Zacks Equity Research

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Aastrom Biosciences, Inc. (ASTM-NASDAQ)

ASTM: Several Near-Time Catalysts For Aastrom Bio…

Current Recommendation	**Neutral**
Prior Recommendation	N/A
Date of Last Change	07/28/2010
Current Price (08/17/10)	$1.51
Target Price	**$2.50**

FULL REPORT

Last month we initiated coverage of Aastrom Biosciences with a Neutral rating and $2.50 price target. Aastrom is pioneering the research effort on adult stem cells for therapeutic applications, specifically for the treatment of cardiovascular diseases such as critical limb ischemia (CLI) and dilated cardiomyopathy (DCM).

Although we are enthusiastic about the company's future, the novel approach to treading disease and the skepticism on Wall Street will keep the stock in "show me" mode for the near future. Aastrom shareholders have real hope however. More data is coming, as soon as November 2010, and what we have seen so far leads us to believe that patience will be rewarded.

SUMMARY DATA

52-Week High	**$3.82**
52-Week Low	**$1.34**
One-Year Return (%)	**-52.50**
Beta	**-0.19**
Average Daily Volume (sh)	**96,293**
Shares Outstanding (mil)	**28**
Market Capitalization ($mil)	**$43**
Short Interest Ratio (days)	**4.81**
Institutional Ownership (%)	**13**
Insider Ownership (%)	**2**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2010 Estimate	**N/A**
P/E using 2011 Estimate	**N/A**
Zacks Rank	**3**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**
Zacks Rank in Industry	**71 of 141**

ZACKS ESTIMATES

Revenue
(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2010	0.07 A	0.02 A	0 A	0 A	0.09 A
2011	0 E	0 E	0 E	0 E	0 E
2012					0.10 E
2013					0.10 E

Earnings per Share
(EPS is operating earnings before non-recurring items)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2010	-$0.18 A	-$0.21 A	-$0.16 A	-$0.18 A	-$0.72 A
2011	-$0.18 E	-$0.18 E	-$0.19 E	-$0.19 E	-$0.74 E
2012					-$0.90 E
2013					-$0.93 E

Zacks Projected EPS Growth Rate - Next 4 Years % **N/A**

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WHAT'S NEW

Financial Review…

On August 17, 2010, Aastrom Biosciences reported financial results for the fiscal fourth quarter and full year ended June 30, 2010. The company did not report any revenues for the fiscal Q4. This was as expected. For the full year 2010, the company reported total revenues of $89k, consisting of product sales and rentals to clinical trial and investigator sites. Net loss for the fiscal Q4 totaled $5.1 million, or -18 cents per share. This was slightly more than our estimate for EPS of -14 cents on higher than expected R&D costs. R&D costs rose in the quarter on the company's phase IIb program for CLI and phase II program for DCM. For the full year 2010, Aastrom reported a net loss of $17.7 million, or -72 cents per share.

The company exited fiscal 2010 ended June 30, 2010 with $19.1 million in cash and investments. We believe this is sufficient cash to fund operations for the next three to four quarters, and includes the necessary funds to initiate the company's planned phase III program in CLI around the middle of calendar 2011.

INVESTMENT THESIS

Two Potential Blockbuster Opportunities…

In July 2010, we initiated coverage of Aastrom Biosciences with a Neutral rating and $2.50 price target. Aastrom is pioneering the research effort on adult stem cells for therapeutic applications, specifically for the treatment of cardiovascular diseases such as critical limb ischemia (CLI) and dilated cardiomyopathy (DCM).

Aastrom's approach involves expansion of a patient's own stem and progenitor cells outside of the body to generate a cell product with significantly increased numbers of highly functional early-stage cells. These autologous cell products can then be used for the repair or regeneration of multiple human tissues. The company has developed a proprietary Tissue Repair Cell technology in which cells are derived from a small amount of bone marrow taken from a patient and expanded in culture to generate a unique cell mixture containing high doses of stem and progenitor cells. Due to the high number of stem and progenitor cells contained in a small volume, Aastrom's strategy seems particularly suitable for direct injection into the affected limb or myocardium.

Aastrom Biosciences has two clinical programs ongoing, one for vascular applications in critical limb ischemia (CLI), the most severe (end-stage) of peripheral arterial disease (PAD), and another for cardiac applications in dilated cardiomyopathy (DCM), the leading cause of heart transplantation.

- ✓ For CLI, management has presented very encouraging proof-of-concept data, as well as statistically significant interim results from a phase IIb program, RESTORE-CLI, on FDA-validated endpoints for CLI – major amputation and amputation-free survival. We have also seen encouraging preliminary data from an investigator-sponsored program conducted in Germany.

- ✓ For DCM, management has demonstrated promising trends from an interim analysis of IMPACT-DCM, which show meaningful improvements in NYHA function class for patients on therapy. The company has also made available encouraging case study data from compassionate use in Europe.

We view Aastrom Biosciences at the premier play for the application of adult stem cells for potential cardiovascular indications. While other stem cell companies such as Cytori Therapeutics (the market leader for cosmetic and reconstructive surgery) and Osiris Therapeutics (the market leader for inflammatory diseases) command higher market capitalizations, no other firm has as an advanced program for peripheral arterial disease or heart failure. Yet, despite the firm's advanced position for two potential billion-dollar "home run" indications, the market has yet to value Aastrom as a leader. We believe this is due to the company's novel approach, the high risk nature of the trials, and the fact that Aastrom must pave the way itself. As such, Aastrom Biosciences is in "show me" mode, and Aastrom must deliver before Wall Street will really start to pay attention. That being said, the next six to nine months is packed with catalysts from a clinical standpoint. We anticipate the first potential big catalyst for the shares, the final six-month data from all 86 patients in RESTORE-CLI, in November 2010.

Adult Stem Cells

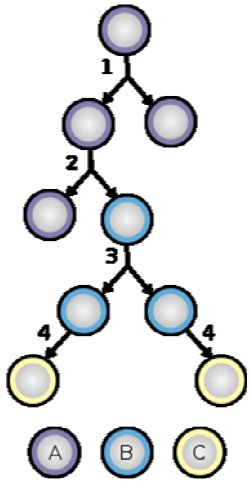
Adult stem cells are undifferentiated cells, found throughout the body after embryonic development, which multiply by cell division to replenish dying cells and regenerate damaged tissues. Also known as somatic stem cells, they can be found in juvenile as well as adult animals and humans. Scientific interest in adult stem cells has centered on their ability to divide or self-renew indefinitely, and generate all the cell types of the organ from which they originate, potentially regenerating the entire organ from a few cells. Unlike embryonic stem cells, the use of adult stem cells in research and therapy is not considered to be controversial as they are derived from adult tissue samples rather than destroyed human embryos.

…Characteristics and Advantages of Adult Stem Cells…

- ✓ Self-Renewal: Ability to self-renew while maintaining an undifferentiated state.
- ✓ Multipotency: Ability to generate progeny of several distinct cell types.
- ✓ Non-controversial: Ability to be derived from adult (healthy) tissue from the patient, as opposed to the destruction of a human embryo.
- ✓ Availability: Ability to be sourced from bone marrow, cord blood, adipose tissue, and mandibular molars.

There are several types of stem cells found in the body. These include, among others, hematopoietic stem cells that are found in bone marrow and give rise to all blood cell types, mammary stem cells that provide the source for growth of the mammary gland during puberty and gestation, endothelial stem cells which give rise to new blood vessels, and mesenchymal stem cells (MSCs) that may differentiate into a variety of tissues. MSCs have the potential to develop or differentiate into many cell types in the body. Lineage differentiation includes adipogenic (fat), cardiomyogenic (heart muscle), leiomygenic (smooth muscle), myogenic (skeletal muscle), chondrogenic (cartilage), osteogenic (bone), neurogenic (nerve), angiogenic (blood vessel), and hematopoietic (blood) cells.

Cell Division & Differentiation



Adult stem cells are also capable of secreting a large number of growth factors including: hepatocyte (HGF), placental (PGF), transforming factor-β (TGFβ), fibroblast (FGF), vascular endothelial (VEGF), and granulocyte / macrophage colony stimulating factors (GM-CSF). Analysis of these growth factors and proteins suggest a strong active role in neovascularization and angiogenesis (the growth of new vessels). The underlying hypothesis for using adult stem cells is that they have the potential to regrow or repair almost any type of damaged tissue found inside the body. This has enormous potential for applications in the medical community.

