Zacks Equity Research

November 18, 2010
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Aastrom Biosciences, Inc. (ASTM-NASDAQ)

ASTM: No Change To Our Thesis Following The RESTORE-CLI Data...

Current Recommendation	**Outperform**
Prior Recommendation	Neutral
Date of Last Change	11/08/2010
Current Price (11/18/10)	$2.57
Target Price	**$5.00**

UPDATE

Aastrom Bio shares will most likely be under significant selling pressure the next few days as the excitement bubble bursts following the 2nd interim update from RESTORE-CLI. We view this as typical biotech trading. In the long-run, we are still very comfortable with Aastrom's position. We are not spooked by the data from RESTORE-CLI at all. This was a small trial will low statistical powering that accomplished its goal – establish proof-of-concept and position the company to enter a phase III registration program. We would be buyers of Aastrom's stock on weakness relating to the RESTORE-CLI data or the impending cash raise. Our NPV calculations peg Aastrom fairly-valued at roughly $5 per share – market capitalization of $140 million.

SUMMARY DATA

52-Week High	**$4.20**
52-Week Low	**$1.34**
One-Year Return (%)	**71.01**
Beta	**-0.06**
Average Daily Volume (sh)	**3,054,582**
Shares Outstanding (mil)	**28**
Market Capitalization ($mil)	**$119**
Short Interest Ratio (days)	**1.30**
Institutional Ownership (%)	**14**
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 2011 Estimate	**N/A**
P/E using 2012 Estimate	**N/A**
Zacks Rank	**3**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**
Zacks Rank in Industry	**72 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 A	0 E	0 E	0 E	0 E
2012					0 E
2013					0 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	-$0.21 A	-$0.21 E	-$0.23 E	-$0.27 E	-$0.92 E
2012					-$1.00 E
2013					-$0.97 E

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

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WHAT'S NEW

RESTORE-CLI Update

On November 18, 2010 at the VEITHsymposium satellite event in NYC, Dr. Richard Powell, principal investigator for the RESTORE-CLI program, presented a second interim update from the trial. The data included an update from an additional 26 patients, 72 in total, who completed the study.

…Backgrounder on RESTORE-CLI…

RESOTRE-CLI was initiated in April 2007. The trial 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.

RESTORE-CLI completed enrollment at 86 patients across 18 clinical sites in March 2010. In June 2010, Aastrom reported the first interim results from RESTORE-CLI at the annual meeting for the Society for Vascular Surgery. Data included 46 patients at the 6 month timeframe and 30 patients at the 12 month timeframe. The results from the second interim update on 72 patients were presented at the VEITHsymposium satellite event in November 2010. The two key points were as follows:

On Time To Treatment Failure…

Efficacy Assessment on ITT Population – 1st Interim

Parameter	TRC (n=32)	Control (n=14)	
Amputation	25%	43%	
De Novo Gangrene	16%	14%	
Doubling in Wound Size	19%	36%	
All Cause Mortality	3%	7%	
Treatment Failure	41%	79%	*p = 0.0053*

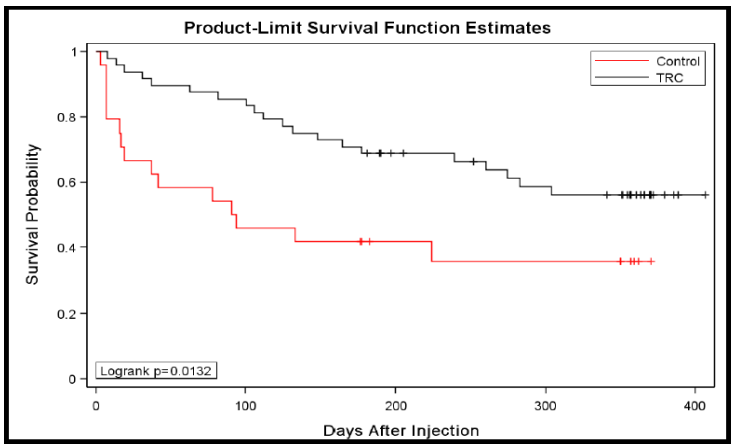
Efficacy Assessment on ITT Population – 2nd Interim

