Zacks Small-Cap Research

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Aastrom Biosciences, Inc. (ASTM-NASDAQ)

ASTM: Cash Crunch Keeps Us On The Sidelines, For Now…

Current Recommendation	**Neutral**
Prior Recommendation	Outperform
Date of Last Change	10/05/2012
Current Price (03/18/13)	$1.31
Target Price	**$2.50**

UPDATE

We continue to rate shares of Aastrom Bio 'Neutral'.

Although we believe the shares remain an attractive long-term investment in the biotech sector, we see a number of issues that are expected to continue to weigh on the shares over the near-term. These issues include: the slower-than-expected enrollment in phase 3 REVIVE, the need for capital at some point in the second half of the year, or the use of the ATM.

Accordingly, we see the stock trending side-ways for the better part of the next year; thus a more neutral position with respect to the stock price is warranted.

SUMMARY DATA

52-Week High	**$2.64**
52-Week Low	**$1.15**
One-Year Return (%)	**-37.86**
Beta	**0.13**
Average Daily Volume (sh)	**484,309**
Shares Outstanding (mil)	**44**
Market Capitalization ($mil)	**$56**
Short Interest Ratio (days)	**9.06**
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 E	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	-$0.18 E	-$0.19 E	-$0.19 E	-$0.17 E	-$0.72 E
2014					-$0.61 E
2015					-$0.64 E

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WHAT'S NEW

Financial Results

On March 18, 2013, Aastrom Biosciences reported financial results for the fourth quarter and full year ended December 31, 2012. The company reported negligible revenues of $0.019 million in the fourth quarter 2012. Revenues for the full year 2012 totaled a similar negligible amount of $0.021 million, all derived from the government's Qualifying Therapeutic Discovery Project. We do not anticipate any meaningful revenues in 2013, a deal for the company's ixmyelocel-T notwithstanding.

Net loss for the fourth quarter totaled $7.9 million, or $0.18 per share. Net loss in the fourth quarter was driven by $6.0 million in R&D and $1.6 million in SG&A. SG&A was essentially in-line with expectations, but R&D was meaningfully lower than expectations, most likely the result of slower-than-anticipated enrollment in the company's phase 3 REVIVE study and delays in starting the company's phase 2b ixCELL-DCM clinical trial. The company also recorded a net gain of $1.0 million associated with the change in fair value of warrant liability and a $1.2 million expense for the accretion of convertible preferred stock during the fourth quarter 2012. For the full year 2012, Aastrom reported a net loss of $33.5 million, or $0.81 per share. Net loss was driven by $26.0 million in R&D and $7.7 million in SG&A.

Operating burn in the fourth quarter was approximately $7.5 million, consistent with management's guidance. As of December 31, 2012, Aastrom reported a cash position of $13.64 million. We remind investors that Aastrom raised net proceeds of approximately $37.6 million back in March 2012 through the issuance of 12,308 shares of Series B-1 non-voting convertible preferred stock to Eastern Capital. During the fourth quarter 2012, the company raised approximately $0.27 million through use of the company's At the Market sales agreement (ATM) with MLV, LLC. The ATM was set into place back in July 2011 for aggregate proceeds up to $20.3 million. Subsequent to the close of the fourth quarter, Aastrom raised net proceeds of $2.38 million through issuance of shares through the ATM agreement.

Operating burn for the first quarter 2013 is expected to be roughly $7.0 million. Thus, we expect the company to report approximately $9.0 million in cash as of March 31, 2013. We find this to be sufficient to fund operations into the third quarter 2013, assuming no additional use of the ATM. However, this seems unlikely. In fact, we would not be surprised to see management use the rest of the outstanding ATM – approximately $17.6 million – to fund operations into 2014. By that time, enrollment in both REVIVE and ixCELL-DCM should be progressing to the point where the company can reassess the status of each and begin to move deeper into partnering discussions pending the outcome of either or both studies. A partnership notwithstanding, we estimate the company needs in the area of $40 million to fund operations to data for both programs.

New CEO

On March 6, 2013, Aastrom announced it had hired Dominick C. Colangelo, Esq. as the company's new President and CEO. Interim CEO, Dan Orlando, will return to his role as the company's Chief Commercial Officer. Mr. Colangelo joins Aastrom with more than twenty years of executive management and corporate development experience in the biopharmaceutical industry, including almost a decade with Eli Lilly & Co. Most recently, he was president and CEO of Promedior, Inc., a clinical-stage biotechnology company developing protein therapeutics for the treatment of fibrovascular diseases. On March 18, 2013, Aastrom registered 5.0 million shares of common stock under the company's Omnibus Incentive Plan for Mr. Colangelo.