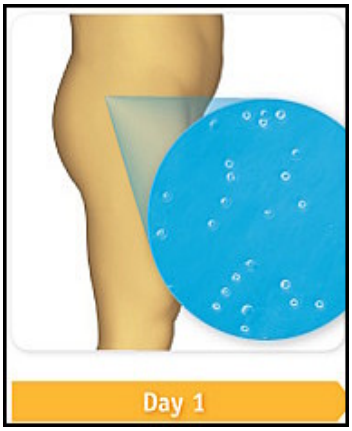
The potential therapeutic application for adult stem cells is enormous. Adult stem cell treatments have been used for many years to successfully treat leukemia and related bone/blood cancers utilizing bone marrow transplants. U.S. government funding has provided for research in this field, as opposed to controversial use of embryonic stem cells which receive no new government funding. Early regenerative applications of adult stem cells have focused on intravenous delivery of blood progenitors known as hematopoietic stem cells (HSCs). Other early commercial applications have focused on mesenchymal stem cells (MSCs). For both cell lines, direct injection or placement of cells into a site in need of repair may be the preferred method of treatment, as vascular delivery suffers from a "pulmonary first pass effect" where intravenous injected cells are sequestered in the lungs.

Several companies are working on stem cell therapies for the treatment or prevention of various conditions. Researchers believe that stem cell therapy has the potential to dramatically change the treatment of human disease. A number of adult stem cell therapies already exist. As noted above, bone marrow transplants are used to treat leukemia. Several advanced clinical studies are currently testing the use of stem cells for the treatment of prevention graft vs. host disease (GvHD) in organ transplant. In the future, physicians may be able to use technologies derived from stem cell research to treat a wider variety of diseases including cancer, diabetes, Parkinson's disease, spinal cord injuries, amyotrophic lateral sclerosis, multiple sclerosis, chronic obstructive pulmonary disease, and muscle damage, amongst a number of other impairments and conditions. Clinical case reports in orthopedic applications and enhancing fat-grafting for cosmetic and reconstructive surgery have also been published. Aastrom Biosciences is pioneering the effort to use adult stem cells for the treatment of various forms of cardiovascular disease, including critical limb ischemia (CLI) and dilated cardiomyopathy (DCM)

Aastrom's Approach to Cell Therapy

Aastrom Biosciences' approach to creating potential therapeutic applications for adult stem cells involves expansion of a patient's own stem and progenitor cells outside of the body to generate a cell product with significantly increased numbers of highly functional early-stage cells. These autologous cell products can then be used for the repair or regeneration of multiple human tissues. The company has developed a proprietary technology in which cells are derived from a small amount of bone marrow taken from a patient and expanded in culture to generate a unique cell mixture containing high doses of stem and progenitor cells. Due to the high number of stem and progenitor cells contained in a small volume, Aastrom's strategy seems particularly suitable for direct injection into the affected limb or myocardium.

…Tissue Repair Cell Technology…



A small quantity (approx 50ml) of bone marrow stem cells are aspirated from the patient's hip, through the iliac crest, in a 15-minute in-office (outpatient) procedure. The procedure is generally performed under a local anesthesia with IV sedation, and can be performed by the attending physician, wound care specialists, or nurse / physician's assistant. The collection kit is supplied by Aastrom Biosciences to simplify and standardize the procedure. Proof-of-concept data has shown that the procedure is generally well-tolerated and can be performed in the most severely ill patients with advanced stages of cardiac or vascular disease.

This bone marrow sample contains a range of cells including hematopoietic and mesenchymal cells. These cells are known to play important roles in the natural healing mechanisms of the human body.



The bone marrow aspirate is then shipped to Aastrom's comprehensive GMP-compliant cell manufacturing and processing facility in Michigan. Over a period of about 12 days, Aastrom's proprietary tissue repair cell technology expands the naturally occurring populations of early stem and progenitor cells found in the extracted bone marrow. The ramped single-pass perfusion (SPP) schedule for the culture medium results in significant expansion of primary early-stage human cells possessing enhanced functionality. Aastrom's patented SPP technology controls gas and cell culture media exchange to enable the replication of these naturally occurring cells. The closed (sterile) procedure is computer automated and optimized for efficiency. The cellular therapy resulting from this process contains expanded populations of mixed stem and progenitor cells to support the regeneration of cardiovascular tissues associated with vasculature and myocardium.



In a single procedure, the cellular therapy produced from the SPP process is then administered to the same patient to promote healing. The cells are injected in multiple sites around the affected tissue. A complete course of therapy is one treatment (1 unit dose), with initial follow-up of patients suggesting a durability of greater than 2 years. Current capacity is for roughly 2,500 doses per year, with the potential to expand in the future as needed.

Aastrom's cell production process works exclusively with adult stem cells derived from and administered to the same patient. This autologous approach reduces the risk of rejection and increases the likelihood of integration with the surrounding tissues, eliminating the need for dangerous immuno-suppressive drugs. Aastrom's use of autologous cells also avoids controversies associated with embryonic or cryo-preserved stem cells.

…Tissue Repair Cell Technology Characteristics…

Aastrom has demonstrated that expansion of stem cells by SPP produces a highly viable cell product. The procedure also produces a highly consistent, reproducible and reliable product. The manufacturing process is a closed (sterile), automated GMP compliant system. Within a single donor, the autologous cell expansion process is reproducible and does not add to the inherent donor variability seen in bone marrow aspirates. For certain cell types, including the mesenchymal CD90+ cells, not only are the numbers of these cells substantially increased, but the donor variability is reduced from the starting bone marrow population. This provides a more standardized final product for all patients. Below is a phenotype representation stem cell analysis for Aastrom's cell product:

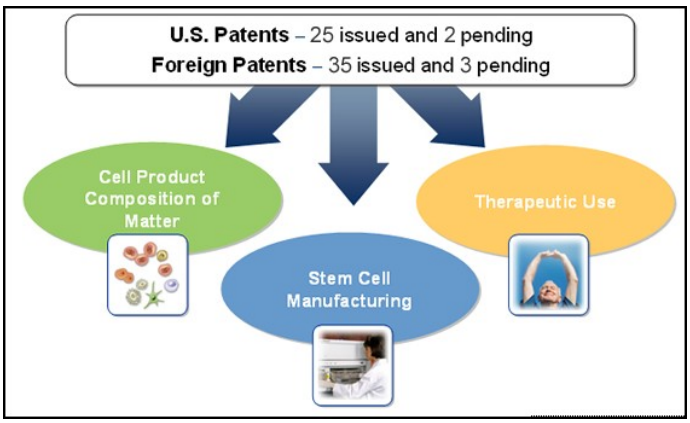
Cell Population	Harvested (BM Input)	Expanded Cells (Output)	Fold Increase
Mononuclear Cells	$300x10^6$	$125 x10^6$	0.4x
Stem & Progenitor Cells (CD90+)	$0.8 x10^6$	$39 x10^6$	49x
RBCs & Erythroid Precursors (GlyA+)	$105 x10^6$	$1 x10^6$	<0.01
All Leukocytes (CD45+)	$290 x10^6$	$86 x10^6$	0.3x
Activated Macrophages (CD14+)	$40 x10^6$	$32 x10^6$	0.8x
Granulocytes (CD66b+)	$183 x10^6$	$20 x10^6$	0.1x
T-Cells (CD3+)	$32 x10^6$	$9 x10^6$	0.3x
B-Cells (CD19+)	$19 x10^6$	$1 x10^6$	0.1x

- ✓ Mesenchymal components, along with macrophage populations are significantly expanded,
- ✓ CXCR4 and VEGFR1 positive cells, believed to be critical for neovascularization, are increased,
- ✓ Cells expressing endothelial cell markers are increased up to 6-fold,
- ✓ Angiogenic factors including VEGFs A, B, and C, are increased,
- ✓ Many hematopoietic components, including red blood cells (RBCs), T-Cells and B-Cells, that may elicit negative immune response, are reduced.

Aastrom has reported positive interim clinical trial results suggesting both the clinical safety and the ability of its expanded autologous cell product to promote healing. The company is also developing clinical programs for expanded autologous cell-based therapies to address cardiovascular regeneration indications. Expanded autologous cells have recently received Orphan Drug Designation from the FDA for use in the treatment of osteonecrosis of the femoral head and the treatment of dilated cardiomyopathy (DCM). The company is seeking U.S. FDA fast track designation for a phase III trial in critical limb ischemia (CLI).

