Zacks Small-Cap Research

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Jason Napodano, CFA
312-265-9421
jnapodano@zacks.com

scr.zacks.com
111 North Canal Street, Chicago, IL 60606

Aastrom Biosciences, Inc. (ASTM-NASDAQ)

ASTM: Strong Rational For Ixmyelocel-T In DCM, But Cash And Catalysts Lacking…

Current Recommendation	**Neutral**
Prior Recommendation	Outperform
Date of Last Change	10/05/2012
Current Price (05/09/13)	$0.59
Target Price	**$1.00**

UPDATE

Aastrom's stock is down 77% over the past 12 months, hitting a new 52-week low early in May on news of the $25 million S-1 filing. Yet, as noted above, once this filing is complete the company should have enough cash to fund operations to the ixCELL-DCM results in the second quarter 2015.

We are not changing our 'Neutral' rating on the stock. Despite optimism that Aastrom's ixmyelocel-T could be a $500 million or bigger drug for DCM, the company is lacking catalysts until the second quarter 2015. It will be a long hold from now until then, and with a $25 million financing under-way, better opportunities to buy-and-hold may emerge over the next several months.

SUMMARY DATA

52-Week High	**$2.56**
52-Week Low	**$0.52**
One-Year Return (%)	**-76.77**
Beta	**0.03**
Average Daily Volume (sh)	**301,259**
Shares Outstanding (mil)	**46**
Market Capitalization ($mil)	**$27**
Short Interest Ratio (days)	**3.37**
Institutional Ownership (%)	**9**
Insider Ownership (%)	**1**
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 2013 Estimate	**N/A**
P/E using 2014 Estimate	**N/A**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue

(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2012	0 A	0 A	0 A	0 A	0 A
2013	0 A	0 E	0 E	0 E	0 E
2014					0 E
2015					0 E

Earnings per Share

(EPS is operating earnings before non-recurring items)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2012	-$0.25 A	-$0.22 A	-$0.17 A	-$0.18 A	-$0.72 A
2013	-$0.15 A	-$0.08 E	-$0.05 E	-$0.04 E	-$0.29 E
2014					-$0.18 E
2015					-$0.19 E

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WHAT'S NEW

Quick Financial Review

On May 8, 2013, Aastrom Biosciences reported financial results for the first quarter 2013. The company did not reported any meaningful revenues in the quarter. Net loss for the quarter was $6.8 million, or 15 cents per share. The company exited the quarter with $9.2 million in cash and investments. Cash burn for the second quarter 2013 is expected to be between $4.5 million and $5.0 million.

We note that on April 29, 2013, the company filed a Form S1 registration statement with the U.S. SEC seeking to raise up to $25 million in cash through the offering of common stock via a fully-marketed public offering. Aastrom hopes to close the offering by the end of the second quarter 2013. If successful in raising a net $23+ million in cash, along with an estimated $4.5 million to still be on hand as of June 30, 2013 from the existing cash balance, the new balance of roughly $28 million should be enough to fund operations to the middle of 2015. We remind investors that results from the company's phase 2b ixCELL-DCM study are expected in the second quarter 2015.

ixCELL-DCM Takes Center Stage

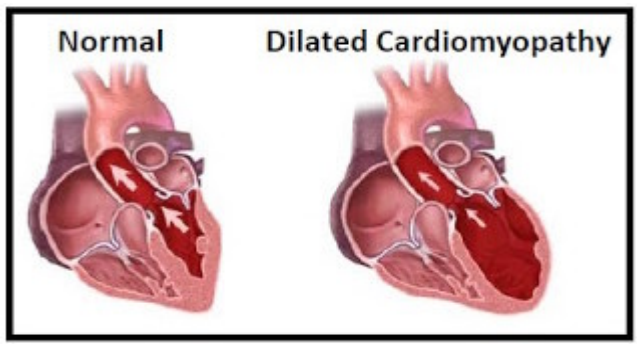
On April 19, 2013, Aastrom announced the first patient had been enrolled in the company's phase 2b ixCELL-DCM study. The phase 2b trial (NCT01670981) is a randomized, placebo-controlled program testing ixmyelocel-T via delivery through the MyoSTAR transendocardial catheter and NOGA mapping system in 108 ischemic DCM patients at around 30 sites all in the U.S. Aastrom plans to enroll patients with NYHA Class-III/IV ischemic DCM that have maximized their use of prescription therapeutics such as ACE inhibitors, ARBs, and beta-blockers, and device therapies, and are no longer candidates for further revascularization procedures such as angioplasty and bypass surgery. The typical patient will have very limited treatment options, and may be a candidate for placement of left ventricular assist devices (LVADs), or eventually heart transplantation.