Phase 3 REVIVE Update

On February 29, 2012, Aastrom Bio announced it had begun patient recruitment in its phase 3 clinical trial, REVIVE (NCT01483898), designed to assess the efficacy and safety of ixmyelocel-T in the treatment of patients with critical limb ischemia (CLI). REVIVE will be conducted at roughly 100 sites in the U.S. and seeks to enroll 594 CLI patients who vascular surgeons have "low confidence" in revascularization. Enrollment criteria also stipulate that the patient must have existing tissue loss due to ischemia. REVIVE will be the largest randomized, double-blind, placebo-controlled, multicenter study ever conducted in patients with CLI, larger than Sanofi's failed phase 3 TAMARIS study conducted in 525 patients.

Patients will be followed for a total of 18 months, including 12 months from randomization for efficacy and an additional six months for safety. The primary endpoint of REVIVE is amputation-free survival at 12 months (AFS-12). The trial is being conducted under a Special Protocol Assessment (SPA) from the U.S. FDA. REVIVE has also been granted Fast Track designation for CLI. Secondary endpoints include adverse events at 18 months, wound closure at 12 months, and incidence of major adverse cardiac events (MACE), including myocardial infarction, chest pain hospitalization, or stroke.

...Slow Enrollment...

On May 9, 2012, Aastrom noted the first patient had been enrolled in the program. On the company's second quarter update call on August 7, 2012, Aastrom noted that 10 patients had been enrolled. On the third quarter call on November 8, 2012, the number grew to only 26 patients. Yesterday, on March 18, 2013, we learned enrollment stood at only 40 patients to date. This despite nearly 70 clinical sites online.

Priority number one of new CEO, Nick Colangelo, is the find a way to speed enrollment in REVIVE. Accordingly, the company has made a number of changes it believes will increase enrollment momentum in the near future. These changes include:

- ✓ Adding clinical sites. The original protocol called for enrolling patients at approximately 80 sites around the U.S. Management is now open to the idea of enrolling up to as many as 120 sites; although, the company believes the final number will be just above 100, with an emphasis on VA hospitals and community clinics rather than large academic centers. We believe moving away from large academic centers does two things for Aastrom. Firstly, it potentially reduces competition from competing technologies and therapeutics for the treatment of CLI, as most companies seek high-profile academic centers as anchors to their clinical programs. Second, it potentially moves enrollment away from vascular surgeons willing to try repeated vascularization procedures with little push-back on reimbursement to more cost-conscious centers willing to try a new therapeutic candidate sponsored via a clinical trial.

- ✓ Changing the nomenclature around the enrollment criteria. This includes dropping the previous "no option" term for one of "low confidence in revascularization". Aastrom is also getting away from the Rutherford-5 classification and moving to simpler terminology such as "confirmed tissue loss". An issue for the company over the past 13 months has been rejecting patients for enrollment because they are too far gone. Aastrom is still looking for no option patients, but not ones that are ready for amputation on day-1.

- ✓ Expanding the criteria to include larger wound sizes and more significant aortic iliac disease, as well as establishing broader immune therapy allowance and parallel cancer screening and higher TcP02 at baseline. This should help facilitate patient referrals to the program and allow the adjudication committee to accept patients that might be outstanding candidates for ixmyelocel-T that have been excluded in the past. If applied retrospectively, management believes enrollment would be 10-15% higher today, which is not monumental, but we see any step forward is a sign of progression at this stage.

Management made it clear on the call yesterday that none of the changes above have a material impact on either the statistical powering assumptions for the trial or the SPA agreement. In fact, Aastrom worked closely with the U.S. FDA on the protocol adjustments and noted on the call that all changes have been confirmed with the FDA. The new language is currently being sent to the clinical sites and management expects little delay before full implementation. In fact, guidance is that all sites should be up and enrolling patients under the new protocol adjustments by May 2013. Chronic kidney disease and end-stage renal disease will remain an exclusion criteria, and may serve as the basis for a small (n=20) separate study once REVIVE has been completed.

We have made little adjustments to our assumptions for the outcome of the study. The trial is 90% powered to show superiority of ixmyelocel-T over the control (no cells). Management used an assumed treatment effect of 36% to design the trial (12% numerical separation). We remind investors that in the phase 2b RESTORE study, ixmyelocel-T showed a 62% risk reduction vs. the control (p=0.0032). For the powering assumptions for REVIVE, management used an event rate for the control group of 34.5%, while expecting that ixmyelocel-T will come in around 22.2%.