…Intellectual Property…

Aastrom's cell processing technology is protected by patents covering strategically important areas of the platform. The IP protection covers a broad range of claims relating to the cell processing technology and products, including composition, process and device claims. New applications include additional composition claims, plus important process claims that aim to protect Aastrom's expanded cellular products. The existing IP suite includes 25 U.S. patents and 2 pending:



For a complete list of Aastrom's patent portfolio, please see:
http://www.aastrom.com/IntellectualProperty.cfm?pagesect=patent

Vascular Application

→ Critical Limb Ischemia (CLI)

One of the most advanced clinical applications currently being studied by Aastrom Biosciences is for the treatment of critical limb ischemia (CLI), the most severe form of peripheral arterial disease (PAD). PAD affects an estimated 10% to 20% of all people over the age of 55, with prevalence increasing with age. Prevalence of PAD is also significantly higher – about 30% to 35% – in people with diabetes. The majority of people with PAD are asymptomatic, which creates the potential for dire consequences, as people living with PAD are four to five-times at higher risk for heart attack or stroke. Only about 25% of the roughly 10 million Americans living with PAD are receiving treatment. Tobacco use in any form has been shown to increase the risk for PAD by tenfold.

PAD is defined as poor circulation to the limbs, and is commonly divided into four stages of disease severity: 1) mild pain when walking (claudication); 2) severe pain when walking relatively short distances (intermittent claudication); 3) pain while resting (rest pain); and 4) biological tissue loss (gangrene). CLI is the most severe form of PAD and affects approximately 1 million people in the U.S. each year – roughly 2% of the population over the age of 50. CLI is defined as inadequate blood flow to the limbs, and if left untreated can result in tissue loss, gangrene, amputation, and death. In fact, CLI leads to an average of 160k major limb amputations each year. CLI has a high mortality rate: 20% after 6-months after initial diagnosis and 25% after 12-months. Nearly 30% of all patients who undergo a major limb amputation will require another amputation at some point in the future. The mortality rate post-amputation remains high, at roughly 20% to 30%.

Therapeutic options for patients with CLI are limited. Besides being at significantly increased risk for heart attack, stroke, or vascular death, patients with CLI often live with several other co-morbidities, including diabetes, angina, dyslipidemia, hypertension, and renal disease. For less severe forms of PAD, physicians will typically recommend smoking cessation (when applicable), and changes to diet and exercise. Medications such as aspirin, statins, and clopidogrel (Plavix) are common first-line therapies for early-stage PAD. Many patients will also be on medications for diabetes and heart failure as well. However, once PAD progresses to the point of CLI, the only real options available to patients are surgical. Patients are passed from the cardiologist, diabetologist, or podiatrist to the care of the vascular surgeon. Surgical procedures include percutaneous transluminal angioplasty, plaque excision, stenting, and bypass grafting. Patients living with CLI suffer from severe pain as a result of the neuropathy, tissue loss, and ischemia.

…Proof-of-Concept…

In September 2005, the Heart and Diabetes Center North Rhine-Westphalia, Germany, conducted an investigator sponsored trial designed to determine the feasibility of using autologous bone marrow stem cells in diabetic patients with ischemia-induced chronic tissue ulcers affecting the lower limbs. This was an independent study in which cells were expanded using Aastrom's proprietary technology. This was a phase I/II, open label program that enrolled patients into 5 groups: 1) standard medication, 2) VRCs administered intramuscularly, 3) VRCs administered intra-arterially, 4) fresh bone marrow administered intramuscularly, and 5) fresh bone marrow administered intra-arterially, with a 12-month follow-up period.

In October 2007, positive interim results from the first 13 patients treated in Germany were presented by investigators at the 2nd Congress of the German Society for Stem Cell Research in Würzburg, Germany. Results reflect treatment experience from: four diabetic patients with ischemia related chronic tissue ulcers who were treated with the cells; seven patients who were treated with normal unexpanded marrow cells; and two standard of care patients who did not receive cells. The investigator reported at twelve months post-treatment that all patients in the interim analysis who were treated with autologous expanded cells reported no major amputations, no cell-related adverse events, and healing of all open wounds. Of the seven patients treated with unexpanded bone marrow cells, five reported results similar to the test patients 12 months post-treatment, one reported similar results to the test patients 18 months post-treatment, and one patient underwent a major amputation. For the two standard of care patients who only received wound care (no cells), one patient received a major amputation and one patient experienced no improvement in wound healing after 12 months.

Full analysis from all the patients enrolled (we estimate 20 to 25) is still ongoing. Nevertheless, this proof-of-concept work, along with other early-stage case study work conducted as Aastrom, lead to the filing of an investigational new drug (IND) application with the U.S. FDA. The agency approved the IND in April 2007.

…RESTORE-CLI…

In April 2007, Aastrom Biosciences initiated a clinical trial designed to assess the use of its cellular therapy (expanded autologous cells) in patients with peripheral arterial disease (PAD) to treat critical limb ischemia (CLI). RESTORE-CLI is a double-blind, multi-center phase IIb program with the primary outcome of the program assessing safely in treating patients with PAD-induced CLI. The ability to reduce the incidence of major amputations in the treated limbs, close open wounds, improve blood flow, and improve overall quality of life was also assessed. Patients enrolling in the program were deemed to have "no acceptable option for revascularization" to treat their condition. The program randomized patients into 2-arms (2:1 ratio) of: 1) expanded cells administered intramuscularly vs. 2) control (electrolyte solution). Both groups continue to also receive the standard of care appropriate for their medical condition.

The first patient received treatment in June 2007. In September 2008, an independent data safety monitoring board (DSMB) granted approval to Aastrom to continue the program after a review of the first 30 patients. RESTORE-CLI completed enrollment at 86 patients across 18 clinical sites in March 2010. In June 2010, Aastrom reported interim results from RESTORE-CLI at the annual meeting for the Society for Vascular Surgery. These results build upon the announcement of the top-line data in February 2010.

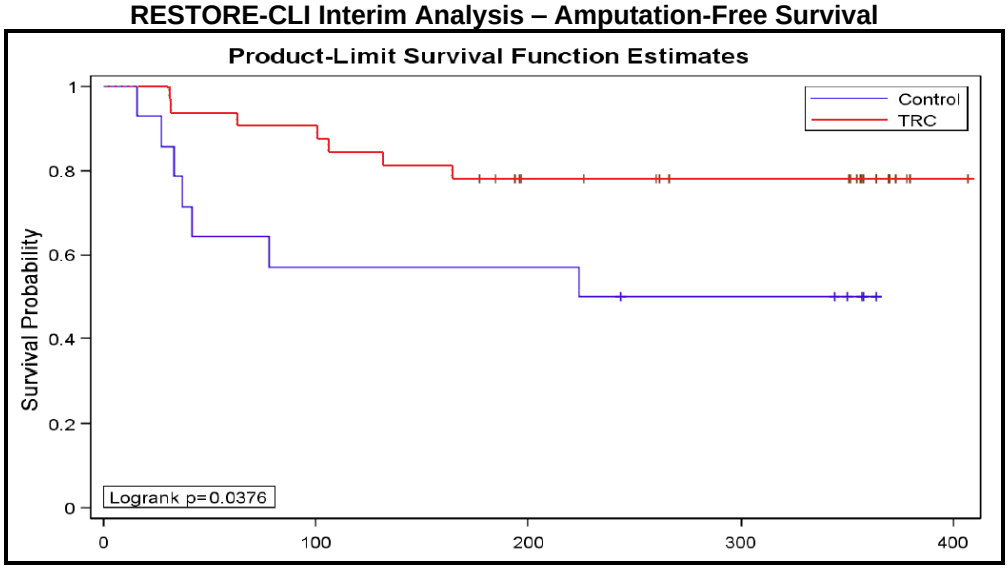
Safety Assessment on ITT Population

Parameter	Expanded Cells (n=32)	Control (n=14)
Number (%) with Adverse Events	30 (94%)	14 (100%)
Number of Deaths	1	1
Number (%) with Serious Adverse Events	14 (44%)	8 (57%)
Number (%) Withdrawal due to AE	0	0

Efficacy Assessment on ITT Population

Parameter	Expanded Cells (n=32)	Control (n=14)	
Any Composite Endpoint	41%	79%	*p = 0.005*
All Cause Mortality	3%	7%	
Major Amputation (6-Months)	19%	43%	*p = 0.14*
Doubling in Wound Size	19%	43%	
Complete Wound Healing (12-Months)	31%	13%	*p = 0.61*
De Novo Gangrene	13%	14%	
Amputation Free Survival (12-Months)	78%	50%	*p = 0.038*

RESTORE-CLI Interim Analysis – Amputation-Free Survival



Interim results from RESTORE-CLI demonstrate statistically significant reductions in the time to first occurrence of treatment failure and in amputation-free survival, as well as a trend toward significance in major amputations and wound healing. We believe that amputation-free survival is the key (gold standard) endpoint with respect to gaining U.S. FDA approval. Accordingly, we are highly encouraged by the data presented in early June 2010. The chart above clearly shows separation of Aastrom's expanded cell therapy group vs. control as soon as two months following treatment, with persistent efficacy maintained over the 12-month assessment period. Adverse events and serious adverse events (including MACE) are common in this patient population. However, management noted that none of the SAE's was related to the expanded cell therapy. We expect management to present full results from the six-month follow up on all 86 patients in RESTORE-CLI in November 2010, perhaps at AHA.