The primary endpoint of the study will be major adverse cardiovascular events (MACE), with 80% powering for statistical significance. Secondary endpoints are expected to include cardio-pulmonary function through imaging, exercise capacity, 6-minute walk test, and safety. We note the biggest challenge for these patients in the marked reduction in exercise capacity. NYHA Class-III/IV patients may have dyspnea (shortness of breath) at rest and an inability to perform even minor physical activity.

We view this as a "registration quality" study, as the data should give Aastrom a clear sign on the profile of ixmyelocel-T before proceeding into a pivotal phase 3 trial. We expect 12 months to enroll, with top-line data expected in the second quarter 2015.

...DCM Backgrounder...

Approximately 5.5 million people in the U.S. suffer from heart failure and there are an estimated 550,000 new cases each year. Medical cost to treat these patients now total more than $25 billion annually, and are expected to triple in the next 20 years.



Dilated cardiomyopathy (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. According to the American Heart Association (AHA), there are an estimated 250k people living (prevalence) in the U.S. with DCM, with roughly 20,000 new cases (incidence) each year. Roughly 60% are of ischemic origin.

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 (source).

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. 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. The long-term costs are upwards of $225,000.

However, for patients with advanced disease who are refractory to medical therapy, cardiac transplantation is the only option. LVADs 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 2,800 heart transplants are done in the U.S. each year. Plus, the mortality rate after a LVAD remains high, at an estimated 50% after year 2. That means of the estimated 125,000 NYHA Class III or IV ischemic DCM 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.

We see DCM as an attractive market opportunity for Aastrom. DCM is an orphan indication, which not only protects Aastrom from direct cell therapy competition in the market for seven years after approval, but also allows for aggressive pricing and effective marketing through a small specialty cardiovascular sales force. If the phase 2b trial is successful, we believe ixmyelocel-T would qualify for Fast Track and Priority Review.

...Preclinical & Phase 2a Data...

Aastrom management believes there is strong scientific rational for testing ixmyelocel-T in DCM. Preclinical results have demonstrated that ixmyelocel-T significantly and reproducibly reduced cardiac tissue damage and had additional cardioprotective effects in relevant disease models. The cell mixture is comprised of multiple key effector cells, such as mesenchymal stromal cells and M2-like macrophages, proven to play a key role in tissue repair and generation that is not found in other cell therapies. M2-like macrophages are known to play a beneficial role in atherosclerosis, providing clear support for the company's efforts to investigate the impact of ixmyelocel-T on the underlying pathology of coronary artery disease.

We point investors to the company's recent presentation at the International Society of Cellular Therapy 2013 Annual Meeting as supportive evidence for ixmyelocel-T in this role. Last June 2012, at the 18th Annual International Society for Cellular Therapy Meeting, the company presented a poster showing that ixmyelocel-T protected the heart from damage in a murine model of heart failure. Most recently, the company presented a poster at the AHA Arteriosclerosis, Thrombosis and Vascular Biology 2013 Scientific Sessions, May 2013, showing that ixmyelocel-T significantly increased nitric oxide (NO) production, reduced oxidative stress and inflammation, and prevented endothelial cell apoptosis. This data suggest that ixmyelocel-T may promote therapeutic effects in the treatment of vascular disease associated with endothelial dysfunction.

In May 2012, Aastrom presented the 12-month follow up results from the phase 2a dilated cardiomyopathy (DCM) study at the Society for Cardiovascular Angiography and Interventions (SCAI) Scientific Sessions. The data presentation, entitled "Safety and Efficacy of Ixmyelocel-T, An Expanded Patient-Specific Mixed Cell Therapy, in Dilated Cardiomyopathy" highlighted injection of Aastrom's expanded multicellular therapy using the NOGA / MyoSTAR transendocardial catheter.

