DCM. We also have an ongoing ixmyelocel-T clinical study for the treatment of craniofacial reconstruction, for which we expect results by the first half of 2016, and have conducted clinical studies for the treatment of CLI.

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 six million patients currently suffering from heart failure in the United States and an estimated 550,000 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 a leading cause of heart failure and 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. 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 approximately $1 million. LVADs are also expensive at an estimated cost of over $175,000 and have a mortality rate of 50% at two years.

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. The estimated incidence of DCM is 148 cases per 100,000 persons, or 444,000 patients. The more severe, or refractory (NYHA Class III/IV) ischemic DCM patient population is difficult to estimate, but we believe it to be approximately one third of the overall DCM population. Ixmyelocel-T has been granted a U.S. Orphan Drug designation by the FDA for the treatment of DCM, which we believe provides the potential for 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. Sixty-one patients were randomized, and of those, 59 received treatment in the phase 2a studies. 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.

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 (IDCM) groups in both studies. In these studies, fewer ischemic patients treated with ixmyelocel-T experienced a major adverse cardiovascular event (MACE) during follow up compared to control patients, representing greater than 50% reduction in the number of patients having a MACE event. A similar benefit was not seen in the non-ischemic patients. Heart failure (HF) exacerbation was the most common MACE. In the combined IDCM 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 greater than 50% 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 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 IDCM groups. The majority of ixmyelocel-T-treated patients with IDCM, but not control patients, had improvement in New York Heart Association (NYHA) Class that was sustained over the 12 months following treatment. Improvement in NYHA Class is considered clinically meaningful. Additionally, a higher percentage of ixmyelocel T-treated IDCM patients showed a clinically meaningful improvement in self-reported quality of life and increased 6 minute walk distance 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 treat 108 patients at approximately 35 sites in the U.S. and Canada. We expect that 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. We expect that 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 2014, and have top-line efficacy results approximately 12 months later.

Production

Cell Manufacturing and Cell Production Components

We acquired two cell manufacturing facilities as part of the acquired CTRM business in Cambridge, Massachusetts and Copenhagen, Denmark. The Cambridge facility, which is approved by the FDA, is used for U.S. manufacturing and distribution of Carticel, Epicel manufacturing and worldwide distribution and also manufactured MACI for the SUMMIT study conducted for approval in Europe. The Cambridge facility also houses the Manufacturing and Technical Services organization, which is responsible for process development, release assay development, and technology transfers between sites and departments. The Copenhagen manufacturing facility, which was approved by the Danish Medicines Agency (DKMA), was responsible for MACI manufacturing and distribution in Europe. As part of the June 2014 restructuring, MACI manufacturing at the Copenhagen manufacturing facility will be discontinued. The lease expires in 2017 by which time we expect to either have found a new tenant to utilize the building with the existing leasehold improvements or we intend to sell the existing equipment and restore the building to its original state prior to occupation by Genzyme Biosurgery ApS. We expect that any future clinical and commercial production of MACI will occur at our Cambridge facility.

We also operate a centralized cell manufacturing facility in Ann Arbor, Michigan. The facility supports the current ixCELL-DCM clinical trial being conducted in the United States and Canada and has sufficient capacity, with minor modifications, to supply our early commercialization requirements. We may establish and operate larger commercial-scale cell manufacturing facilities for the United States market in the future to accommodate potential market growth. We have reached agreement with the FDA on Chemistry, Manufacturing and Control (CMC) which was completed as part of the SPA process with the FDA for the Phase 3 REVIVE clinical trial.

Our ixmyelocel-T patient-specific multicellular therapies are manufactured using our proprietary Aastrom Replicell System (ARS) cell manufacturing system. Our manufacturing process is conducted in a highly-automated, fully-closed and rigorously controlled system. Our system is modular and thus both highly scalable and reproducible and is located in a 5,000-square-foot centralized manufacturing facility in Ann Arbor, Michigan. We believe the ARS based production is conducted under current Good Manufacturing Practices (cGMP) guidelines required by the FDA and has a current annual capacity to treat up to 1,500 patients. Upon approval we can scale-up to meet demand simply by adding additional ARS modules into existing and new clean rooms.

We have established relationships with manufacturers that are registered with the FDA as suppliers of medical products to produce various components of our patented cell manufacturing system.

We have established relationships with various third parties who manufacture and/or supply certain components, equipment, disposable devices and other materials used in our cell manufacturing process to develop our cell products, as well as our final assemblies, component parts, subassemblies and associated spare parts used in the instrumentation platform of our cell production system.

In October 2010, we entered into a contract manufacturing and supply agreement (Supply Agreement) with ATEK Medical, LLC (ATEK) for the manufacture of our proprietary cell cassette for use in our manufacturing process. In November 2011, ATEK was purchased by Vention and currently operates as a division of Vention. There have been no changes to the terms of the Supply Agreement as a result of this purchase.

Pursuant to the terms of the Supply Agreement, we have granted Vention the exclusive right to manufacture our proprietary cell cassette, which includes assembly, labeling, packaging and sterilization. Vention is responsible for obtaining all of our approved components pertaining to the cassettes and we are obligated to order and purchase the cassettes from Vention on an agreed upon schedule and in agreed upon quantities. In addition, we provided Vention with reasonable engineering support to initiate and ramp up manufacturing of the cassettes and expect to supply all manufacturing equipment.

Research & Development

The bulk of our ongoing research is based on ixmyelocel-T, our unique multicellular product produced from the patient's bone marrow using Aastrom's proprietary manufacturing system. We have demonstrated in the laboratory that the cells in our therapy are capable of multiple biological activities thought to play a critical role in repairing diseased and damaged tissues. These activities include aspects of tissue remodeling, promotion of angiogenesis and resolution of inflammation. In addition to these properties demonstrated *in vitro*, we have also shown that the therapy increases blood perfusion in both rat and mouse models of CLI. We have ongoing preclinical studies designed to further characterize the mechanism of action of our product in the treatment of cardiovascular diseases as well as explore other potential disease states which may benefit from the use of ixmyelocel-T.

In addition, our proprietary cell manufacturing system has demonstrated the capability to produce other types of cells. In the future, we may continue to explore the application of our manufacturing technology for the production of other cell types where there are potential opportunities to collaborate in the development of new cell therapies.

Patents and Proprietary Rights

Our success depends in part on our ability, and the ability of our licensors, to obtain patent protection for our products and processes.

As part of the acquired CTRM business, we acquired a multinational intellectual property estate. The intellectual property estate includes patents and patent applications directed to chondrocyte implants and related technologies. Although we do not own any patents or patent applications relating to Epicel, many of the processes and techniques are trade secrets and would be difficult to replicate without significant investment and time. We do own issued patents directed to the combinations of chondrocytes and collagen membranes used in Carticel and MACI, which are scheduled to expire in August of 2016 in the U.S. and in August of 2017 abroad. In certain foreign countries, selected patent rights covering Carticel are scheduled to expire in 2022.

We also own a broadly filed trademark portfolio with registrations for Carticel, MACI, and Epicel.

The processes and technologies related to the ixmyelocel-T and ARS system platform include 17 unexpired issued United States patents. Eleven of these patents are material patents that protect our cellular therapy. We own ten of these patents and one has been licensed exclusively from the University of Michigan. These patents present various claims relating to (i) the composition of our ixmyelocel-T cellular therapy, (ii) methods to manufacture or administer the ixmyelocel-T cellular therapy, and

(iii) the ARS bioreactor device that is used to make ixmyelocel-T products. The number of United States patents of each type with expiration range is listed in the table below.

Patent Type	Number	Expiry (Years)
Composition of Matter	2	1 and 15
Methods	2	13
Bioreactor Device	7	1 - 2

Certain patent equivalents to the United States patents have also been issued in other jurisdictions including Australia, United Kingdom, and Canada, and under the European Patent Convention. In addition, we have filed applications for patents in the United States and equivalent applications in certain other countries claiming other aspects of our cell products and manufacturing processes. Our most significant patent that protects the composition of the cellular therapy directly, "Mixed cell populations for tissue repair and separation technique for cell processing" (US Patent 7,871,605), was issued in January 2011 and will expire in 2029. A divisional application of 7,871,605 for administration of this composition to patients was allowed by the USPTO in January 2012 and was issued in the April 2012 and will expire in 2027. A second divisional application of 7,871,605 directed to the methods of manufacture of our cell compositions was issued in March 2013 and will expire in 2027. Patents that protect our automated bioreactor device and culture system expire in 2015, but we will continue to rely on trade secrets and un-patentable know-how.

In 2007, the use of ixmyelocel-T for the treatment of DCM received an Orphan Drug Designation from the FDA, which provides seven years of market exclusivity, should ixmyelocel-T receive FDA approval for this indication. The validity and breadth of claims in medical technology patents involve complex legal and factual questions and, therefore, may be highly uncertain. No assurance can be given that any patents based on pending patent applications or any future patent applications by us, or our licensors, will be issued, that the scope of any patent protection will exclude competitors or provide competitive advantages to us, that any of the patents that have been or may be issued to us or our licensors will be held valid if subsequently challenged or that others will not claim rights in or ownership of the patents and other proprietary rights held or licensed by us. Furthermore, there can be no assurance that others have not developed or will not develop similar products, duplicate any of our products or design around any patents that have been or may be issued to us or our licensors. Since patent applications in the United States are maintained in secrecy until they are published 18 months after filing, we also cannot be certain that others did not first file applications for inventions covered by our and our licensors' pending patent applications, nor can we be certain that we will not infringe any patents that may be issued to others on such applications.