…Phase III Plans…

On June 30, 2010, Aastrom Biosciences met with the U.S. FDA to discuss plans for initiating a pivotal phase III program for the treatment of CLI using its expanded cell therapy. The company will pursue this program under the FDA's special protocol adjustment (SPA) process, which allows for close discussion with the agency and agreed-upon endpoints and trial design. The benefits of pursuing a SPA are that if these protocols are followed and the clinical trial endpoints achieved, and there is a favorable risk-benefit profile, trial data may serve as the primary basis of an efficacy claim in support of a biologic license application (BLA). Aastrom plans to file the first submission of the SPA in late September / early October 2010. In July 2010, management filed for "Fast Track" development status with the FDA, again allowing for close and expedited consultation on trial design and endpoints. We expect the FDA to respond on the Fast Track application early in the fourth quarter 2010.

We expect that the phase III program will look similar to the phase IIb RESTORE-CLI program. Management may focus the patient population to be more homogeneous in nature to lower variability and risk. We expect there to be two phase III trials in the program, with in the area of 500 patients total between two arms. The primary endpoint will most likely be amputation-free survival at 6 months, with secondary endpoints including amputation free survival at 12 months, de novo gangrene, wound healing, and all cause mortality. Enrollment should proceed faster than the phase IIb program now that management has identified the key wound care centers and vascular surgeons from the RESTORE-CLI program. We expect approximately 50 sites in the U.S. and Canada to participate.

Our assumption is that this program could initiate around the middle of 2011 and take up to two years to complete. The total cost should be roughly $15 million, or $30k per patient. We note this is relatively inexpensive for a pivotal phase III program. The design and costs are more in-line with a medical device than a small molecule pharmaceutical. The biggest impediment we see in enrollment would be a potentially competing CLI program from an oral small molecule or medical device company and funding. Neither is a concern at this point.

…Market Opportunity & Commercialization Plans…

As discussed above, CLI represents a significant and wide-open opportunity for Aastrom Biosciences. PAD affects an estimated 10% to 20% of all people over the age of 55, with prevalence increasing with age. CLI is the most severe form of PAD and affects approximately 1 million people in the U.S. each year – roughly 2% of the population over the age of 50. CLI leads to an average of 160k major limb amputations each year. The mortality rate is 20% after 6-months and 25% after 12-months following diagnosis. Nearly 30% of all patients having undergone a major limb amputation will require another amputation at some point in the future. Therapeutic options for patients with CLI are limited. In fact, the only real options available to patients are surgical.

The market for cell-based therapies is growing. Aastrom will be able to follow the pathway paved by Genzyme with Carticel, an autologous cell therapy for knee injuries, and Dendreon with Provenge, an activated immunotherapy of antigen presenting cells for prostate cancer. However, we note that Aastrom's approach seems more efficient (single dose from a single bone marrow aspirate vs. three doses) and elegant (no need to add activator compounds) in procedure than Dendreon's.

Aastrom's cell therapy could capture sizable market share as a rescue medication prior to surgery. A major limb amputation can cost upwards of $50,000, and the long-term care cost associated with an elderly patient post-amputation are even greater. We note that the mortality rate post amputation remains high, at roughly 20% to 30%. Vascular surgeons could use Aastrom's cell therapy in an effort to save a limb, and in-turn, a life. At this point Aastrom is in the driver's seat with CLI. The company has the most advanced stem cell therapy for CLI, ahead of competitors such as Pluristem and Harvest Technologies. We expect management to develop its autologous cell therapy all the way up to, and most likely through the BLA filing. With positive phase III data under a SPA, and a BLA filed, management will then have the opportunity to partner for commercialization, or move forward on its own.

Cardiac Application

→ Dilated Cardiomyopathy (DCM)

Aastrom Biosciences is currently studying the use of its expanded autologous cell therapy for the treatment of dilated cardiomyopathy (DCM) in mid-stage clinical trials. DCM is a condition in which the heart becomes weakened and enlarged, and cannot pump blood efficiently. The expansion of the heart and the decreased function results in poor blood circulation and affect the lungs, liver, and other body systems. In patients with DCM, the left or right ventricular systolic pump function of the heart becomes impaired, leading to progressive cardiac enlargement and hypertrophy, a process called remodeling.

The cause of DCM are often varied, but most frequently is the result of damage to the myocardium produced by a variety of ischemic toxic, metabolic, or infectious (bacterial or viral) agents. It may be due to fibrous change of the myocardium from a previous myocardial infarction; or, it may be the late sequel of acute viral myocarditis, possibly mediated through an immunologic response. DCM is often reversible when the result of alcohol abuse, pregnancy (peripartum cardiomyopathy), thyroid disease, and chronic uncontrolled tachycardia. About 20-40% of all patients have familial (genetic) forms of the disease. However, many cases of non-ischemic DCM remain idiopathic in nature. There are two forms of DCM:

- Ischemic DCM: Weakening of the heart muscle is a result of coronary artery disease or myocardial infarction. This is the most common cause of DCM.

- Non-ischemic DCM: Weakening of the heart muscle is a result of external factors, including alcohol abuse, drug abuse, viral or bacterial infections, genetics, or idiopathic causes.

There are an estimated 120k to 150k people living (prevalence) in the U.S. with DCM, with roughly 10,000 to 15,000 new cases (incidence) each year. DCM occurs more frequently in men than in women, and is most common between the ages of 20 and 60 years. Vague chest pain may be present, but typical angina pectoris is unusual and suggests the presence of ischemic heart disease as well. Syncope due to arrhythmias and systemic embolism may occur, as well as dyspnea. About one in three cases of congestive heart failure (CHF) is due to DCM. The 1-year survival rate for a patient diagnosed with DCM is roughly 75%. The 5-year survival rate drops to only 30% because many patients with DCM go un-diagnosed until the disease has progressed to the most severe stages. As a general rule for idiopathic DCM, after 1-year, 1/3rd of patients exhibit improved cardiac function, 1/3rd have stable cardiac dysfunction, and 1/3rd progress to significant cardiac dysfunction. These 1/3rd that progress to severe cardiac dysfunction will require a heart transplant.

Standard of care for patients with DCM is often to treat secondary co-morbid conditions such as hypertension or renal failure. As such, patients with DCM are often prescribed angiotensin-converting enzyme (ACE) inhibitors, diuretics, beta-blockers, and sometimes digitalis. Anticoagulants may also be used. Alcohol should be avoided. Artificial pacemakers and left ventricular assist devices (LVADs) may be used in patients with intra-ventricular conduction delay, and implantable cardioverter-defibrillators in those at risk of arrhythmia. These forms of treatment have been shown to improve symptoms and reduce hospitalization. They can cost upward of $75,000 each, and many patients will require re-implantation or an upgraded or new device in a year. However, for patients with advanced disease who are refractory to medical therapy, cardiac transplantation is the only option. LVAD are commonly known as a "bridge to transplantation". The problem however, and the reason this is such as a significant medical problem, is that only about 2,000 heart transplants are done in the U.S. each year. That means of the estimated 150k NYHA Class 3 or 4 patients with dilation, over 95% will never get a transplant. Accordingly, this is why mortality rates start to rise dramatically after a patient has been diagnosed with DCM.

…IMPACT-DCM…

Aastrom is currently conducting a phase II (proof-of-concept) program in the U.S. studying its cell therapy for the treatment of DCM. The company received U.S. FDA clearance to begin this program via the approval of its investigational new drug (IND) application in June 2008. The trial, IMPACT-DCM (Intramyocardial Delivery of Autologous Bone Marrow Cells in Patients with Heart Failure Due to Dilated Cardiomyopathy) is designed to determine if expanded autologous cells delivered by direct injection into the myocardium can safely and effectively treat patients with DCM compared to standard-of-care treatment. This is an indication for which the U.S. FDA granted Aastrom Biosciences an 'Orphan Drug' designation in February 2007 as a result of the limited therapeutic treatment options available and high mortality rate for patients.