We remind investors that the phase 2a program enrolled 22 patients with ischemic or idiopathic DCM that had no other options available for revascularization (meaning the next available options are surgical – a heart transplant or LVAD). The study took place at three centers all in the U.S. Patients were randomized 2:1 to receive Ixmylocel-T + standard of care vs. standard of care alone. The primary endpoint of the study was safety, with a planned interim analysis conducted when all subjects completed 6 months. There was also a planned final analysis conducted when all subjects completed 12 months, with control patients being able to crossover to the Ixmyelocel-T group after 6 months. As noted above, a total of 22 subjects were randomized. One subject in the control with idiopathic DCM withdrew prior to day-1 so was not included in the safety assessment. One subject in the ixmyelocel-T group with idiopathic DCM discontinued due to heart failure on day 322.

Investigators concluded that transendocardial injection of Ixmyelocel-T was well tolerated in patients with DCM. In fact, management noted that the tolerability of the procedure was significantly better than the previous study (IMPACT-DCM) conducted by Aastrom in which patients received the cells via a minithoracotomy. Adverse events were similar between the Ixmyelocel-T and control group, a clear positive considering the control group underwent no transendocardial injection procedure. A total of 14 out of 15 (93%) of the ixmyelocel-T patients completed the trial versus 5 of the 7 (83%) on the control.

Secondary objectives were included to investigate signs of efficacy, including:

- Major Adverse Cardiovascular Events (MACE) – The key clinical endpoint
- Cardiopulmonary stress and 6-minute walk – Key functional endpoints
- Echo and left-ventricle ejection fraction (LVEF) – Key structural endpoints
- New York Heart Associate (NYHA classification) – Subjective / Quality of Life endpoints

Proof-of-Concept was clearly evident by analyzing the data. Given the small size of the trial, no results are statistically significant, but the signs point to a reduction in MACE and improvement in quality of life measures with Ixmyelocel-T. Also, similar to the IMPACT-DCM results, the data shows an improved outcome for the ischemic DCM patients far greater than for the idiopathic DCM patients. We believe that efficacy observations related to structural and functional end points including major adverse cardiovascular events (MACE), New York Heart Association (NYHA) functional classification, 6-minute walk distance were consistent with improved function of impaired myocardium.

The key clinical endpoint was MACE. Below (Figure-1) is a graphical representation of the Time to First Occurrence of MACE. The results show an observational benefit in favor of the Ixmyelocel-T group, although not statistically significant due to the small number of patients (n=19) completing the study. The data in Figure-2 shows the clear separation of benefit for patients with ischemic DCM verses idiopathic DCM.