We think ixmyelocel-T works. Therefore, the biggest risk we see with REVIVE is control group doing better than management's assumption, which was based on the TAMARIS and RESTORE-CLI studies. Aastrom will have a blinded interim update after the first 297 patients have been enrolled in REVIVE and completed the 6 month follow-up. Management can add patients to the trial based if the overall blinded data is showing an event rate lower than expectations. An overall event rate lower than expect could mean the control is doing better, the treatment group is doing better, or both are doing better than the powering assumptions. We like the fact that management has baked in this blinded look after 297 patients; it provides the ability to enhance the power of REVIVE if necessary. We expect this to take place in 2015.

We also note at the data safety monitoring board (DSMB) will be monitoring the trial with unblinded data. The DSMB can stop the trial at any time for safety or efficacy reasons. Efficacy reasons can include futility, or clear statistical separation prior to enrolling the 594 patients.

Results from the phase 2b RESTORE-CLI study give us confidence in the outcome of REVIVE. Full data from RESTORE-CLI was published in the Journal of Molecular Therapy in March 2012 (doi:10.1038/mt.2012.52). We estimate there are approximately 250,000 patients in the U.S. that are ideal candidates for Aastrom's ixmyelocel-T product for CLI. We believe the product can be effectively priced at $40,000 per treatment, given the high both direct and indirect cost of amputation. We arrive at a peak U.S. market opportunity for ixmyelocel-T at around $500 million given the following assumptions:

There are approximately 10-12 million Americans with PAD.

- 10% have progressed to critical limb ischemia (CLI)
  - 25% are candidates for ixmyelocel-T (i.e. "low confidence / no option")
- That's ~ 250,000 patients
  - 5% market penetration for ixmyelocel-T at a cost of $40,000 per treatment
- ~ $500 million U.S. sales

Phase 2b ixCell-DCM Finally Underway

Late 2012, Aastrom met with the FDA to outline the design and necessary endpoints for a phase 2b study. Patient screening has begun and the first patients should be enrolled soon in the phase 2b ixCELL-DCM (NCT01670981) study. The trial is a randomized, placebo-controlled program using the MyoSTAR transendocardial catheter and NOGA mapping system, seeking to enroll about 108 ischemic DCM patients at around 30 sites all in the U.S. We note the original plan was to seek enrollment at only 20 sites, but the company recently expanded the number of sites to 30 in an effort to speed enrollment along.

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 view this as a "registration quality" study, as the data should give Aastrom – and potential partners – a clear sign on the profile of Ixmyelocel-T before proceeding into phase 3. We expect 12 months to enroll, with top-lie data expected early 2015.

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.

There are an estimated 250k people living (prevalence) in the U.S. with DCM, with roughly 20,000 new cases (incidence) each year. Roughly 65% 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.

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.

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. 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 remind investors that the FDA has granted Orphan Drug designation to Aastrom for use of its ixmyelocel-T in patients with DCM.

Given a potential population of 125,000 potential 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:

There are 125,000 patients in the U.S. with ischemic DCM

- 5% market penetration for ixmyelocel-T at a cost of $75,000 per treatment
- ~ $500 million U.S. sales

Recommendation

We currently rate shares of Aastrom Bio 'Neutral'. Our concerns over the slow enrollment to date in RENEW and the need for cash either through usage of the ATM or a secondary offering keep us on the side-lines. That being said, we encourage investors to keep an eye on the story because if the changes in lexicon and nomenclature to REVIVE actually do work to accelerate patient enrollment, both investor and partner interest in Aastrom could soar.

We would love to see Aastrom form a development and commercialization partnership with a larger pharmaceutical company in 2013. However, absent that news, investors should be cautious with establishing a full position. We do believe the stock remains attractively valued for long-term investors even at today's "pre-financing" price, but catalysts are lacking and we may not see the acceleration in enrollment to REVIVE until the second half of the year. We are also watching to see how Aastrom manages its financial position and burn ahead of any potential clinical trial enrollment surge. Our DCF model, largely based on partnering both for CLI and DCM given the peak U.S. market opportunity outlined above for both drugs, yields a price of roughly $2.50 per share, but use of the ATM could keep a lid on the shares despite the already depressed valuation.