IMPACT-DCM is a randomized, open-label program that enrolled 20 patients with ischemic DCM and 20 patients with non-ischemic DCM in a 3:1 ratio for cell therapy vs. control, with a 12-month follow-up period. Participants in IMPACT-DCM must have a left ventricular ejection fraction (LVEF) of less than or equal to 30% (60-75% is typical for a healthy person) and meet certain other eligibility criteria. Patients will be treated with cell therapy through direct injection into the heart muscle during minimally invasive (mini thoracotomy) open heart surgery. The CRCs are injected directly into the heart in 20 to 25 sites. While the primary objective of this study is to assess the safety of cell therapy in patients with DCM, efficacy measures including LVEF, heart failure stage and other measures of cardiac function will be monitored.

Aastrom enrolled the first patient in the program in November 2008. Shortly after, in February 2009, the U.S. FDA enforced a hold on patient enrollment when one patient experienced a serious adverse event (SAE) associated with anesthesia management during treatment at one of the active clinical sites. The DSMB reviewed the incident and determined it was not related to Aastrom's cell therapy, and allowed enrollment to resume in March 2009. Unfortunately, in May 2009, enrollment was suspended again when one patient, on active cell therapy, died at home after being released from the hospital. Once again, the DSMB reviewed the incidence and determined the death was due to disease progression, not a serious adverse event associated with the cell therapy. Enrollment was allowed to resume in June 2009, and eventually completed in March 2010 at 40 patients.

In November 2009, the lead investigator in the IMPACT-DCM program, Dr. Amit N. Patel, M.D., M.S., provided an encouraging interim update via an oral presentation at the American Heart Association (AHA) annual meeting. Dr. Patel's talk highlighted data suggesting that the majority of patients treated to date with cell therapy have shown improvements in their heart failure classification, while patients in the control group did not.

Interim IMPACT-DCM Data

New York Heart Association Functional Class Assessment:
Of the 7 treatment patients who have completed the 1-month follow-up visit, 1 patient had improved to NYHA Class I and 3 patients had improved to Class II. In contrast, at the 1-month follow-up visit, the NYHA Class did not improve in 3 of the 5 control patients.
Of the 6 treatment patients who have completed the 3-month follow-up visit, 1 patient improved to NYHA Class I and 2 patients improved to Class II. In contrast, at the 3-month follow-up visit, the NYHA Class did not improve in 4 of the 5 control patients.
Of the 5 treatment patients who have completed the 6-month follow-up visit, 2 patients improved to NYHA Class I, 2 patients improved to Class II and 1 patient deteriorated to NYHA Class IV. In contrast, at the 6-month follow-up visit, the NYHA Class did not improve in 3 of the 5 control patients, including 1 patient who deteriorated to NYHA Class IV.

We view these results as very encouraging. After six months, 5 of the 6 patients receiving cell therapy demonstrated improvement NYHA functional class. This compares extremely well to the control group. Deterioration in NYHA class correlates to increased surgical procedure, including implantable pacemakers and cardioverter-defibrillators, and eventually heart transplantation. According to the American Heart Association, there are only roughly 2,200 heart transplants in the U.S. each year. This levels a significant number of patients without an option. Complete interim results from all 40 patients at the 6-month follow-up should become available early next year. There is also a 6-month open-label extension study currently ongoing allowing control patients to crossover cell therapy. This should put management in position to discuss the plans for a larger phase IIb program during the first half of 2011. Final results from IMPACT-DCM will be available during the second half of 2011.

…Catheter-DCM…

Aastrom Biosciences is currently conducting another U.S. phase II clinical trial in DCM studying a catheter-based transendocardial delivery system that channels the cell therapy directly into the heart via threading a catheter through the femoral artery. This is in contrast to IMPACT-DCM where the cells are injected directly into the heart muscle via lateral thoracotomy or minimally invasive thoracoscopy. However, similar to IMPACT-DCM, this is a prospective, open-label, program testing cell therapy as a monotherapy that seeks to enroll patients with both ischemic and non-ischemic DCM. The program began enrollment in April 2010. Patients must have a left ventricular ejection fraction < 30%, and no other cardiac intervention options likely to improve clinical status. The trial seeks to enroll 12 ischemic DCM patients and 12 non-ischemic DCM patients. Within each stratum, patients will be randomized to receive either autologous cellular therapy treatment along with standard-of-care, or control treatment (standard-of-care only) in a 2:1 ratio (8 patients per cell therapy treatment group and 4 patients per control group). Management has guided to completing patient dosing by the end of the year 2010. Interim results are expected in the second quarter 2011.

…EU Compassionate Use Continues…

In certain non-U.S. regions, autologous cells, such as Aastrom's cell therapy products, do not require prior marketing authorization for commercial distribution. This has enabled management to gain product-use experience and refine the clinical development strategies through compassionate use and standard of care patient treatment in Europe. In January 2008, Aastrom announced that the first patient had been treated with its cellular therapy in Germany for the treatment of DCM. Other compassionate use case studies have been conducted in Spain.

In April 2008, Aastrom Biosciences reported data from two compassionate use patients treated in Germany with its autologous stem cell therapy for DCM. A cardiothoracic surgeon experienced with cell therapy at the University Hospital in Dusseldorf, Germany performed the first human application of the cell therapy product through direct injection into the heart muscle during open heart surgery for these two patients in late 2007. The data from these two critically ill patients upon discharge from the surgical center was described as encouraging. Per typical treatment practices in Germany, once these patients were released from the surgical center, they were followed by regional rehabilitation hospitals or local physicians.

- Patient #1 had an LVEF of approximately 10% prior to the cell therapy treatment in November 2007. Over the course of two months, this patient's LVEF improved to 25-30% and clinical improvement of his heart failure stage was noted. As reported by the surgeon, during his stay at a rehabilitation hospital, this critically ill patient refused all further medical treatment and discharged himself from the hospital against medical advice. This patient's subsequent death due to natural causes was unrelated to the cell therapy treatment.

- Patient #2 had an LVEF of 25-30% prior to being treated with cell therapy in December 2007. Upon discharge from the surgical center in February 2008, her LVEF had improved to 45%. In September 2008, at a 7 month follow-up visit with the treating surgeon, this patient's LVEF was again measured at 45% and the patient reported further improvement in her heart failure symptoms.

Management continues to gain clinical experience through the compassionate use protocol. In total, a few dozen patients have been treated in the EU. This has allowed management to gain valuable experience real-world efficacy and safety data on the use of CRCs. This will assist management in planning for the next steps in the U.S.

What Do We Know So Far?

Aastrom Biosciences has two clinical programs ongoing, one for vascular applications in critical limb ischemia (CLI), the most severe (end-stage) of peripheral arterial disease (PAD), and another for cardiac applications in dilated cardiomyopathy (DCM), the leading cause of heart transplantation.

- ✓ For CLI, management has presented very encouraging proof-of-concept data, as well as statistically significant interim results from a phase IIb program, RESTORE-CLI, on FDA-validated endpoints for CLI – major amputation and amputation-free survival. We have also seen encouraging preliminary data from an investigator-sponsored program conducted in Germany.

- ✓ For DCM, management has demonstrated promising trends from an interim analysis of IMPACT-DCM, which show meaningful improvements in NYHA function class for patients on therapy. The company has also made available encouraging case study data from compassionate use in Europe.

More data is coming. By the end of the year, Aastrom should have 6-month interim data from both IMPACT-DCM and RESTORE-CLI, as well as be fully-enrolled in the Catheter-DCM program. Management's meeting with the U.S. FDA on June 30, 2010, went very well. The company received clearance to move forward into a phase III program, and management is now preparing the filings for the SPA. The Fast Track designation filing is currently under review. If all goes well, Aastrom should be in phase III trials with its cell therapy for CLI by the middle of calendar 2011.

We note that Aastrom is not the only company pursuing cellular therapies as a treatment of vascular or cardiac applications. We highlight below the progress of some other pharmaceutical companies in the area. And, despite the fact that these companies may ultimately end up being competitors to Aastrom, at this point in the development phase the more proof-of-concept we can find, the better. Accordingly, we have been very encouraged by what we have seen so far.