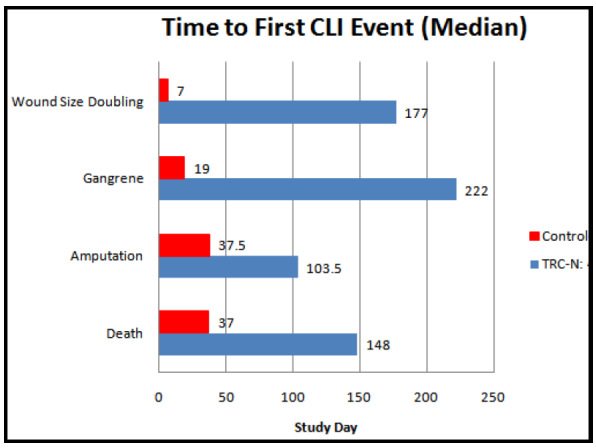
Parameter	TRC (n=16)	Control (n=10)	
Amputation	13%	0%	
De Novo Gangrene	6%	30%	
Doubling in Wound Size	19%	20%	
All Cause Mortality	13%	0%	
Treatment Failure	42%	63%	*p < 0.05*

Efficacy Assessment on ITT Population – TOTAL

Parameter	TRC (n=48)	Control (n=24)	
Amputation	21%	25%	
De Novo Gangrene	13%	21%	
Doubling in Wound Size	19%	29%	
All Cause Mortality	6%	4%	
Treatment Failure	42%	63%	*p = 0.0132*

Results for the primary endpoint of the phase 2b program were statistically significant for Time to Treatment Failure at p = 0.0132. The graph below shows the clear separation between TRC and the control for the entire population. The bar chart breaks down the individual components of Treatment Failure, where we see that each was meaningfully in-favor of TRC vs. the control.





Conclusion: The Time to Treatment Failure composite endpoint was clearly a success in RESTORE-CLI. The p-value of 0.0132 is incredibly strong considering only 72 patients were included. We would have liked to see better data with respect to "Death" and "Amputation", but these are things we expect will continue to separate upon the final analysis of the program expected in May 2011.

On Amputation Free Survival…

Efficacy Assessment on ITT Population – 1st Interim

Parameter	TRC (n=32)	Control (n=14)	
Amputation Free Survival	78%	50%	*p = 0.0376*

Efficacy Assessment on ITT Population – TOTAL

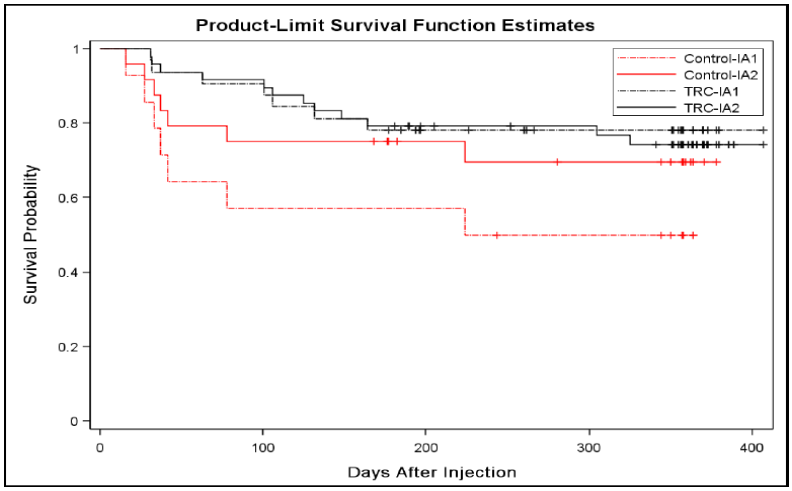
Parameter	TRC (n=48)	Control (n=24)	
Amputation Free Survival	75%	71%	*p = 0.5541*

This is the key endpoint in the eyes of the U.S. FDA. This is what Aastrom will design the upcoming phase III to detect. The results from RESTORE-CLI show a favorable trend, but failed to meet statistical significance. We believe this was due to a number of factors. Mainly, the control group at the backend of the trial responded significantly better than expected. Some reasons why:

- Excitement from the medical community grew significantly following the 1st interim update. It is possible that patients received a significant step-up in quality-of-care in-between the 1st and 2nd analysis. The step-up in medical care could have reduced the event rate.

- Patients may have skewed a little "less sick" as the trial completed enrollment. There is nothing mechanistically speaking that would cause TRC to not work in this population, but a less sick population will certainly have less events (MACE, amputation, death) in a 12-month time period. Management noted that of the 10 new control patients that were added between the 1st and 2nd analysis, there were no events during months 7-12. Just 2 or 3 events, which you would assume given the ~30% net event rate, would have made the this endpoint statistically significant at p<0.05.