We rely on certain licenses granted by a number of third parties, including Sanofi and the University of Michigan for certain patent rights. If we breach such agreements or otherwise fail to comply with such agreements, or if such agreements expire or are otherwise terminated, we may lose our rights in such patents.

We also rely on trade secrets and un-patentable know-how that we seek to protect, in part, by confidentiality agreements. It is our policy to require our employees, consultants, contractors, manufacturers, outside scientific collaborators and sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific limited circumstances. We also require signed confidentiality or material transfer agreements from any company that is to receive our confidential information. In the case of employees, consultants and contractors, the agreements generally provide that all inventions conceived by the individual while rendering services to us shall be assigned to us as the exclusive property of Aastrom. There can be no assurance, however, that these agreements will not be breached, that we

would have adequate remedies for any breach, or that our trade secrets or un-patentable know-how will not otherwise become known or be independently developed by competitors.

Our success will also depend in part on our ability to develop additional commercially viable products without infringing the proprietary rights of others. We do not believe any of our approved products or our currently contemplated products or processes infringe any existing valid issued patent. However, the results of patent litigation are unpredictable, and no assurance can be given that patents do not exist or could not be filed which would have an adverse effect on our ability to market our products or maintain our competitive position with respect to our products. If our technology components, designs, products, processes or other subject matter are claimed under other existing United States or foreign patents, or are otherwise protected by third-party proprietary rights, we may be subject to infringement actions. In such event, we may challenge the validity of such patents or other proprietary rights or we may be required to obtain licenses from such companies in order to develop, manufacture or market our products. There can be no assurances that we would be able to obtain such licenses or that such licenses, if available, could be obtained on commercially reasonable terms. Furthermore, the failure either to develop a commercially viable alternative or obtain such licenses could result in delays in marketing our proposed products or the inability to proceed with the development, manufacture or sale of products requiring such licenses, which could have a material adverse effect on our business, financial condition and results of operations. If we are required to defend ourselves against charges of patent infringement or to protect our proprietary rights against third parties, substantial costs will be incurred regardless of whether we are successful. Such proceedings are typically protracted with no certainty of success. An adverse outcome could subject us to significant liabilities to third parties and force us to curtail or cease our development and sale of our products and processes.

Certain of our and our licensors' research has been or is being funded in part by the Department of Commerce and by a Small Business Innovation Research Grant obtained from the Department of Health and Human Services. As a result of such funding, the United States government has certain rights in the technology developed with such funding. 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 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 United States government may use the invention for its own needs.

Sales and Marketing

Both our marketed and development stage products are specialty products with focused physician and institutional call points. The U.S. Carticel commercial organization is comprised of approximately 25 employees, including Clinical Account Executives, Regional Sales Directors and a Government Accounts Manager. The target audience is a small (well under 1,000) set of sports medicine orthopedic surgeons. We expect to utilize the same sales force for MACI.

Reimbursement coverage for Carticel is widespread. The 15 largest payers, representing approximately 98% of commercial lives, have a formal medical policy that allows treatment with Carticel within labeled indications. These 15 plans represent approximately 132 million covered lives and include the top five national plans —WellPoint, United Healthcare, Aetna, CIGNA and Humana.

US Bioservices Corporation (USB) is the exclusive distributor of Carticel in the United States. USB purchases and takes title to Carticel upon shipment of the product. USB works with the payers on behalf of patients and surgeons to ensure medical coverage and to obtain reimbursement for Carticel implantation procedures. We retain all responsibility for shipment of the product to the surgical suite and may have certain indemnification obligations to USB. USB would also be the exclusive distributor of MACI in the United States, if and when it is approved by the FDA.

Sales of Epicel are supported by three Clinical Account Executives and Medical Science Liaisons. This represents an expansion over past support levels. Since there are under 150 specialized burn centers in the U.S. increasing coverage to the majority of the target audience should be feasible with only a small number of incremental Clinical Account Executives and Medical Science Liaisons.

If and when ixmyelocel-T is approved, we anticipate utilizing parts of the existing organization, such as Sales Operations, Sales Management, and Government Accounts, as well as augmenting our existing sales and marketing organization to cover the expanded physician audience. The target physician population will likely be heart failure specialists and interventional cardiologists in secondary and tertiary cardiac facilities, a specialty audience which can be covered by a modest sized sales force. However, we intend to explore other options, including partnerships, to help minimize costs and increase penetration if and when the product is commercialized.

Government Regulation

Our research and development activities and the manufacturing and marketing of our products are subject to the laws and regulations of governmental authorities in the United States and other countries in which our products will be marketed. Specifically, in the United States, the FDA, among other activities, regulates new product approvals to establish safety and effectiveness of these products. Governments in other countries have similar requirements for testing and marketing. In the United States, in addition to meeting FDA regulations, we are also subject to other federal laws, such as the Occupational Safety and Health Act and the Environmental Protection Act, as well as certain state laws.

Our cell products are somatic cell therapies regulated as biologics. With this classification, commercial production of our products will need to occur in registered/licensed facilities in compliance with cGMP for biologics (cellular products).

Regulatory Process

Our products are subject to regulation as biological products under the Public Health Service Act which is incorporated into the FFDCA. Different regulatory requirements may apply to our products depending on how they are categorized by the FDA under these laws. The FDA has indicated that it intends to regulate products based on our technology as licensed biologics through the FDA's Center for Biologics Evaluation and Research (CBER). As current regulations exist, the FDA requires regulatory approval for certain human cellular- or tissue-based products, including our cell products, through a Biologics License Application (BLA) submission.

Approval of new biological products is a lengthy procedure leading from development of a new product through preclinical and clinical testing. This process takes a number of years and the expenditure of significant resources. There can be no assurance that our product candidates will ultimately receive regulatory approval.

Regardless of how our product candidates are regulated, the FFDCA and other Federal and State statutes and regulations govern or influence the research, testing, manufacture, safety, labeling, storage, record-keeping, approval, distribution, use, product reporting, advertising and promotion of such products. Noncompliance with applicable requirements can result in civil penalties, recall, injunction or seizure of products, refusal of the government to approve or clear product approval applications or to

allow us to enter into government supply contracts, withdrawal of previously approved applications and criminal prosecution.

Product Approval

In order to obtain FDA approval of a new biological product, sponsors must submit proof of safety and effectiveness. In most cases, such proof entails extensive nonclinical, also known as preclinical studies and clinical trials. The testing, preparation of necessary applications and processing of those applications by the FDA is expensive, may take several years to complete and is uncertain as to outcome. There can be no assurance that the FDA will act favorably or in a timely manner in reviewing submitted applications, and we may encounter significant difficulties or costs in our efforts to obtain FDA approvals, in turn, which could delay or preclude us from marketing any products we may develop. The FDA may also require post-marketing testing and surveillance of approved products, or place other conditions on the approvals. These requirements could cause it to be more difficult or expensive to sell the products, and could therefore restrict the commercial applications of such products. Product approvals may be withdrawn if compliance with applicable regulations is not maintained or if problems occur following commercialization. For patented technologies, delays imposed by the governmental approval process may materially reduce the period during which we will have the exclusive right to exploit such technologies.

If clinical trials of a proposed biological product are required, the manufacturer or distributor of a biologic will have to submit an Investigational New Drug (IND) application with the FDA prior to commencing human clinical trials. The submission must be supported by data, typically including the results of preclinical and laboratory testing. The conduct of the preclinical tests must comply with federal regulations, including good laboratory practice, or GLP, requirements. The results of preclinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted. Following submission of the IND, the FDA has 30 days to review the application and raise safety and other clinical trial issues. If we are not notified of objections within that period, clinical trials may be initiated, and human clinical trials may commence at a specified number of investigational sites with the number of patients approved by the FDA. We have submitted several INDs for our cell products, and we have conducted clinical trials under these INDs.

Our products are and our product candidates will be regulated by the FDA as a licensed biologic, although there can be no assurance that the FDA will not choose to regulate our products in a different manner in the future. The FDA categorizes human cell- or tissue-based products as either minimally manipulated or more than minimally manipulated, and has determined, among other things, that more than minimally manipulated products require clinical trials to demonstrate product safety and effectiveness and the submission of a BLA for marketing authorization. For products that may be regulated as biologics, the FDA requires: (i) preclinical laboratory and animal testing; (ii) submission to the FDA of an IND application, which must become effective prior to the initiation of human clinical trials; (iii) adequate and well-controlled clinical trials to establish the safety and effectiveness of the product for its intended use; (iv) submission to the FDA of a BLA; and (v) review and approval of the BLA as well as inspections of the manufacturing facility by the FDA prior to commercial marketing of the product.

For purposes of BLA approval, human clinical trials are typically conducted in three sequential phases that may overlap:

- Phase 1—The biological product is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial

human testing is often conducted in patients. These trials may also provide early evidence on effectiveness.