Company	Product	Indication	Status
Cytori Therapeutics (CYTX)	Adipose-Derived Regenerative & Stem Cells (ADRC) obtained from the company's proprietary Celution System	Acute Myocardial Infarction (AMI)	Phase II (APOLLO) program demonstrated safety and feasibility, as well as a significant improvement in perfusion rate and ejection fraction, and a significant decrease in left ventricle infarct size (LVI) and mean infarct size at 6-months post therapy, in May 2010.
		Chronic Myocardial Ischemia	Phase II (PRECISE) program demonstrated safety and feasibility, as well as a significant improvement in myocardial oxygen consumption (MVO_2), Metabolic equivalent (MET), NYHA functional class, and a significant decrease in left ventricle infarcted size (LVI) at 6-months post therapy, in May 2010.
BioHeart, Inc. (BHRT)	MyoCell SDF-1 (gene-modified autologous skeletal myoblast cells – precursors to muscle)	Severe heart damage in patients with congestive heart failure (CHF).	Phase II (MARVEL) program demonstrated statistically significant evidence of the safety and efficacy in treating patients with severe, chronic damage to the heart on primary endpoint of improvement in 6-minute walk distance (6MWD) in Sept. 2009. Phase II (SEISMIC) program demonstrated safety and feasibility, as well as improvement in 6MWD and NYHA classification for MyoCell program (vs. control) delivered via the company's proprietary MyoCath endoventricular needle-injection catheter.
Osiris Therapeutics, Inc. (OSIR)	Prochymal (mesenchymal stem cells processed and formulated for non-specific intravenous infusion)	Acute Myocardial Infarction (AMI)	Phase I program demonstrated safety, and statistically significant improvement in LVEF and FEV1, as well as fewer arrhythmic events, fewer ventricular contractions, and less required re-hospitalization in February 2008. Phase II (Protocal-403) is a 220-patient program designed to study Prochymal vs. placebo in patients post AMI with LVEF between 20% and 45%. Primary endpoint is safety, with key secondary endpoints of end systolic volume (ESV), change in LVEF, functional and quality of life assessments. Currently ongoing.
Advanced Cell Technology (ACTC)	Autologous Skeletal Myoblast (adult progenitor stem) cells	Congestive Heart Failure (CHF) - Ischemic Cardiomyopathy.	Phase I program demonstrated safety and initial signs of improved heart function leading to improvement in quality of life assessments. Currently planning phase II program in 160 patients with heart failure who are not eligible for angioplasty or coronary artery bypass surgery.
Athersys, Inc. (ATHX)	MultiStem (stem cells obtained from adult bone morrow or other non-embryonic sources, expanded on large scale for non-specific injection)	Acute Myocardial Infarction (AMI)	Phase I clinical trial to evaluate the safety of MultiStem administered via catheter to patients who have suffered an acute myocardial infarction reported positive results in July 2010. The data showed good tolerability, with no dose-limiting toxicities or significant changes to vital signs or allergic reactions, and no MultiStem related SAEs. Heart function analysis showed improvement in LVEF at 4 months post dose compared to baseline, vs. control.
Pluristem Therapeutics. (PSTI)	Placental expanded (PLX) cells (allogeneic adherent stromal cells obtained from the placenta after birth)	Peripheral Arterial Disease (PAD) – Critical Limb Ischemia (CLI)	Preclinical animal (mice) data suggests revascularization and neovascularity of the treated limb with intramuscular PLX-PAD. Currently in phase I/II program in patients with Grade III or IV Critical Limb Ischemia (CLI).

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SUMMARY RECOMMENDATION & VALUATION

Neutral Rating, With Positive Bias…

In July 2010 we initiated coverage of Aastrom Biosciences with a Neutral rating and $2.50 price target. Aastrom is pioneering the research effort on adult stem cells for therapeutic applications, specifically for the treatment of cardiovascular diseases such as critical limb ischemia (CLI) and dilated cardiomyopathy (DCM). The company has presented very encouraging proof-of-concept data on both indications over the past year.

The company's approach involves expansion of a patient's own stem and progenitor cells outside of the body to generate a cell product with significantly increased numbers of highly functional early-stage cells. These autologous cell products can then be used for the repair or regeneration of multiple human tissues. The company has developed a proprietary Tissue Repair Cell technology in which cells are derived from a small amount of bone marrow taken from a patient and expanded in culture to generate a unique cell mixture containing high doses of stem and progenitor cells. Due to the high number of stem and progenitor cells contained in a small volume, Aastrom's strategy seems particularly suitable for direct injection into remodeled myocardium.

…Two Potential Blockbuster Opportunities…

- For CLI, we expect that management will file its special protocol assessment (SPA) with the U.S. FDA in the third quarter 2010 for a pivotal phase III program to begin in 2011. We also expect that management will file for, and receive, FDA fast track designation for this potentially enormous market opportunity. CLI is the most severe form of peripheral artery disease (PAD) and affects approximately 1 million people in the U.S. each year. Patients living with CLI suffer from severe pain as a result of the neuropathy, tissue loss, and ischemia. In fact, CLI leads to an average of 160k major limb amputations each year. The mortality rate is high, at roughly 20% after only 6-months post-amputation, and 25% after 12-months. Therapeutic options are limited. Medications such as aspirin, statins, and clopidogrel (Plavix) are common first-line therapies for early-stage PAD, but once PAD progresses to the point of CLI, the only real options available to patients are surgical. Surgical procedures include percutaneous transluminal angioplasty, plaque excision, stenting, and bypass grafting. A therapeutic application, such as Aastrom's expanded autologous cell therapy is a potential billion-dollar product in our view. Interim phase IIb data from the company's RESTORE-CLI trial demonstrate statistically significant reductions in key endpoints, including amputation-free survival and time to first occurrence of treatment failure, as well as a trend toward significance in major amputations and wound healing. We expect management to present the full six-month results from all 86 patients in RESTORE-CLI in November 2010, potentially at the American Heart Association (AHA) meeting.

- DCM is a condition in which the heart becomes weakened and enlarged, and cannot pump blood efficiently. Causes of DCM are often varied, but most frequently is the result of damage to the myocardium produced by a variety of toxic, metabolic, or infectious (bacterial or viral) agents. There are an estimated 120k to 150k people living in the U.S. with DCM, with roughly 10,000 to 15,000 new cases each year. About one in three cases of congestive heart failure (CHF) is due to DCM. The 1-year mortality rate for a patient diagnosed with DCM is roughly 25%. It is a significant market opportunity given the lack of therapeutic treatment options. Artificial pacemakers and left ventricular assist devices (LVADs) may be used in patients with intra-ventricular conduction delay, and implantable cardioverter-defibrillators in those at risk of arrhythmia. However, these are generally viewed as bridge to heart transplantation surgery. Unfortunately, there are only about 2,200 heart transplants are done in the U.S. each year. That means of the estimated 150k NYHA Class 3 or 4 patients with dilation, over 95% will never get a transplant. Accordingly, DCM is an indication for which the U.S. FDA granted Aastrom an 'Orphan Drug' designation. Aastrom is currently studying the use of its expanded autologous cell therapy in mid-stage clinical trial for DCM called IMPACT-DCM. Interim results, presented in November 2009 at AHA, demonstrated the majority of patients treated with CRCs have shown improvements in their NYHA functional classification. Deterioration in NYHA class correlates to increased surgical procedure, including implantable pacemakers and cardioverter-defibrillators, and eventually heart transplantation. Complete results should become available early next year.

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The Market Leader for Cardiovascular Indications…

We view Aastrom Biosciences at the premier play for the application of adult stem cells for potential cardiovascular indications. While other stem cell companies such as Cytori Therapeutics (the market leader for cosmetic and reconstructive surgery) and Osiris Therapeutics (the market leader for inflammatory diseases) command higher market capitalizations, no other firm has as an advanced program for peripheral arterial disease or heart failure. Yet, despite the firm's advanced position for two potential billion-dollar "home run" indications, the market has yet to value Aastrom as a leader.