- Amputations are subjective and a placebo effect was clearly evident. Pain scores are a major contributor to the decision to amputate. Things like de novo gangrene and wound size are clearly not subjective and showed statistical significance in favor of TRC. However, pain is subjective and with less reported pain it is possible physicians were delaying amputations accordingly. This is something we expect will mitigate as the trial progresses to the final analysis. Placebo response does not actually delay disease progression.



Conclusion: The chart above clearly shows the big change in control response from the 1st to 2nd update. We are encouraged by the fact that TRC behaved remarkably consistent throughout the trial. Assuming management can alleviate some of the placebo effect in the phase III trial through better patient selection and more standardized care, if TRC offers up an amputation free survival rate of ~25%, while the control trends to the expected ~35%, the phase III trial will most definitely meet statistical significance with 450-500 patients.

On Safety Assessment…

Safety was a paramount concern during the trial. Management enrolled a total of 86 patients. Only 72 progressed to treatment. Fourteen (14) patients were not treated for various reasons:

- ✓ Some did not meet entry criteria upon further review prior to bone aspiration.
- ✓ Some could not tolerate the bone aspiration.
- ✓ Some of the bone aspirate was contaminated or could not be expanded under Aastrom's technology.
- ✓ Some had amputations in-between the bone aspiration and the injection (2-weeks).
- ✓ Some had significant adverse events in-between the bone aspiration and the injection (2-weeks).
- ✓ Some provided bone aspirate for expansion, but never returned for injection.

Patients that did undergo the procedure generally responded well. Adverse events (AEs) were high, as expected, but nothing was significantly higher in the TRC group vs. the control.

Safety Assessment on ITT Population - TOTAL

Parameter	TRC (n=53)	Control (n=24)
Number (%) with Adverse Events	46 (87%)	22 (92%)
Number of Deaths	3 (6%)	1 (4%)
Number (%) with Serious Adverse Events	23 (43%)	12 (50%)
Number (%) Withdrawal due to AE	1 (2%)	0

What's Next?

…SPA Under Review…

In mid-October 2010, Aastrom announced that it had submitted a special protocol assessment (SPA) on the company's phase III clinical development program in CLI. The SPA allows for close consultation with the agency on the protocol design and necessary endpoints for approval. We expect the FDA will respond back in mid-December 2010 (approx. 60 days from filing). We expect that Aastrom will need to make some minor adjustments to the protocol based on the FDA's response in December, and thus one additional round of filing and response may push the initiation of the program back to late March / early April 2011. This actually works in management favor, as they can now incorporate minor changes given what the company has learned from the 2nd interim update on RESTORE-CLI and Sanofi-Aventis' phase III failure with NV1-FGF in the TALSIMAN-201 program.

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 be amputation-free survival at 12 months, with secondary endpoints including amputation, de novo gangrene, wound healing, and all cause mortality. Management may look to enroll a "less sick" population in one of the two phase III programs, but at this time we are still waiting for the final protocol.

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. Site selection and enrollment criteria will be instrumental to the success of the program. Enrollment should take between 12 to 18 months to complete.

The total cost should be roughly $15 to $20 million, or $30-40k 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. In late October 2010, Aastrom Bio signed a new strategic manufacturing partnership with ATEK Medical. ATEK will supply the disposable cassettes used during the cell therapy procedure. The relationship puts a more comprehensive and long-term supply agreement into place ahead of the phase III program. This should work to alleviate supply or logistic issues that could materialize during the program.

…FDA Grants Fast Track Status for CLI…

Also in October 2010, the U.S. FDA granted a Fast Track designation to Aastrom's cell therapy development program for CLI. The FDA's fast track program is designed to facilitate the development and expedite the review of new drugs and biologics intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs. CLI clearly falls into this category.