- Phase 2—These trials are conducted in a limited number of patients in the target population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

- Phase 3—Phase 3 trials are undertaken to provide statistically significant evidence of clinical efficacy and to further evaluate dosage, potency, and safety in an expanded patient population at multiple clinical trial sites. They are performed after preliminary evidence suggesting effectiveness of the product has been obtained, and are intended to establish the overall benefit-risk relationship of the investigational product, and to provide an adequate basis for product approval and labeling.

Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials may be required by the FDA as a condition of approval and are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up. The FDA now has express statutory authority to require post-market clinical trials to address safety issues. All of these trials must be conducted in accordance with good clinical practice, or GCP, requirements in order protect the health and safety of human subjects and for the data to be considered reliable for regulatory purposes.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA and the investigators for serious and unexpected adverse events; any findings from other studies, tests in laboratory animals or in vitro testing that suggest a significant risk for human subjects; or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information.

Phase 1, Phase 2, and Phase 3 clinical trials may not be completed successfully or within any specified period, if at all. Regulatory authorities, a data safety monitoring board or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the participants are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the biological product has been associated with unexpected serious harm to patients.

Our ongoing and planned clinical trials for our product candidates may not begin or be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including delays in:

- Obtaining regulatory approval to commence a trial;

- Reaching agreement with third-party clinical trial sites and their subsequent performance in conducting accurate and reliable trials on a timely basis;

- Obtaining IRB approval to conduct a trial at a prospective site;

- Recruiting patients to participate in a trial; and

- Supply of the biological product.

Typically, if a biological product is intended to treat a chronic disease, safety and efficacy data must be gathered over an extended period of time, which can range from six months to three years or more. Success in early stage clinical trials does not ensure success in later stage clinical trials. Data obtained from clinical activities are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the physical characteristics of the biological product as well as finalize a process for manufacturing the product in commercial quantities in accordance with GMP requirements. To help reduce the risk of the introduction of adventitious agents with the use of biological products, the PHS Act emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency, and purity of the final biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life.

After completion of the required clinical testing, a BLA is prepared and submitted to the FDA. FDA review and approval of the BLA is required before marketing of the product may begin in the United States. The BLA must include the results of all preclinical, clinical, and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture, and controls and must demonstrate the safety and efficacy of the product based on these results. The BLA must also contain extensive manufacturing information. The cost of preparing and submitting a BLA is substantial. Under federal law, the submission of most BLAs is additionally subject to a substantial application user fee, as well as annual product and establishment user fees, which may total several million dollars and are typically increased annually.

The FDA has 60 days from its receipt of a BLA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of BLAs. Most such applications for standard review biologics are reviewed within ten months from the date the application is accepted for filing. Although FDA often meets its user fee performance goals, the FDA can extend these timelines if necessary, and FDA review may not occur on a timely basis at all. The FDA usually refers applications for novel biologics, or biologics which present difficult questions of safety or efficacy, to an advisory committee—typically a panel that includes clinicians and other experts—for review, evaluation, and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving a BLA, the FDA will typically inspect one, or more, clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the biologic is manufactured. The FDA will not approve the product unless it verifies that compliance with requirements for current good manufacturing practice, or cGMP, is satisfactory and the BLA contains data that provide substantial evidence that the biologic is safe and effective in the indication studied.

After the FDA evaluates the BLA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, or information, in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the BLA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. The

FDA approval is never guaranteed, and the FDA may refuse to approve a BLA if applicable regulatory criteria are not satisfied.

Under the PHSA, the FDA may approve a BLA if it determines that the product is safe, pure and potent and the facility where the product will be manufactured meets standards designed to ensure that it continues to be safe, pure, and potent. An approval letter authorizes commercial marketing of the biologic with specific prescribing information for specific indications. The approval for a biologic may be significantly more limited than requested in the application, including limitations on the specific diseases and dosages or the indications for use, which could restrict the commercial value of the product. The FDA may also require that certain contraindications, warnings, or precautions be included in the product labeling. In addition, as a condition of BLA approval, the FDA may require a risk evaluation and mitigation strategy (REMS) to help ensure that the benefits of the biologic outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use (ETASU). ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS or use of a companion diagnostic with a biologic can materially affect the potential market and profitability of the biologic. Moreover, product approval may require, as a condition of approval, substantial post-approval testing and surveillance to monitor the biologic's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Under current requirements, facilities manufacturing biological products for commercial distribution must be licensed. To accomplish this, an establishment registration must be filed with the FDA. In addition to the preclinical studies and clinical trials, the BLA includes a description of the facilities, equipment and personnel involved in the manufacturing process. An establishment registration/license is granted on the basis of inspections of the applicant's facilities in which the primary focus is on compliance with cGMP and the ability to consistently manufacture the product in the facility in accordance with the BLA. If the FDA finds the results of the inspection unsatisfactory, it may decline to approve the BLA, resulting in a delay in production of products.

FDA Post-Approval Requirements

Maintaining substantial compliance with applicable federal, state, local, and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Rigorous and extensive FDA regulation of biological products continues after approval, particularly with respect to cGMP. We will rely, and expect to continue to rely, on third parties to manufacture or supply certain components, equipment disposable devices and other materials used in our manufacturing process for any products that we may commercialize. Manufacturers of our products are required to comply with applicable requirements in the cGMP regulations, including quality control and quality assurance and maintenance of records and documentation. We cannot be certain that we or our present or future suppliers will be able to comply with the cGMP and other FDA regulatory requirements. Other post-approval requirements applicable to biological products include reporting of cGMP deviations that may affect the identity, potency, purity and overall safety of a distributed product, record-keeping requirements, reporting of adverse effects, reporting updated safety and efficacy information, periodic reporting requirements and complying with electronic record and signature requirements.

After a BLA is approved, the product also may be subject to official lot release. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. The FDA also may perform certain confirmatory tests on lots of some

products, such as viral vaccines, before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products. After approval of biologics, manufacturers must address any safety issues that arise, are subject to recalls or a halt in manufacturing, and are subject to periodic inspection after approval.

Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements, by us or our suppliers, may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical hold, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Biological product manufacturers and other entities involved in the manufacture and distribution of approved biological products are required to register their facilities with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. In addition, changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

Humanitarian Device Exemption

An Humanitarian Use Device (HUD) is a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year. A device manufacturer`s research and development costs could exceed its market returns for diseases or conditions affecting small patient populations. The HUD provision of the regulations provides an incentive for the development of devices for use in the treatment or diagnosis of diseases affecting these populations.

To obtain approval for an HUD, an humanitarian device exemption (HDE) application is submitted to FDA. An HDE is similar in both form and content to a premarket approval (PMA) application, but is exempt from the effectiveness requirements of a PMA. An HDE application is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose. The application, however, must contain sufficient information for FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury, and that the probable benefit to health outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. Additionally, the applicant must demonstrate that no comparable devices are available to treat or diagnose the disease or condition, and that they could not otherwise bring the device to market.

U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration, and specifics of the FDA approval of the use of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. Patent term restoration can compensate for time lost during product development and the regulatory review process by returning up to five years of patent life for a patent that covers a new product or its use. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The period of patent term restoration is generally one-half the time between the effective date of an IND (falling after

issuance of the patent) and the submission date of a BLA, plus the time between the submission date of the BLA and the approval of that application, provided the sponsor acted with diligence. Only one patent applicable to an approved biological product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The application for patent term extension is subject to approval by the United States Patent and Trademark Office, or PTO, in consultation with the FDA.

A patent term extension is only available when the FDA approves a biological product for the first time. We believe our product and the manner in which it is manufactured have not been previously approved by the FDA. However, we cannot be certain that the PTO and the FDA will agree with our analysis or will grant a patent term extension.

A biological product can obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

Biosimilars

The Patient Protection and Affordable Care Act signed into law on March 23, 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009. That Act created an approval pathway authorizing the FDA to approve biosimilars and interchangeable biosimilars. Biosimilars are biological products which are "highly similar" to a previously approved biologic product or "reference product" and for which there are no clinically meaningful differences between the biosimilar product and the reference product in terms of the safety, purity, and potency as shown through analytical studies, animal studies and a clinical study or studies. For FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biosimilar and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. However, complexities associated with the larger, and often more complex, structures of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation, which are still being worked out by the FDA.

A reference biologic is granted 12 years of exclusivity from the time of first licensure of the reference product. A biosimilar application may be filed four (4) years after the approval of the reference biologic. Although the patents for the reference biologic may be challenged by the biosimilar applicant during that time period pursuant to the BPCIA statutory patent challenge framework, no biosimilar or interchangeable product will be licensed by FDA until the end of the exclusivity period. The first biologic product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against other biologics submitting under the abbreviated approval pathway for the lesser of (i) one year after first commercial marketing, (ii) 18 months after the initial application if there is no legal challenge, (iii) 18 months after the resolution in the applicant's favor of a lawsuit challenging the biologics' patents if an application has been submitted, or (iv) 42 months after the application has been approved if a lawsuit is ongoing within the 42-month period. At this juncture, it is unclear whether products deemed "interchangeable" by FDA, in fact, will be readily substituted by pharmacies, which are governed by state pharmacy law.