Company	Product	Market Cap
Cytori Therapeutics (CYTX)	Adipose-Derived Regenerative & Stem Cells (ADRC) obtained from the company's proprietary Celution System.	$218 million
BioHeart, Inc. (BHRT)	MyoCell SDF-1 (gene-modified autologous skeletal myoblast cells – precursors to muscle).	$8 million
Osiris Therapeutics, Inc. (OSIR)	Prochymal (mesenchymal stem cells processed and formulated for non-specific intravenous infusion).	$224 million
Advanced Cell Technology (ACTC)	Autologous Skeletal Myoblast (adult progenitor stem) cells.	$70 million
Athersys, Inc. (ATHX)	MultiStem (stem cells obtained from adult bone morrow or other non-embryonic sources, expanded on large scale for non-specific injection).	$56 million
Pluristem Therapeutics. (PSTI)	Placental expanded (PLX) cells (allogeneic adherent stromal cells obtained from the placenta after birth).	$24 million
NeoStem, Inc. (NBS)	Provides adult stem cell collection, processing, and storage services for healthy individuals to store their stem cells for personal therapeutic use.	$95 million
Opexa Therapeutics, Inc. (OPXA)	Personalized T-cell therapeutic vaccine (Tovaxin) derived from T-cells isolated from peripheral blood and expanded ex vivo.	$19 million
StemCells, Inc. (STEM)	Cell-based therapeutics (HuCNS-SC) for central nervous system disorders, and cell cultures and technologies for stem cell-based research.	$104 million
	Average Market Capitalization	$91 million
Aastrom Biosciences, Inc. (ASTM)	Autologous stem cell products derived from adult bone marrow for the treatment of cardiovascular diseases.	$43 million

Unfortunately, we expect that the market will continue to under-value Aastrom Biosciences over the near-term. Given the limited therapeutic treatment options available, the high risk nature of the trials, and the fact that Aastrom must pave the way itself, these are "show me" indications from a valuation standpoint to the Street. Plus, the market is skeptical of new therapeutic classes like stem cells, as well aware of the fact that Aastrom must find funding and sign development and commercialization partnerships at some point in the future. As a result, Aastrom must deliver before Wall Street will really start to pay attention.

That being said, what we have seen so far from RESTORE-CLI and IMPACT-DCM is very encouraging. In November 2010, perhaps at this year's AHA, we will see final data from RESTORE-CLI. This will be followed by six-month data from IMPACT-DCM in early 2011. These data, if positive, should convince Wall Street that Aastrom's cell therapy viable and approvable; and as a result, drive the shares significantly higher.

…Tough To Value…

We estimate peak sales in the CLI indication are in the area of $800 million in the U.S. We assume 10% market penetration in the 160,000 major amputations per year, with a cost of around $50,000 cellular therapy dose. The DCM breaks out in similar fashion, with peak sales at around $675 million based on135,000 patients, 10% market share, and a cost of $50,000 per dose. Upside exists based on the phase III data. Given the limited treatment options available for both patient groups, market share achievement far beyond 10% is plausible. For now we choose to be conservative.

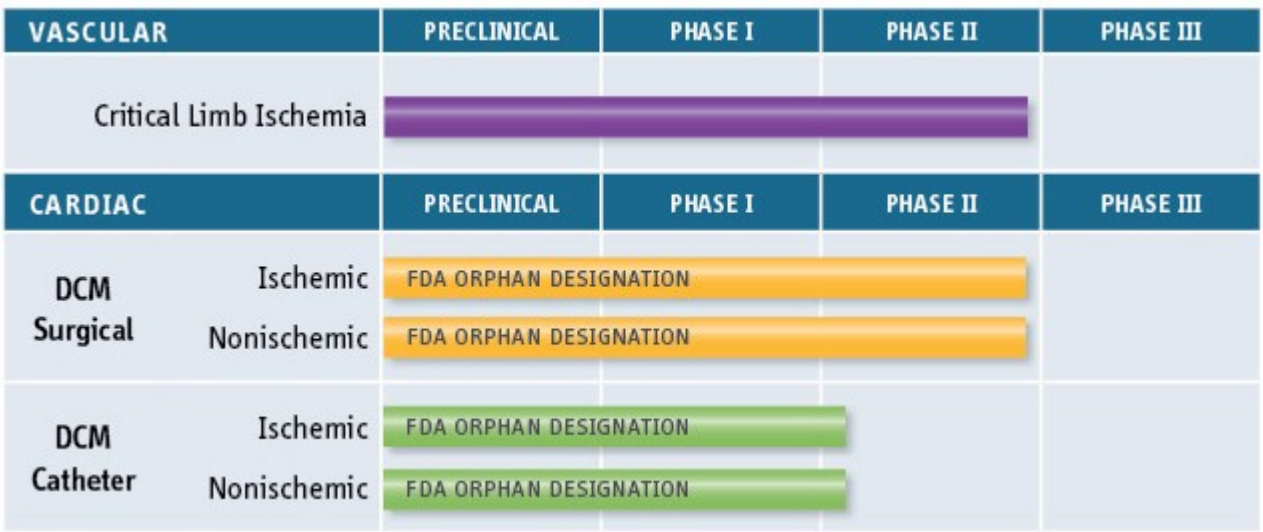
Management has not said much regarding the potential for commercialization partnerships in CLI or DCM. We expect that Aastrom will take its cell therapy development program through the biologic license application (BLA) filing for CLI. The size and scope of the partnership really depends on the phase III data, and potentially the FDA's response on the BLA. However, we can be sure that most large-cap pharmaceutical companies will be interested in a product with nearly $1 billion in peak sales potential. A partnership could be worth several hundred million, with over $100 million upfront to Aastrom. We point to Genzyme's development and commercialization partnership with Osiris Therapeutics in November 2008 for Prochymal: → $75 million upfront + $880 million in milestones + royalties on sales as an example for future cell therapy deals. The Genzyme-Osiris deal centered on Prochymal for GvHD and Crohn's disease, and offered another $500 million in upside for the opt-in on early-stage stem cell product, Chondrogen, for arthritis.

We easily envision a scenario where a pharmaceutical company pays Aastrom Bio server hundred million for the licensing of its cell therapy for CLI in 2012 or 2013, with upside for the DCM indication in 2014 or 2015, if the phase III data so warrants. Potential deals could looks as such:

- CLI: Project a $650 million total deal, plus royalties in 2012-2013. Peak sales at $800 million in 2018.
- DCM: Project a $600 million total deal, plus royalties in 2014-2015. Peak sales at$675 million in 2019.

If we apply a steep probability-adjustment (adjusted based on risk of phase III trials and probability of approval) and discount rate (based on time-value) on these deals, we arrive at a firm value of around $75 million. This equates to a price per share of around $2.50. The steep probability-adjustment discount will ease as additional positive data becomes available. Accordingly, Aastrom has significant upside based on the outcome of pivotal trials.

PIPELINE



Source: http://www.aastrom.com/ClinicalPrograms.cfm

MANAGEMENT PROFILE

Timothy M. Mayleben, Chief Executive Officer, President, and Director

Mr. Mayleben joined Aastrom as a member of the company's board of directors in June 2005. Previously he was an advisor to life science and healthcare companies through his advisory and investment firm, ElMa Advisors. He has also been president, COO and a director of NightHawk Radiology Holdings, Inc. Mr. Mayleben also served as COO of Esperion Therapeutics, where he led the raising of more than $200 million in venture capital and institutional equity funding and later negotiated the acquisition of Esperion by Pfizer in December 2003. He holds an MBA with distinction from the J.L. Kellogg Graduate School of Management at Northwestern University and a BA in business administration from the University of Michigan.

Ronnda L. Bartel, Ph.D., Chief Scientific Officer

Ronnda L. Bartel, Ph.D., joined Aastrom in 2006 and is responsible for research, development and manufacturing and engineering operations. Dr. Bartel has more than 20 years of research and product development experience and most recently was Executive Director, Biological Research at MicroIslet and Vice president, Scientific Development at StemCells Inc. Earlier in her career, she was Senior Principal Scientist, Cell Biology at Advanced Tissue Sciences and was involved in the development and approval of some of the first cell based products approved by the FDA. She has also worked as Senior Director, Science and Technology at SRS Capital, LLC evaluating life science investments and has also held positions in clinical development, drug delivery, business development and manufacturing. Dr. Bartel holds a Ph.D. in Biochemistry from the University of Kansas, completed postdoctoral work at the University of Michigan and received a B.A. in Chemistry and Biology from Tabor College.

Scott Durbin, Chief Financial Officer

Scott Durbin brings more than 15 years of healthcare-related banking, financial and corporate development experience to Aastrom. Formerly he was the COO and CFO of Prescient Medical, Inc., which develops diagnostic and therapeutic catheter-based medical devices for the treatment of severe coronary artery disease. While at Prescient, Mr. Durbin raised more than $60 million in private equity financing and helped advance the company through early-stage research, development and regulatory approval. Previously he served as a finance and corporate development consultant for Scios, Inc. (a Johnson & Johnson subsidiary) and Alteon, Inc. Prior to this consulting work, he was an investment banker with Lehman Brothers, Inc. where he completed more than $5 billion in financings and M&A transactions for life science companies. Mr. Durbin earned an MPH in health management from the Yale University School of Medicine & School of Management and a BS from the University of Michigan.