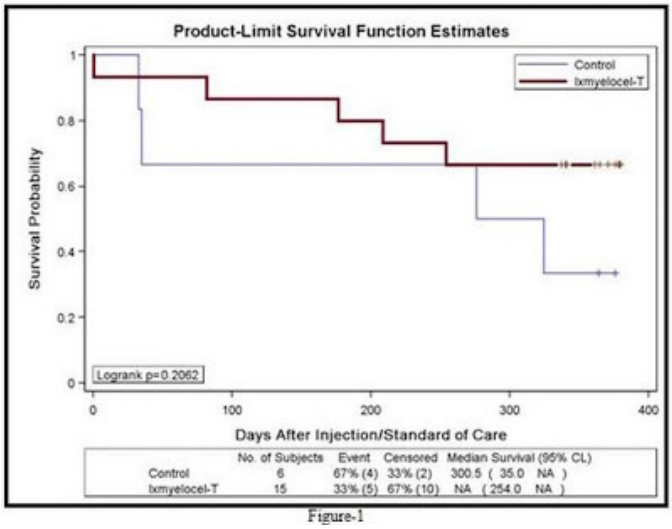


Figure-1

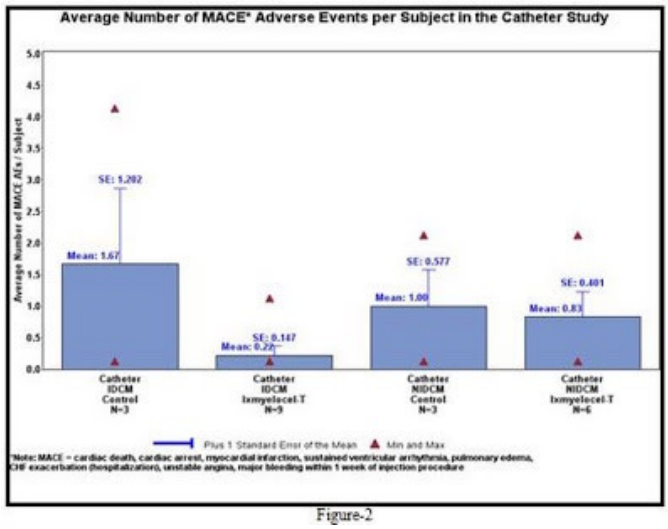


Figure-2

We believe the data above from both the IMPACT-DCM and the Cather-DCM studies, as well as the preclinical animal model data, provides excellent proof-of-concept for ixmyelocel-T in ischemic DCM. This is clearly a larger market opportunity for the company, and will cost around 1/3rd of the phase 3 CLI study. We think the opportunity to partner in DCM is high. Aastrom is going after a subset of NYHA Class III / IV patients that have progressed to DCM. We believe this patient population is an excellent fit for the company's autologous cell therapy where safety and mechanism of action is paramount.

Given a potential population of 150,000 patients seeking an alternative treatment option, we see Aastrom's ixmyelocel-T as a potential $500 million opportunity. We arrive at this opportunity as such:

- Approximately 125,000 ischemic DCM patients in the U.S.
- 5% market penetration for ixmyelocel-T at a cost of $75,000 per treatment
= ~ $500 million U.S. sales

PROJECTED FINANCIALS

Aastrom Biosciences
Income Statement

Aastrom Biosciences	Dec-11	Dec-12	Mar-13	Jun-13	Sep-13	Dec-13	Dec-13	Dec-14	Dec-15
	2011 A	2012 A	Q1 A	Q2 E	Q3 E	Q4 E	2013 E	2014 E	2015 E
R&D Agreements / Grants	**$0**	**$0.021**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	*0%*	*0.0%*	-	-	-	-	*0%*	*0%*	*0%*
Product Sales	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	*0.0%*	*0.0%*	-	-	-	-	*0.0%*	*0.0%*	*0.0%*
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	-	-
Cost of Product Sales & Rentals	$0	$0	$0	$0	$0	$0	$0	$0	$0
Product Gross Margin	-	-	-	-	-	-	-	-	-
Research & Development	$21.3	$26.0	$5.5	$4.0	$3.2	$3.0	$15.7	$12.5	$15.0
% R&D	-	-	-	-	-	-	-	-	-
Selling, General, and Admin	$7.7	$7.8	$1.6	$2.0	$1.4	$1.1	$6.1	$5.0	$5.5
% SG&A	-	-	-	-	-	-	-	-	-
Operating Income	($29.1)	($33.8)	($7.2)	($6.0)	($4.6)	($4.1)	($21.9)	($17.5)	($20.5)
Operating Margin	-	-	-	-	-	-	-	-	-
Other Income (Expenses)	$9.4	$4.3	$0.4	$0.5	$0.4	$0.3	$1.6	$1.2	$1.1
Pre-Tax Income	($19.7)	($29.5)	($6.8)	($5.5)	($4.2)	($3.8)	($20.3)	($16.3)	($19.4)
Taxes	$0	$0	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	($19.7)	($29.5)	($6.8)	($5.5)	($4.2)	($3.8)	($20.3)	($16.3)	($19.4)
Net Margin	-	-	-	-	-	-	-	-	-
Reported EPS	**($0.51)**	**($0.72)**	**($0.15)**	**($0.08)**	**($0.05)**	**($0.04)**	**($0.29)**	**($0.18)**	**($0.19)**
YOY Growth	-	-	-	-	-	-	-	-	-
Weighted Ave. Shares Out	38.6	41.2	44.9	70.0	85.0	85.0	71.2	90.0	100.0