On April 10, 2013, President Obama released his proposed budget for fiscal year 2014 and proposed to cut this twelve year period of exclusivity down to seven years. He also proposed to prohibit additional periods of exclusivity for brand biological products due to minor changes in product formulation, a practice often referred to as "evergreening." The BPCIA is complex and is only

beginning to be interpreted and implemented by the FDA. As a result, its ultimate impact, implementation and meaning are subject to uncertainty.

Pediatric Research Equity Act

Under the Pediatric Research Equity Act, or PREA, a BLA or BLA supplement must contain data to assess the safety and effectiveness of the biological product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The intent of PREA is to compel sponsors whose products have pediatric applicability to study those products in pediatric populations, rather than ignoring pediatric indications for adult indications that could be more economically desirable. FDA may grant deferrals for submission of data or full or partial waivers. By its terms, PREA does not apply to any biological product for an indication for which orphan designation has been granted, unless the FDA issues regulations saying otherwise. Because the FDA has not issued any such regulations, submission of a pediatric assessment is not required for an application to market a product for an orphan-designated indication.

Advertising and Promotion

Once a BLA is approved, a product will be subject to continuing post-approval regulatory requirements. For instance, FDA closely regulates the post-approval marketing and promotion of biologics, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. Failure to comply with these regulations can result in significant penalties, including the issuance of warning letters directing a company to correct deviations from FDA standards, a requirement that future advertising and promotional materials be precleared by the FDA, and federal and state civil and criminal investigations and prosecutions.

Biologics may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new BLA or BLA supplement before the change can be implemented. A BLA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing BLA supplements as it does in reviewing BLAs.

While doctors are free to prescribe any product approved by the FDA for any use, a company can only make claims relating to safety and effectiveness of a biological product that are consistent with FDA approval, and the company is allowed to actively market a biological product only for the particular use and treatment approved by the FDA. In addition, any claims we make for our products in advertising or promotion must be appropriately balanced with important safety information and otherwise be adequately substantiated. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising, injunctions and potential civil and criminal penalties.

Orphan Drug

Under the Orphan Drug Act, the FDA may grant orphan drug designation to biologics intended to treat a rare disease or condition—generally a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the generic identity of the biologic and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not necessarily convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first BLA applicant to receive FDA approval for a particular product to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for

that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan drug exclusivity, which would most likely run concurrently with exclusivity, if any, received from the time of first licensure of a reference product, does not prevent the FDA from approving a different biologic for the same disease or condition, or the same biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application user fee.

Anti-Kickback and False Claims Laws

In the United States, the research, manufacturing, distribution, sale and promotion of biological products are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare & Medicaid Services, other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General), the U.S. Department of Justice, state Attorneys General, and other federal, state and local government agencies. For example, sales, marketing and scientific/educational grant programs must comply with the Anti-Kickback Statute, as amended, the False Claims Act, as amended, the privacy regulations promulgated under the Health Insurance Portability and Accountability Act, or HIPAA, and similar state laws. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. All of these activities are also potentially subject to federal and state consumer protection and unfair competition laws.

As noted above, in the United States, we are subject to complex laws and regulations pertaining to healthcare "fraud and abuse," including, but not limited to, the Anti-Kickback Statute, the federal False Claims Act, and other state and federal laws and regulations. The Anti-Kickback Statute makes it illegal for any person, including a biological product manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer, or pay any remuneration that is intended to induce the referral of business, including the purchase or order of an item for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Violations of this law are punishable by up to five years in prison, criminal fines, administrative civil money penalties, and exclusion from participation in federal healthcare programs. In addition, many states have adopted laws similar to the Anti-Kickback Statute. Some of these state prohibitions apply to the referral of patients for healthcare services reimbursed by any insurer, not just federal healthcare programs such as Medicare and Medicaid. Due to the breadth of these federal and state anti-kickback laws and the potential for additional legal or regulatory change in this area, it is possible that our future sales and marketing practices and/or our future relationships with physicians might be challenged under anti-kickback laws, which could harm us. Because we intend to commercialize products that could be reimbursed under a federal healthcare program and other governmental healthcare programs, we plan to develop a comprehensive compliance program that establishes internal controls to facilitate adherence to the rules and program requirements to which we will or may become subject.

The federal False Claims Act prohibits anyone from, among other things, knowingly presenting, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services, including biological products, that are false or fraudulent. Although we would not submit claims directly to payers, manufacturers can be held liable under these laws if they are deemed to "cause" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. In addition, our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state, and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law. For example, pharmaceutical companies have been prosecuted under the federal False Claims Act in connection with their off-label promotion of drugs. Penalties for a False

Claims Act violation include three times the actual damages sustained by the government, plus mandatory civil penalties of between $5,500 and $11,000 for each separate false claim, the potential for exclusion from participation in federal healthcare programs, and, although the federal False Claims Act is a civil statute, conduct that results in a False Claims Act violation may also implicate various federal criminal statutes. If the government were to allege that we were, or convict us of, violating these false claims laws, we could be subject to a substantial fine and may suffer a decline in our stock price. In addition, private individuals have the ability to bring actions under the federal False Claims Act and certain states have enacted laws modeled after the federal False Claims Act.

There are also an increasing number of state laws that require manufacturers to make reports to states on pricing and marketing information. Many of these laws contain ambiguities as to what is required to comply with the laws. In addition, a similar recent federal law, referred to as the Sunshine Act, requires biological product manufacturers to track and report to the federal government certain payments or transfers of value made to physicians and teaching hospitals made in the previous calendar year. These laws may affect our sales, marketing, and other promotional activities by imposing administrative and compliance burdens on us. In addition, given the lack of clarity with respect to these laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent state, and soon federal, authorities.

International Regulation

In addition to regulations in the United States, a variety of foreign regulations govern clinical trials, commercial sales, and distribution of product candidates. The approval process varies from country to country and the time to approval may be longer or shorter than that required for FDA approval.

Pharmaceutical Coverage, Pricing, and Reimbursement

In the United States and other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of reimbursement from third-party payors, including government health administrative authorities, managed care providers, private health insurers, and other organizations. Third-party payors are increasingly examining the medical necessity and cost effectiveness of medical products and services in addition to safety and efficacy and, accordingly, significant uncertainty exists as to the reimbursement status of newly approved therapeutics. Third-party reimbursement adequate to enable us to realize an appropriate return on our investment in research and product development may not be available for our products.

We do not expect to generate positive cash flows from our consolidated operations for the next several years and then only if we achieve some combination of the following: increased sales of Carticel and Epicel, gain FDA approval for MACI and generate significant revenue, or gain approval for ixmyelocel-T in one or more indications and generate significant revenue. In addition to Carticel and Epicel revenues, our revenue sources have also included minor sales of our cell products and manufacturing supplies to our academic collaborators, grant revenue, research funding and potential licensing fees or other financial support from potential future corporate collaborators.

We expect that we will need to raise significant additional funds or pursue strategic transactions or other strategic alternatives in order to complete our product development programs, complete clinical trials needed to market our products, and commercialize our products. To date, we have financed our operations primarily through public and private sales of our equity securities, and we expect to continue to seek to obtain the required capital in a similar manner. We have never been profitable and do not anticipate having net income unless and until sales significantly increase. To generate revenue from MACI and ixmyelocel-T we will need to obtain significant additional funding, complete the required clinical trials for regulatory approvals, and receive the necessary approvals to market our products. 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. Through June 30, 2014, we have accumulated a deficit of $298,398,000. We cannot provide any assurance that we will be able to achieve profitability on a sustained basis, if at all, obtain the required funding, obtain the required regulatory approvals, or complete additional corporate partnering or acquisition transactions.

Competitive Environment For Cell Therapy and Regenerative Medicine

The biotechnology and medical device industries are characterized by rapidly evolving technology and intense competition. Our competitors include major multinational medical device companies, pharmaceutical companies, biotechnology companies and stem cell companies operating in the fields of tissue engineering, regenerative medicine, cardiac, vascular, orthopedics and neural medicine. Many of these companies are well-established and possess technical, research and development, financial, and sales and marketing resources significantly greater than ours. In addition, many of our smaller potential competitors have formed strategic collaborations, partnerships and other types of joint ventures with larger, well established industry competitors that afford these companies potential research and development and commercialization advantages in the technology and therapeutic areas currently being pursued by us. Academic institutions, governmental agencies and other public and private research organizations are also conducting and financing research activities which may produce products directly competitive to those being commercialized by us. Moreover, many of these competitors may be able to obtain patent protection, obtain FDA and other regulatory approvals and begin commercial sales of their products before us.

For patients diagnosed with cartilage defects, there are several treatment options, including arthroscopic debridement/chondroplasty, marrow stimulation techniques such as microfracture, osteochondralautografts for smaller cartilage injuries, allografts, and autologous chondrocyte implants for larger, more complex injuries.

The main competitor for Carticel in the U.S. is the microfracture procedure. Microfracture is a minimally invasive procedure that can be performed during the initial arthroscopic procedure. Short term results are generally considered good in smaller cartilage defects. Other competitive treatments in the U.S. include autograft/allograft procedures and a juvenile donor-derived allograft product DeNovo NT from Zimmer, Inc. However, none of these products have the documented long term duration of response which Carticel offers. One trial has followed patients for over 20 years, with the majority still benefitting from a positive response.