Sheldon A. Schaffer, Ph.D., Vice President, Corporate Development

Dr. Schaffer joined Aastrom in 2006 and is responsible for corporate and business development and intellectual property. He has more than 30 years of experience in life sciences and most recently was a business development consultant to a range of life science companies. Previously, Dr. Schaffer served as president and CEO of Inveresk Research, N.A., vice president of pharmaceutical development at DepoTech, and vice president of business development at Cholestech. Dr. Schaffer has also been a postdoctoral and teaching fellow at Harvard Medical School, holds a Ph.D. in chemistry from the University of Illinois and a BS in chemistry from the University of California, Berkeley.

Sharon Watling, PharmD, Vice President, Clinical and Regulatory

Sharon Watling joined Aastrom in February 2010 and is responsible for clinical development, clinical operations and regulatory affairs. Dr. Watling has over 12 years of experience in clinical development, with an emphasis on translational and early stage development, as well as development of clinical strategies. Her industry career started in late stage development within Warner-Lambert/Parke Davis and evolved while at Pfizer to include an early clinical leadership role in cardiovascular-metabolic diseases. Following Pfizer, she was Site Leader and Senior Director, Clinical Development at Metabasis, Inc. Most recently, she served as the Research and Development Strategy Leader at Cognigen Corporation. Dr. Watling received a Doctor of Pharmacy Degree from the University of Michigan College of Pharmacy.

PROJECTED FINANCIALS

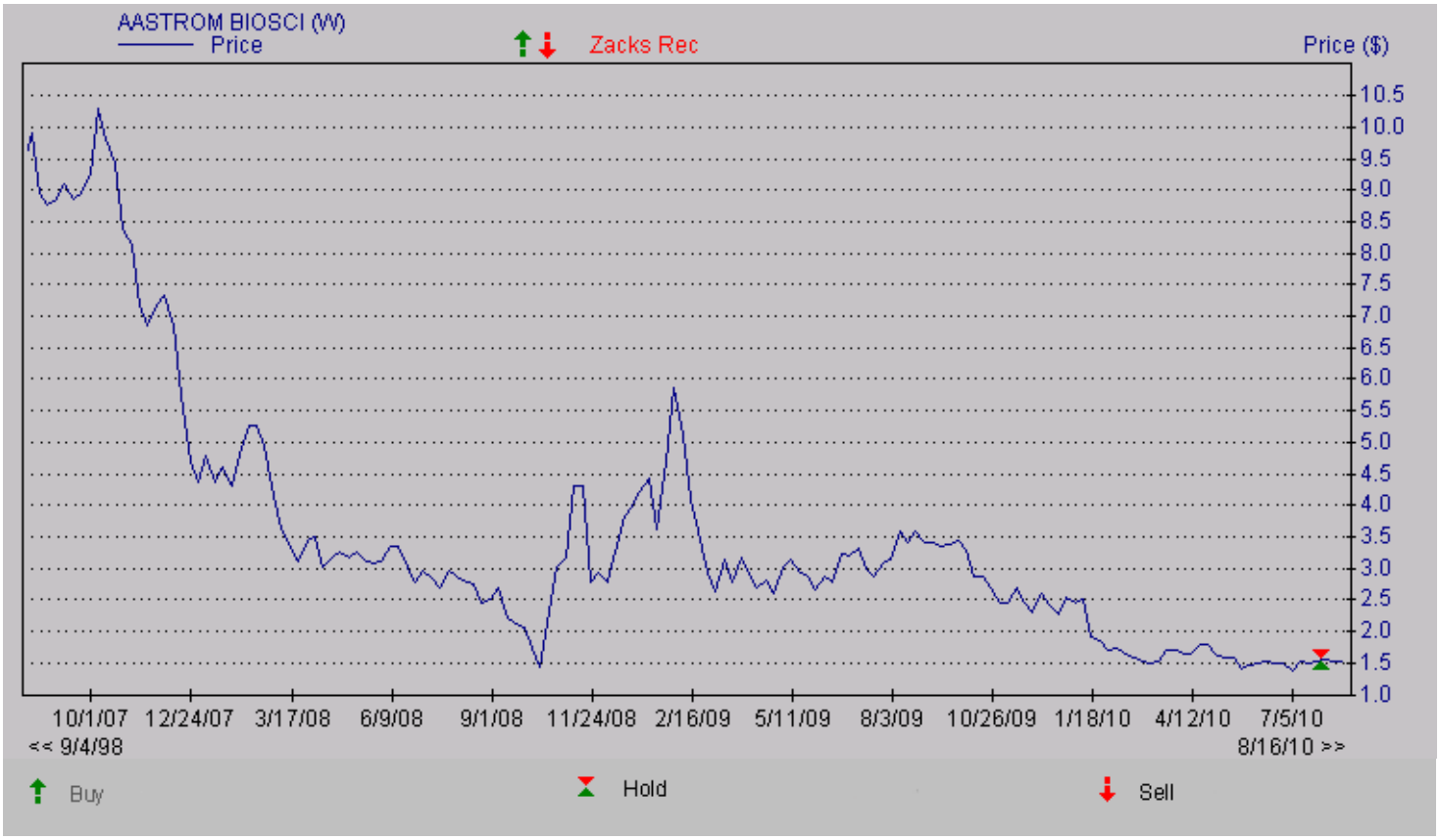
Aastrom Biosciences
Income Statement

Aastrom Biosciences	Jun-09	Jun-10	Sep-10	Dec-10	Mar-11	Jun-11	Jun-11	Jun-12	Jun-13	Jun-14
	2009 A	2010 A	Q1 E	Q2 E	Q3 E	Q4 E	2011 E	2012 E	2013 E	2014 E
R&D Agreements / Grants	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0.0**
YOY Growth	-	*0%*	-	-	-	-	*0%*	*0%*	*0%*	*0%*
Product Sales & Rentals	**$0.182**	**$0.089**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0.100**	**$0.100**	**$0.100**
YOY Growth	-	-	-	-	-	-	-	*#DIV/0!*	*0.0%*	*0.0%*
Total Revenues	**$0.182**	**$0.089**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0.100**	**$0.100**	**$0.100**
YOY Growth	*-65.1%*	*-51.1%*	-	-	-	-	*-100.0%*	*#DIV/0!*	*0.0%*	*0.0%*
Cost of Product Sales & Rentals	$0.112	$0.034	$0	$0	$0	$0	$0	$0.040	$0.040	$0.040
Product Gross Margin	*38%*	*0%*	-	-	-	-	*#DIV/0!*	*60%*	*60%*	*60%*
Research & Development	$11.289	$12.658	$3.500	$3.700	$3.800	$4.000	$15.000	$22.500	$25.000	$20.000
% R&D	*6202.7%*	*14222.5%*	-	-	-	-	*#DIV/0!*	*22500.0%*	*25000.0%*	*20000.0%*
Selling, General, and Admin	$4.950	$5.201	$1.550	$1.550	$1.600	$1.650	$6.350	$6.500	$6.750	$7.000
% SG&A	*2719.8%*	*5843.8%*	-	-	-	-	*#DIV/0!*	*6500.0%*	*6750.0%*	*7000.0%*
Operating Income	($16.169)	($17.804)	($5.050)	($5.250)	($5.400)	($5.650)	($21.350)	($28.940)	($31.690)	($26.940)
Operating Margin	*-8884.1%*	*-20004.5%*	-	-	-	-	*#DIV/0!*	*-28940.0%*	*-31690.0%*	*-26940.0%*
Other Income (Expenses)	$0.223	$0.075	$0.025	$0.025	$0.025	$0.025	$0.100	$0.120	$0.130	
Pre-Tax Income	($15.9)	($17.729)	($5.025)	($5.225)	($5.375)	($5.625)	($21.250)	($28.820)	($31.560)	($26.940)
Taxes & Other Charges	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	($15.946)	($17.729)	($5.025)	($5.225)	($5.375)	($5.625)	($21.250)	($28.820)	($31.560)	($26.940)
Net Margin	-	*-19920.2%*	-	-	-	-	*#DIV/0!*	*-28820.0%*	*-31560.0%*	*-26940.0%*
Reported EPS	**($0.89)**	**($0.72)**	**($0.18)**	**($0.18)**	**($0.19)**	**($0.19)**	**($0.74)**	**($0.90)**	**($0.93)**	**($0.75)**
YOY Growth	-	*-19.6%*	-	-	-	-	*3.4%*	*21.5%*	*3.1%*	*-19.4%*
FAS-123R Expense	$1.4	$0.5	$0.1	$0.1	$0.1	$0.1	$0.4	$0.5	$0.6	$0.7
Weighted Ave. Shares Out	17.9	24.7	28.5	28.6	28.7	28.9	28.7	32.0	34.0	36.0

Source: Zacks Investment Research, Inc. *Jason Napodano, CFA*

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