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

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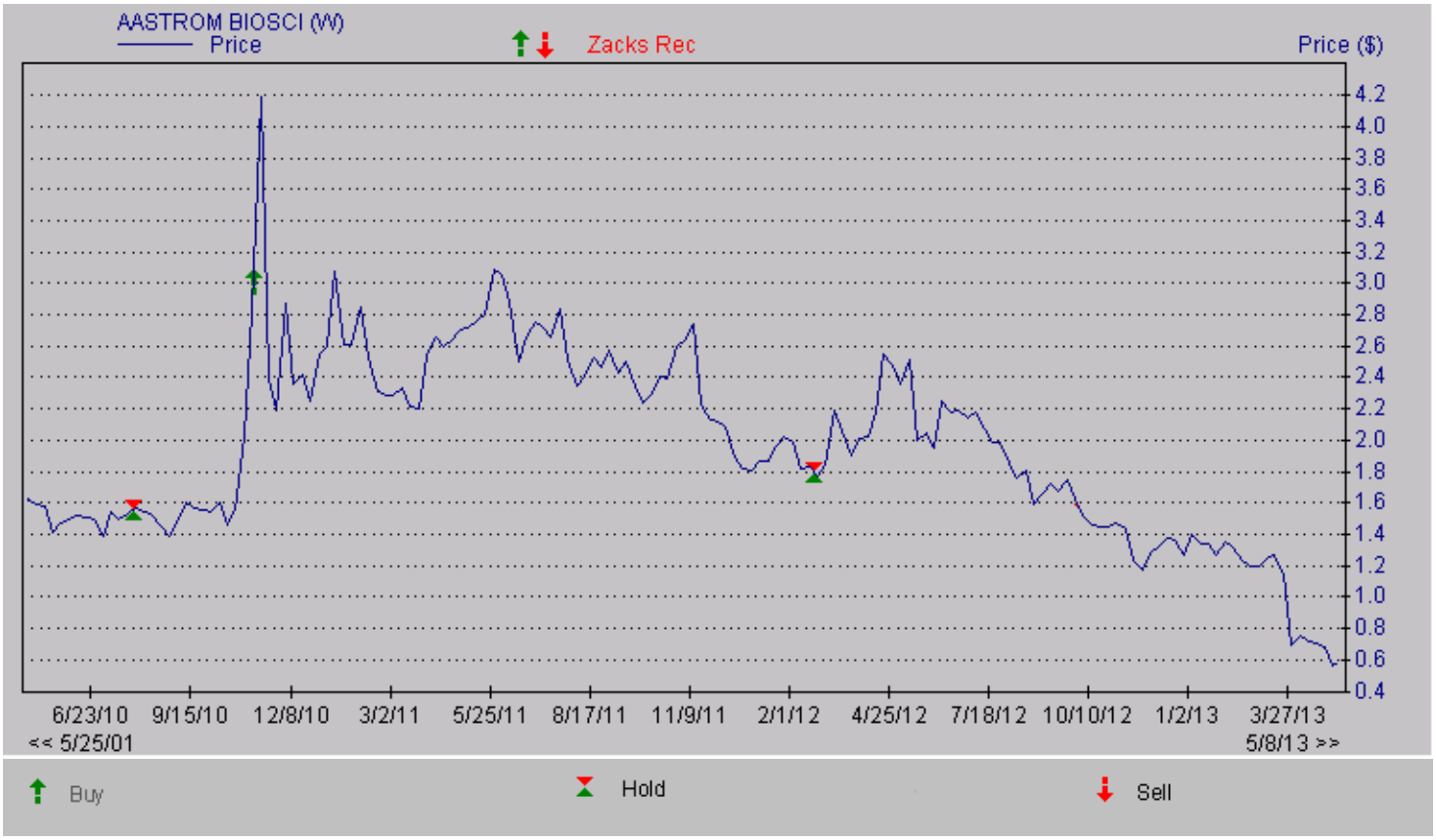

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