Carticel is the only FDA-approved ACI product on the market in the United States. We are aware of one ACI product in development. Histogenics Corporation began a Phase 3 study of its Neocart implant in February 2010. Neocart is an autologous chondrocyte tissue implant under development for treatment of symptomatic articular cartilage lesions on the femur.

The competitive treatment alternatives to MACI in the EU are the same as those for Carticel in the U.S., including debridement/chondroplasty, microfracture, and osteochondralautografts. Although there is very little use of allografts or allograft-derived products, the competitive product environment is much more robust. Competitors include microfracture augmentation products such as ChondroGide® from Geistlich Pharma AG and direct ACI competitors including ChondroCelect® from TiGenix NV.

Patients suffering catastrophic burns over a significant portion of total body surface area have few options for permanent skin coverage. When undamaged skin is available, a procedure known as meshed split-thickness auto-grafting can be considered. However, this option becomes less viable as the

percentage of total body surface area burn increases. Epicel is a lifesaving therapy and represents the only option for patients with TBSA burns greater than 70%.

Aastrom is investigating ixmyelocel-T, an autologous cell therapy, in ischemic dilated cardiomyopathy (ischemic heart failure) and is currently enrolling a Phase 2b clinical trial. Competitor cell (autologous and allogeneic) and gene therapies are currently under clinical development in phases 1, 2 and 3 in heart failure patients. Examples are, Mesoblast Ltd., which is conducting a Phase 3 trial with allogeneic cell therapy and Harvest Technologies is conducting a phase 1 trial with an autologous therapy. Gene therapies are being evaluated in Phase 2 trials by Juventas Therapeutics, Inc. and Celladon Corporation.

Our potential commercial products address a broad range of existing and emerging therapeutic markets, in which cell-based therapy is a new and as of yet, unproven, commercial strategy. In a large part, we face primary competition from existing medical devices and drug products. Some of our competitors have longer operating histories and substantially greater resources. These include companies such as Baxter International, Inc. (Baxter), Biomet, Inc., Johnson & Johnson, Inc., Medtronic, Inc. (Medtronic), and others.

In the general area of cell-based therapies, we potentially compete with a variety of companies, most of whom are specialty medical products or biotechnology companies. Some of these, such as Baxter, Johnson & Johnson, Medtronic and MiltenyiBiotec are well-established and have substantial technical and financial resources compared to ours. However, as cell-based products are only just emerging as viable medical therapies, many of our most direct competitors are smaller biotechnology and specialty medical products companies. These include Advanced Cell Technology, Inc., Cytomedix, Inc. (formerly Aldagen, Inc.), Arteriocyte Medical Systems, Inc., Athersys, Inc., Bioheart, Inc., Cytori Therapeutics, Inc., International Stem Cell Corporation, Neostem, Inc., Terumo Medical Corporation (formerly Harvest Technologies Corporation), Mesoblast Ltd., Osiris Therapeutics, Inc., Pluristem, Inc. Stem Cells, Inc., Tengion, Inc., and others.

Employees

As of June 30, 2014, we employed approximately 190 full-time employees. A significant number of our management and professional employees have had prior experience with pharmaceutical, biotechnology or medical product companies. None of our employees are covered by collective bargaining agreements, and management considers relations with our employees to be good.

Facilities

We lease approximately 36,000 square feet in Ann Arbor, Michigan and 50,000 square feet in Cambridge, Massachusetts. The lease agreements expire in April 2018 and February 2017, respectively. Both facilities include clean rooms, laboratories and office space. We believe that our facilities are adequate to meet our current needs.

Legal Proceedings

From time to time we may be involved in legal proceedings arising in the ordinary course of business. We believe there is no litigation currently pending that could have, individually or in the aggregate, a material adverse effect on our results of operations or financial condition.

Corporate Information

Aastrom is incorporated under the laws of the State of Michigan. Our principal executive offices are located at 24 Frank Lloyd Wright Drive, Lobby K, Ann Arbor, Michigan 48105. Our telephone number is (734) 418-4400. The address of our website is 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.

MANAGEMENT

The following table presents our executive officers and key employees and their respective ages and positions as of June 30, 2014:

Name	Position(s)	Age	Executive Officer Since
Dominick C. Colangelo(1)	President and Chief Executive Officer	50	2013
Gerard Michel(1)	Chief Financial Officer and VP of Corporate Development	51	2014
Daniel R. Orlando	Chief Operating Officer	49	2012
David Recker, M.D.	Chief Medical Officer	56	2014
Ross Tubo, Ph.D.	Chief Scientific Officer	55	2014

(1) Denotes Executive Officer.

Dominick C. Colangelo — Mr. Colangelo joined Aastrom in March 2013 with more than twenty years of executive management and corporate development experience in the biopharmaceutical industry, including nearly a decade with Eli Lilly and Company. Most recently, he was President and Chief Executive Officer of Promedior, Inc. from 2008 to 2012. During his career, he has held a variety of executive positions of increasing responsibility in product development, pharmaceutical operations, sales and marketing, and corporate development. He has extensive experience in the acquisition, development and commercialization of therapies to treat fibrovascular, metabolic and cardiovascular diseases. During his tenure at Eli Lilly and Company, he held positions as Director of Strategy and Business Development for Lilly's Diabetes Product Group and also served as a founding Managing Director of Lilly Ventures. Mr. Colangelo received his B.S.B.A. in Accounting, Magna Cum Laude, from the State University of New York at Buffalo and a J.D. degree, with Honors, from the Duke University School of Law.

Gerard Michel — Mr. Michel joined Aastrom in June of 2014 with over 25 years of experience in the pharmaceutical industry across multiple functional areas. He has considerable experience in business development, raising capital and executing successful financial transactions. Mr. Michel was formerly Chief Financial Officer and Vice President, Corporate Development of Biodel from November 2007 to May 2014, where he oversaw strategic development, fundraising and capital structure management, marketing efforts, investor relations, and financial reporting and internal controls. From August 2002 to November 2007, Mr. Michel served as Chief Financial Officer and Vice President of Corporate Development of NPS Pharmaceuticals, where he led the first syndicated royalty monetization, the structure of which has been widely copied. Prior to that, Mr. Michel was a Principal at Booz Allen and also held a variety of commercial roles at both Lederle Labs and Wyeth Labs. Mr. Michel holds a M.S. in Microbiology from the University of Rochester School of Medicine, an M.B.A. from the Simon School of Business, and a B.S. in both Biology and Geology from the University of Rochester.

Daniel R. Orlando — Mr. Orlando joined Aastrom as Chief Commercial Officer in August of 2012. Mr. Orlando served as interim Chief Executive Officer of Aastrom from December 2012 to March 2013. He has more than 20 years of commercial product preparation and launch experience including leadership roles in sales, marketing and most recently as a vice president of business development for North and South America at Takeda Pharmaceuticals. As an employee at Takeda North America, he served as the original brand director for Actos, a branded anti-diabetic agent in the United States. Mr. Orlando's initial pharmaceutical experience came in progressively expanding roles in sales and marketing at Abbott Laboratories. He holds an M.B.A. from Florida Atlantic University and a B.A. in economics with Honors from the University of Florida.

David Recker, M.D. — Dr. Recker joined Aastrom in April 2014 and has more than 20 years of experience in drug development, most recently at Takeda Global Research and Development where he served as Senior Vice President for Clinical Science from 2002 to 2012. Dr. Recker has had responsibility for multiple development programs in a variety of therapeutic areas in his career which have resulted in many successful regulatory filings throughout the world. He is a Fellow of the American College of Physicians as well as a Fellow of the American College of Rheumatology. He holds an M.D. with Distinction from the University of Michigan where he completed his internship and residency and served as Chief Resident in Internal Medicine. He did his fellowship in training at the National Institutes of Health.

Ross Tubo, Ph.D. — Dr. Tubo joined Aastrom in April 2014 with more than twenty years of experience in cell therapy, regenerative medicine, and stem cell biology. Dr. Tubo was a pioneer in the research, development, and commercialization of the first autologous cell therapy for articular cartilage repair, known as Carticel. As Vice President of Stem Cell and Chemokine Biology for Genzyme Corporation, a position he held from 1998 to 2010, he developed a world-class research organization designed to understand the underlying cell and molecular mechanism(s) of action of mesenchymal stem cells (MSCs) in autoimmune disease and cancer. These efforts led to the identification of specific therapeutic targets for treatment of these diseases. He holds a Ph.D. in Cell and Molecular Biology from State University of New York at Buffalo and completed post-doctoral studies at Harvard Medical School.

DESCRIPTION OF SECURITIES

The following briefly summarizes the general terms and provisions of our shares of common and preferred stock. You should read the provisions of our articles of incorporation, as amended (Charter), our amended and restated bylaws (Bylaws) and other relevant instruments and agreements relating to our securities before you make an investment decision with respect to our shares of common and preferred stock.