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 E	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	$6.1	$6.5	$7.0	$7.5	$27.1	$30.0	$35.0
% R&D	-	-	-	-	-	-	-	-	-
Selling, General, and Admin	$7.7	$7.8	$1.7	$1.8	$1.9	$2.0	$7.4	$8.0	$8.5
% SG&A	-	-	-	-	-	-	-	-	-
Operating Income	($29.1)	($33.8)	($7.8)	($8.3)	($8.9)	($9.5)	($34.5)	($38.0)	($43.5)
Operating Margin	-	-	-	-	-	-	-	-	-
Other Income (Expenses)	$9.4	$4.3	($0.5)	($0.5)	($0.5)	($0.5)	($2.0)	($1.5)	($1.0)
Pre-Tax Income	($19.7)	($29.5)	($8.3)	($8.8)	($9.4)	($10.0)	($36.5)	($39.5)	($44.5)
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)	($8.3)	($8.8)	($9.4)	($10.0)	($36.5)	($39.5)	($44.5)
Net Margin	-	-	-	-	-	-	-	-	-
Reported EPS	**($0.51)**	**($0.72)**	**($0.18)**	**($0.19)**	**($0.19)**	**($0.17)**	**($0.72)**	**($0.61)**	**($0.64)**
YOY Growth	-	-	-	-	-	-	-	-	-
Weighted Ave. Shares Out	38.6	41.2	45.0	47.0	50.0	60.0	50.5	65.0	70.0

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

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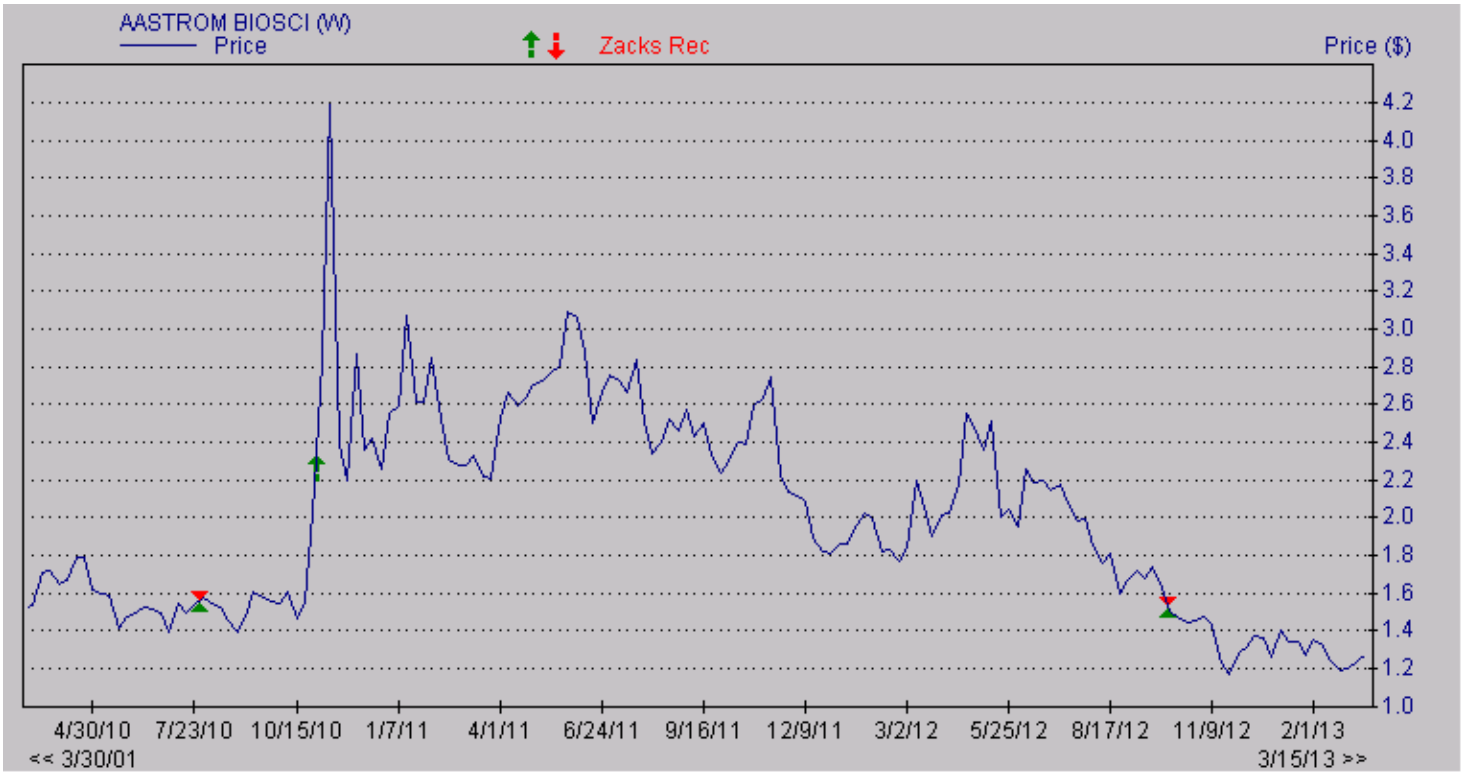

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