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

Our authorized capital stock consists of 75,000,000 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" 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 the Company 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 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, out of legally available funds for dividends, subject to any preferences that may be applicable to any shares of preferred stock that may be outstanding at that time. The rights, preferences and privileges of holders of common stock are set forth in our Charter, which may be amended by the holders of a majority of the outstanding shares of common stock. We have adopted a shareholder rights plan, which could make it more difficult for a third party to acquire, or could discourage a third party from acquiring, our company or a large block of our common stock. Please see the description above in "Certain Provisions of Michigan Law and of our Charter and Bylaws; Transfer Agent and Registrar."

Preferred Stock

Our Board may issue 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 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.

Shareholder Rights Agreement—Series A Junior Participating Cumulative Preferred Stock

On August 11, 2011, our Board adopted a shareholder rights agreement (Rights Agreement), the purpose of which is, among other things, to enhance the Board's ability to protect shareholder interests and to ensure that shareholders receive fair treatment in the event any coercive takeover attempt of Aastrom is made in the future. The Rights Agreement could make it more difficult for a third-party to acquire, or could discourage a third party from acquiring, us or a large block of our common stock.

The following summary description of the Rights Agreement should be read in conjunction with the Rights Agreement, which was filed with the SEC as an exhibit to a Registration Statement on Form 8-A on August 12, 2011 and amended in March 2012 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 Rights Agreement.

In connection with the adoption of the Rights Agreement, the Board declared a dividend distribution of one preferred stock purchase right (Right) for each outstanding share of common stock to shareholders of record as of the close of business on August 15, 2011. In addition, one Right will automatically attach to each share of common stock issued between August 15, 2011 and the distribution date. As a result of the October 2013 reverse stock split, the number of Rights associated with each share of common stock was automatically proportionately adjusted so that (i) twenty rights were then associated with each outstanding share of common stock and (ii) so long as the Rights are attached to the common stock, twenty rights shall be deemed to be delivered for each share of common stock issued or transferred by the Company in the future. The Rights currently are not exercisable and are attached to and trade with the outstanding shares of common stock. Under the Rights Agreement, the Rights become exercisable if a person or group becomes an "acquiring person" by acquiring 15% or more of the outstanding shares of common stock or if a person or group commences a tender offer that would result in that person owning 15% or more of the common stock. On the tenth day after a person or group becomes an "acquiring person," each holder of a Right (other than the acquiring person and its affiliates, associates and transferees) would be entitled to purchase, at the then-current exercise price, such number of shares of our preferred stock which are equivalent to shares of common stock having a value of twice the exercise price of the Right. If we are is acquired in a merger or other business combination transaction after any such event, each holder of a Right would then be entitled to purchase, at the then-current exercise price, shares of the acquiring company's common stock having a value of twice the exercise price of the Right.

Each share of preferred stock is entitled to payment of a quarterly dividend, an increased vote multiple, and a liquidation preference. In addition, each share of preferred stock is granted the exclusive right to vote for two additional members of the Board whose positions are created upon the vesting of such rights upon holders of preferred stock. Except in certain limited circumstances, once purchased, said shares are not redeemable by us.

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

Series B Convertible Preferred Stock

On March 9, 2012, we completed the sale of 12,308 shares of Series B-1 Non-Voting Convertible Preferred Stock (Series B-1 Preferred Stock) at an offering price of $3,250 per share. We received approximately $37,620,000 in net proceeds from the sale of the shares, after offering expenses. In addition to the Series B-1 Preferred Stock, which was issued at the closing, we also authorized Series B-2 Voting Convertible Preferred Stock (Series B-2 Preferred Stock). The Series B-1 Preferred Stock and Series B-2 Preferred Stock collectively are referred to as the Series B Preferred Stock. The following is a summary of the powers, privileges and rights, and the qualifications, limitations or restrictions in respect of the Series B Preferred Stock.

Exchange

Subject to our receipt of the requisite shareholder approval for purposes certain limitations pursuant to NASDAQ Marketplace Rule 5635(b), each share of Series B-1 Preferred Stock may be exchanged at any time without payment of additional consideration into one share of Series B-2 Preferred Stock. On May 3, 2012, we obtained shareholder approval in accordance with NASDAQ Marketplace Rule 5635(b). Subsequently, Eastern Capital exchanged all of its then outstanding shares of Series B-1 Preferred Stock for Series B-2 Preferred Stock.

Conversion

The Series B Preferred Stock is convertible, at the option of the holder thereof at any time after March 9, 2017, into shares of our common stock at a conversion price of $65 per share of common stock. We may elect to convert any or all of the outstanding shares of Series B Preferred Stock common stock at any time after March 9, 2017, subject to certain limitations.

Dividends

Dividends on the Series B Preferred Stock will be cumulative and compound daily, at a rate of 11.5% per annum, payable upon conversion, liquidation, redemption or other similar events, and payable in cash or Series B Preferred Stock until March 9, 2017. Following March 9, 2017, if we do not elect to convert all outstanding shares of Series B Preferred Stock into common stock, until the earlier of March 9, 2022 and the date no Series B Preferred Stock remain outstanding, dividends will accrue at a rate of 8% per annum and will be payable in cash or Series B-1 Preferred Stock, at our option.

Voting

The Series B-1 Preferred Stock is not entitled to vote on matters on which the common shareholders are generally entitled to vote. The Series B-2 Preferred Stock is entitled to vote with the holders of the common stock as a single class, with each share of Series B-2 Preferred Stock having the number of votes equal to the number of shares of common stock issuable upon conversion of such Series B-2 Preferred Stock. Following our October 2013 reverse stock split, each share of Series B-2 Preferred Stock currently has one vote per 1/50 share of Series B-2 Preferred Stock (subject to adjustment).

Redemption

Unless prohibited by Michigan law governing distributions to shareholders, the Series B-1 Preferred Stock, if any, that remains outstanding after March 9, 2017 and cannot be exchanged for Series B-2 Preferred Stock, or upon a liquidation, winding up, dissolution or other similar events, shall be redeemable at the option of holder of the Series B-1 Preferred Stock, subject to certain terms and limitations.

The redemption price of the Series B-1 Preferred Stock, prior to March 9, 2017, is currently equal to $7,430 multiplied by the number of Series B-1 preferred shares redeemed minus our closing stock price multiplied by the number of common shares into which the outstanding Series B-2 preferred stock are convertible. The redemption price of the Series B-1 Preferred Stock, after March 9, 2017, is the amount equal to the greater of the Series B Preferred Stock offering price plus accrued dividends or the conversion value in common stock.

Liquidation

The Series B Preferred Stock will, with respect to dividend rights and rights on liquidation, winding-up and dissolution, rank on parity with any other class or series of our capital stock that we may issue in the future which is designated as being on parity with the Series B Preferred Stock, and rank senior to our common stock and Series A Preferred Stock.

Transfer Agent

The transfer agent of our common stock is Continental Stock Transfer & Trust Company.

CERTAIN PROVISIONS OF MICHIGAN LAW AND OF OUR CHARTER AND BYLAWS

We are subject to certain anti-takeover provisions of the Michigan Business Corporation Act (MBCA) that could delay or make more difficult a merger or tender offer involving us. 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; (b) the interested shareholder has been an interested shareholder for at least five years and has not acquired beneficial ownership of any additional shares of the corporation subsequent to the transaction which resulted in such shareholder being classified as an interested shareholder, and meets certain requirements, including provisions relating to the fairness of the price and the form of consideration paid; or (c) the board of directors, by resolution, exempts a particular interested shareholder from these provisions prior to the interested shareholder becoming an interested shareholder. The MBCA also contains certain other provisions that could have anti-takeover effects.

Our Charter does not provide shareholders with the right to act without a meeting and does not provide for cumulative voting in the election of directors. The amendment of any of these provisions would require approval by holders of at least a majority of the shares of our outstanding common stock.

These and other provisions of our Charter or Bylaws, as well as our Rights Agreement described above under "Description of Capital Stock," could have the effect of deterring certain takeovers or delaying or preventing certain changes in control or changes in our management, including transactions in which shareholders might otherwise receive a premium for their shares over then-current market prices.

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS

The following is a summary of the material U.S. federal income tax consequences of the ownership and disposition of our common stock to non-U.S. holders, but does not purport to be a complete analysis of all the potential tax considerations relating thereto. This summary is based upon the provisions of the Internal Revenue Code of 1986, as amended, or the Code, Treasury regulations promulgated thereunder, administrative rulings and judicial decisions, all as of the date hereof. These authorities may be changed or subject to differing interpretations, possibly with retroactive effect, so as to result in U.S. federal income tax consequences different from those set forth below. We have not sought any ruling from the Internal Revenue Service, or the IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions.

This summary also does not address the tax considerations arising under the laws of any U.S. state or local or any non-U.S. jurisdiction, the Medicare tax on net investment income or any alternative minimum tax consequences. In addition, this discussion does not address tax considerations applicable to an investor's particular circumstances or to investors that may be subject to special tax rules, including, without limitation:

- Banks, insurance companies or other financial institutions;
- Tax-exempt organizations;
- Dealers in securities or currencies;
- Traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;
- Persons that own, or are deemed to own, more than five percent of our capital stock;
- Certain former citizens or long-term residents of the United States;
- Persons who hold our common stock as a position in a hedging transaction, "straddle," "conversion transaction" or other risk reduction transaction;
- Persons who do not hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, for investment purposes);
- Persons deemed to sell our common stock under the constructive sale provisions of the Code;
- Regulated investment companies;
- Real estate investment trusts;
- Individual retirement or tax-deferred accounts;
- Pension plans;
- Hybrid entities;
- Corporations that accumulate earnings to avoid U.S. federal income tax;
- Integral parts of controlled entities of a foreign sovereign;
- Controlled foreign corporations;
- Passive foreign investment companies; or
- Persons that acquire our common stock as compensation for services.

In addition, if a partnership, including any entity or arrangement classified as a partnership for U.S. federal income tax purposes, holds our common stock, the tax treatment of a partner generally

will depend on the status of the partner and upon the activities of the partnership. Accordingly, partnerships that hold our common stock, and partners in such partnerships, should consult their tax advisors.

You are urged to consult your tax advisor with respect to the application of the U.S. federal income tax laws to your particular situation, as well as any tax consequences of the purchase, ownership and disposition of our common stock arising under the U.S. federal estate or gift tax rules or under the laws of any U.S. state or local or any non-U.S. or other taxing jurisdiction or under any applicable tax treaty.

Non-U.S. Holder Defined

For purposes of this discussion, you are a non-U.S. holder if you are a beneficial owner of our common stock that is for United States federal income tax purposes (i) a foreign corporation, (ii) a nonresident alien individual, or (iii) a foreign estate or trust that in either case is not subject to U.S. federal income tax on a net-income basis on income or gain from a note or share of common stock.

Distributions

If we make distributions on our common stock, those payments will constitute dividends for U.S. tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed both our current and our accumulated earnings and profits, they will constitute a return of capital and will first reduce your basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock.

Any dividend paid to you generally will be subject to U.S. withholding tax either at a rate of 30% of the gross amount of the dividend or such lower rate as may be specified by an applicable income tax treaty. In order to receive a reduced treaty rate, you must provide us with an IRS Form W-8BEN (generally including a U.S. taxpayer identification number), IRS Form W-8-BEN-E or another appropriate version of IRS Form W-8 (or a successor form), in each case, certifying qualification for the reduced rate.

Dividends received by you that are effectively connected with the conduct of a U.S. trade or business (and, if an income tax treaty applies, are attributable to a permanent establishment maintained by you in the United States) generally are exempt from such withholding tax. In order to obtain this exemption, you must provide us with an IRS Form W-8ECI or successor form or other applicable IRS Form W-8 properly certifying such exemption. Such effectively connected dividends, although not subject to withholding tax, are taxed at the same graduated rates applicable to U.S. persons, net of certain deductions and credits, subject to an applicable income tax treaty providing otherwise. In addition, if you are a corporate non-U.S. holder, dividends you receive that are effectively connected with your conduct of a U.S. trade or business (and, if an income tax treaty applies, are attributable to a permanent establishment maintained by the you in the United States) may also be subject to a branch profits tax at a rate of 30% or such lower rate as may be specified by an applicable income tax treaty.

If you are eligible for a reduced rate of withholding tax pursuant to a tax treaty, you may be able to obtain a refund of any excess amounts currently withheld if you file an appropriate claim for refund with the IRS.

Gain on Sale or Other Disposition of Common Stock

Subject to the discussion below regarding backup withholding and FATCA, a non-U.S. Holder generally will not be required to pay U.S. federal income tax on any gain realized upon the sale or other disposition of our common stock unless:

- The gain is effectively connected with the conduct of a U.S. trade or business (and, if an income tax treaty applies, the gain is attributable to a permanent establishment maintained by you in the United States), in which case you will be required to pay tax on the net gain derived from the sale under regular graduated U.S. federal income tax rates, and for a non-U.S. holder that is a corporation, such non-U.S. holder may be subject to the branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty;

- You are an individual who is present in the United States for a period or periods aggregating 183 days or more during the calendar year in which the sale or disposition occurs and certain other conditions are met, in which case you will be required to pay a flat 30% tax on the gain derived from the sale, which tax may be offset by U.S. source capital losses (even though you are not considered a resident of the United States) (subject to applicable income tax or other treaties); or

- Our common stock constitutes a U.S. real property interest by reason of our status as a "U.S. real property holding corporation" for U.S. federal income tax purposes, a USRPHC, at any time within the shorter of the five-year period preceding the disposition or your holding period for our common stock. We believe that we are not currently and will not become a USRPHC. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property relative to the fair market value of our other business assets, there can be no assurance that we will not become a USRPHC in the future. Even if we become a USRPHC, however, as long as our common stock is regularly traded on an established securities market, such common stock will be treated as U.S. real property interests only if you actually or constructively hold more than five percent of such regularly traded common stock at any time during the applicable period that is specified in the Code.

Federal Estate Tax

Our common stock beneficially owned by an individual who is not a citizen or resident of the United States (as defined for U.S. federal estate tax purposes) at the time of their death will generally be includable in the decedent's gross estate for U.S. federal estate tax purposes, unless an applicable estate tax treaty provides otherwise.

Backup Withholding and Information Reporting

Generally, we must report annually to the IRS the amount of dividends paid to you, your name and address, and the amount of tax withheld, if any. A similar report will be sent to you. Pursuant to applicable income tax treaties or other agreements, the IRS may make these reports available to tax authorities in your country of residence.

Payments of dividends or of proceeds on the disposition of stock made to you may be subject to additional information reporting and backup withholding at a current rate of 28% unless you establish an exemption, for example by properly certifying your non-U.S. status on an IRS Form W-8BEN, IRS Form W-8BEN-E or another appropriate version of IRS Form W-8 (or a successor form). Notwithstanding the foregoing, backup withholding and information reporting may apply if either we or our paying agent has actual knowledge, or reason to know, that you are a U.S. person.

Information reporting and backup withholding generally will apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S.

or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Backup withholding is not an additional tax; rather, the U.S. income tax liability of persons subject to backup withholding will be reduced by the amount of tax withheld. If withholding results in an overpayment of taxes, a refund or credit may generally be obtained from the IRS, provided that the required information is furnished to the IRS in a timely manner.

Foreign Account Tax Compliance Act (FATCA)

Provisions commonly referred to as "FATCA" may impose withholding tax on certain types of payments made to "foreign financial institutions" and certain other non-U.S. entities. The legislation imposes a 30% withholding tax on dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a foreign financial institution or to certain non-financial foreign entities, unless (i) the foreign financial institution undertakes certain diligence and reporting obligations or (ii) the non-financial foreign entity either certifies it does not have any substantial U.S. owners or furnishes identifying information regarding each substantial U.S. owner and such entity meets certain other specified requirements. If the payee is a foreign financial institution, it must enter into an agreement with the U.S. Treasury requiring, among other things, that it undertake to identify accounts held by certain U.S. persons or U.S.-owned foreign entities, annually report certain information about such accounts, and withhold 30% on payments to account holders whose actions prevent it from complying with these reporting and other requirements. If the country in which a payee is resident has entered into an "intergovernmental agreement" with the United States regarding FATCA, that agreement may permit the payee to report to that country rather than to the U.S. Treasury. Under final regulations and published guidance, any obligation to withhold from payments made to a foreign financial institution or a foreign non-financial entity under the new legislation with respect to dividends on our common stock began on July 1, 2014, but with respect to the gross proceeds of a sale or other disposition of our common stock will not begin until January 1, 2017. Prospective investors should consult their tax advisors regarding FATCA.

The preceding discussion of U.S. federal tax considerations is for general information only. It is not tax advice. Each prospective investor should consult its own tax advisor regarding the particular U.S. federal, state and local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed change in applicable laws.

UNDERWRITING

Ladenburg Thalmann & Co. Inc. is acting as the sole book-running manager of the offering and as representative of the underwriters. Subject to the terms and conditions set forth in an underwriting agreement dated the date of this prospectus among us and the representative of the underwriters named below, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase from us, the number of shares of common stock listed next to its name in the following table.

Underwriters	Number of Shares
Ladenburg Thalmann & Co. Inc.	11,666,667
Trout Capital LLC	2,058,823
Total	13,725,490

The underwriters are committed to purchase all the shares of common stock offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of nondefaulting underwriters may be increased or the offering may be terminated. The underwriters are not obligated to purchase the shares of common stock covered by the option to purchase additional shares described below.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officer's certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Discounts and Commissions

The underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover page of this prospectus and to dealers at that price less a concession not in excess of $0.092 per share. After the initial offering of the shares, the public offering price and other selling terms may be changed by the representative.

The following table shows the public offering price, underwriting discounts and commissions and proceeds before expenses to us. The information assumes either no exercise or full exercise of the option we granted to the underwriters to purchase additional shares.

	Per Share	Total Without Option to Purchase Additional Shares	Total With Option to Purchase Additional Shares
Public offering price	$ 2.55	$ 35,000,000	$ 40,250,000
Underwriting discounts and commissions	$ 0.153	$ 2,100,000	$ 2,415,000
Proceeds, before expenses, to us	$ 2.397	$ 32,900,000	$ 37,835,000

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately $200,000.

We have also agreed to reimburse the underwriters for certain of their expenses incurred in connection with this offering, of which $22,900 will be considered by FINRA to be underwriting compensation.

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase, from time to time, in whole or in part, up to 2,058,823 additional shares from us at the public offering price set forth on the cover page of this prospectus, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares proportionate to that underwriter's initial purchase commitment as indicated in the table above.

Lock-Up Agreements

We, our officers, directors and certain of our shareholders have entered into lock-up agreements with the underwriters. Under these agreements, we and these other individuals have agreed, subject to specified exceptions, not to sell or transfer any common stock or securities convertible into, or exchangeable or exercisable for, common stock, during a period ending 90 days after the date of this prospectus, without first obtaining the written consent of the representative.

Specifically, we and these other individuals have agreed not to:

- Offer, pledge, assign, encumber, announce the intention to sell, sell, contract to sell, sell any option or con-tract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock owned either of record or beneficially or may be deemed to be beneficially owned (as defined in the Exchange Act) by the respective locked-up party on the date of the lock-up agreement or acquired thereafter;

- Enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock, whether any such transaction is to be settled by delivery of common stock or such other securities, in cash or otherwise;

- Make any demand for or exercise any right with respect to, the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock; or

- Publicly announce an intention to do any of the foregoing.

The restrictions described above do not apply to:

- The sale of shares of our common stock to the underwriters pursuant to the underwriting agreement;

- Transfers of shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock (i) as a bona fide gift, or gifts, (ii) to an immediate family member or a trust for the direct or indirect benefit of the respective locked-up party or such immediate family member of the respective locked-up party, or (iii) by will or intestacy;

- Equity securities issued pursuant to our equity incentive plans in effect as of the date of the lock-up agreement or pursuant to bona fide equity incentive plans thereafter established and the grant by us of stock options or other stock-based awards, or the issuance of shares of our common stock upon exercise thereof, to eligible participants pursuant to employee benefit or equity incentive plans described in this prospectus; provided that, prior to the grant of any such stock options or other stock-based awards that vest within the restricted period, each recipient of such grant shall sign and deliver a lock-up agreement agreeing to be subject to the restrictions on transfer described above;

- Transfers of shares of common stock to us (i) as forfeitures to satisfy tax withholding and remittance obligations of the undersigned in connection with the vesting or exercise of equity awards granted pursuant to our equity incentive plans, or (ii) pursuant to a net exercise or cashless exercise by the shareholder of outstanding equity awards pursuant to our equity incentive plans;

- The establishment of a trading plan that complies with Rule 10b5-1 under the Exchange Act; provided, however, that (i) the restrictions shall apply in full force to sales or other dispositions pursuant to such Rule 10b5-1 plan during the 90-day lock-up period described above and (ii) no public announcement or disclosure of entry into such Rule 10b5-1 plan is made or required to be made, including any filing with the SEC under Section 13 or Section 16 of the Exchange Act;

- Transfers of shares of our common stock to a charity or education institution;

- If our shareholders are, directly or indirectly, controlled by a corporation, partnership, limited liability company or other business entity, any transfers of our common stock to any shareholder, partner or member of, or owner of similar equity interests in our shareholders, as the case may be; and

- Transactions relating to our common stock acquired in open market transactions after the completion of the offering; provided that no filing under Section 16(A) of the Exchange Act shall be required or shall be voluntarily made in connection with subsequent sales of Common Stock acquired in such open market transactions.

Indemnification

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make for these liabilities.

Stabilization

The underwriters have advised us that they, pursuant to Regulation M under Exchange Act and certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering.

These activities may have the effect of stabilizing or maintaining the market price of the common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either "covered" short sales or "naked" short sales.

"Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

"Naked" short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of shares of common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our common stock in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Offer, Sale and Distribution of Shares

A prospectus in electronic format may be made available on the websites maintained by one or more underwriters or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares of common stock to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' websites and any information contained in any other website maintained by the underwriters is not part of this prospectus or the registration statement of which this prospectus forms a part.

Notice to Non-U.S. Investors

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus.

This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

European Economic Area

In relation to each member state of the European Economic Area that has implemented the Prospectus Directive, each of which we refer to as a relevant member state, with effect from and including the date on which the Prospectus Directive is implemented in that relevant member state, or the relevant implementation date, an offer of securities described in this prospectus may not be made to the public in that relevant member state other than:

- To legal entities that are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;
- To any legal entity that has two or more of (i) an average of at least 250 employees during the last financial year; (ii) a total balance sheet of more than €43,000,000 and (iii) an annual net turnover of more than €50,000,000, as shown in its last annual or consolidated accounts
- To fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of representative for any such offer; or
- In any other circumstances that do not require the publication of a prospectus pursuant to Article 3 of the Prospectus Directive;

provided that no such offer of securities shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer of shares to the public" in relation to any shares of common stock in any relevant member state means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe for the shares, as the same may be varied in that member state by any measure implementing the Prospectus Directive in that member state and the expression "Prospectus Directive" means Directive 2003/71/EC and includes any relevant implementing measure in each relevant member state.

Other Relationships

From time to time, certain of the underwriters and their affiliates have provided, and may provide in the future, various advisory, investment and commercial banking and other services to us in the ordinary course of business, for which they have received and may continue to receive customary fees and commissions. The Trout Group LLC, an affiliate firm of Trout Capital LLC, has been retained as investor relations advisor for us since April 2010 and we currently pay a monthly cash retainer to The Trout Group LLC. During the period beginning 180 days prior to the original filing of the registration statement of which this prospectus forms a part and ending 90 days after the effectiveness of such registration statement, we have paid and expect to pay The Trout Group LLC no more than an aggregate amount of $85,591 in fees and as reimbursement for certain of their expenses. Such amount will be considered by FINRA to be underwriter compensation in connection with this offering.

Except as described above and for services provided in connection with this offering, no underwriter has provided any investment banking or other financial services during the 180-day period preceding the date of this prospectus and we do not expect to retain any underwriter to perform any investment banking or other financial services for at least 90 days after the date of this prospectus.

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. In connection with the offering, other legal matters will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Certain legal matters in connection with this offering will be passed upon for the underwriters by Lowenstein Sandler LLP, New York, New York.

EXPERTS

The consolidated financial statements incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2013 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.

The audited special purpose combined financial statements of the Cell Therapy and Regenerative Medicine Business, a product portfolio of Sanofi, included as Exhibit 99.1 to Aastrom Biosciences Inc.'s Current Report on Form 8-K dated June 2, 2014 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, independent accountants, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the securities offered by this prospectus. This prospectus, which forms a part of the registration statement, does not contain all the information set forth in the registration statement, as permitted by the rules and regulations of the SEC. For further information with respect to us and the securities offered by this prospectus, reference is made to the registration statement.

Statements contained in this prospectus as to the contents of any contract or other document that we have filed as an exhibit to the registration statement are qualified in their entirety by reference to the exhibits for a complete statement of their terms and conditions.

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, including the registration statement, 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). You may also inspect the registration statement on this website.

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. We incorporate by reference the documents listed below:

- Our quarterly reports on Form 10-Q for the quarters ended March 31, 2014, filed with the SEC on May 15, 2014, and June 30, 2014, filed with the SEC on August 14, 2014;

- Our annual report on Form 10-K for the period ended December 31, 2013, filed with the SEC on March 13, 2014;

- Our current reports on Form 8-K, filed with the SEC on January 14, 2014, January 27, 2014, April 1, 2014, April 23, 2014, May 1, 2014, May 9, 2014, May 12, 2014, June 2, 2014, as amended on June 16, 2014 and August 29, 2014, June 4, 2014, June 16, 2014, and July 11, 2014 respectively (excluding any information furnished in such reports under Item 2.02, Item 7.01 or Item 9.01);

- The portions of our definitive Proxy Statements on Schedule 14A for the Annual Meeting of Shareholders, filed with the SEC on March 31, 2014, that are deemed "filed" with the SEC under the Exchange Act;

- 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 our registration statements on Form S-1, filed with the SEC on November 1, 1996, filed with the SEC on 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 (734) 418-4400. 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.

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.

TERM	DEFINITION
IND—Investigational New Drug	An application submitted to the FDA for a new drug or biologic that, if allowed, will be used in a clinical trial.
Ischemia	A shortage or inadequate flow of blood to a body part (commonly an organ or tissue) caused by a constriction or obstruction of the blood vessels supplying it.
LVEF—Left Ventricular Ejection Fraction	The fraction of blood pumped out of the left ventricle with each heart beat.
Open-label Clinical Trial	A trial in which both the treating physician and the patient know whether they are receiving the experimental treatment or control/placebo treatment.
Orphan Drug Designation	"Orphan drug" refers to a drug or biologic that is intended for use in the treatment of a rare disease or condition. Orphan drug designation from the U.S. Food and Drug Association (FDA) qualifies the sponsor to receive certain benefits from the Government in exchange for developing the drug for a rare disease or condition. The drug must then go through the FDA marketing approval process like any other drug or biologic which evaluates for safety and efficacy. Usually a sponsor receives a quicker review time and lower application fees for an orphan product.
Periosteal Flap	A graft taken from the periosteum, a fibrous membrane of connective tissue that snugly covers all bones.
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.

TERM	DEFINITION
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.

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13,725,490 Shares of Common Stock

PROSPECTUS

Sole Book-Running Manager

Ladenburg Thalmann

September 11, 2014