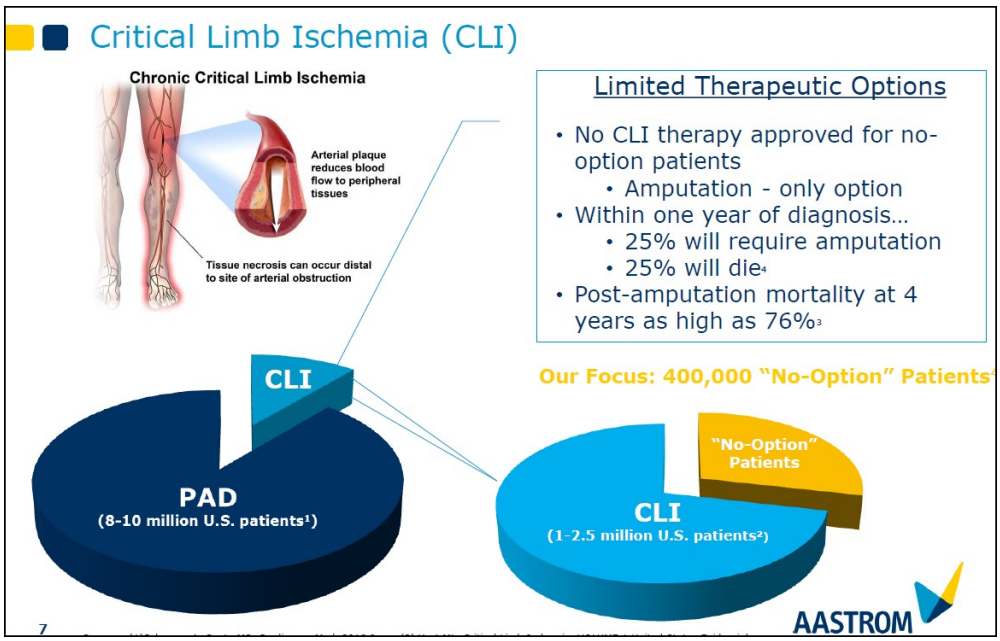
- Critical limb ischemia (CLI) affects approximately 1 million people in the U.S. each year -- roughly 2% of the population over the age of 50. Over 25% of patients with PAD will eventually development CLI. CLI is defined as inadequate blood flow to the limbs, and if left untreated can result in tissue loss, gangrene, amputation and death. In fact, CLI leads to an average of 150,000 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 25%.

Fast track-designated drugs and biologics ordinarily qualify for priority review, thereby expediting the review process. In addition, the designation may allow Aastrom to submit portions of the biologic license application (BLA) on a rolling submission basis. For a company of Aastrom's size, it's a significant benefit in our view.

…Market for CLI Remains Wide Open…

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. The healthcare burden associated with PAD-related amputations in the U.S. is greater than $10 billion per year.



Cash Raise Coming Soon…

Management has guided to external R&D costs associated with the RESTORE-CLI program of $15 to $20 million. We expect approximately half of these costs to take place in calendar 2011. Our financial model forecasts cash at the end of calendar 2010 of approximately $10.5 million.

On November 12, 2010, Aastrom filed a $75 million mixed securities shelf. We do not expect the company to see to raise this much cash at one time. More likely is that the company finances to the next major event, which will be the 1st interim analysis of the phase III trial after 200-250 patients have completed treatment. This will most likely be around mid-2012. We note there are several other catalysts before this time, including the full analysis from RESTORE-CLI in May 2011, along with meaningful updates from the Dilated Cardiomyopathy (DCM) program during the first half of 2011.

We suspect that management will look to raise cash of approximately $25 million before the end of the year. This will be enough to fund operations in 2012. We are also aware that the company has entered "CDA" with several firms on collaborating for both CLI and DCM. We believe these talks center around the Ex-North American rights to TRC in CLI or DCM. Management is looking to commercialize TRC in North America alone. After all, they are footing the bill for the phase III trial and will be in close contact with approximately 50 centers around the U.S. and Canada throughout the next few years while the trial is active. No company will be in better position from a market awareness standpoint than Aastrom. A deal Ex-N.A. for sizable upfront cash could fund the expansion of an internal sales force to promote TRC post-approval. This is not a primary-care "pound-the-street" indication. Aastrom could easily build and manage the small specialty sales force necessary to see TRC achieve blockbuster sales if the data backs up the claim.

Outperform Rating / $5 Price Target

Aastrom Bio shares will most likely be under significant selling pressure the next few days as the excitement bubble bursts following the 2nd interim update from RESTORE-CLI. We view this as typical biotech trading. In the long-run, we are still very comfortable with Aastrom's position. We are not spooked by the data from RESTORE-CLI at all. This was a small trial will low statistical powering that accomplished its goal – establish proof-of-concept and position the company to enter a phase III registration program. We would be buyers of Aastrom's stock on weakness relating to the RESTORE-CLI data or the impending cash raise. Our NPV calculations peg Aastrom fairly-valued at roughly $5 per share – market capitalization of $140 million.

PROJECTED FINANCIALS

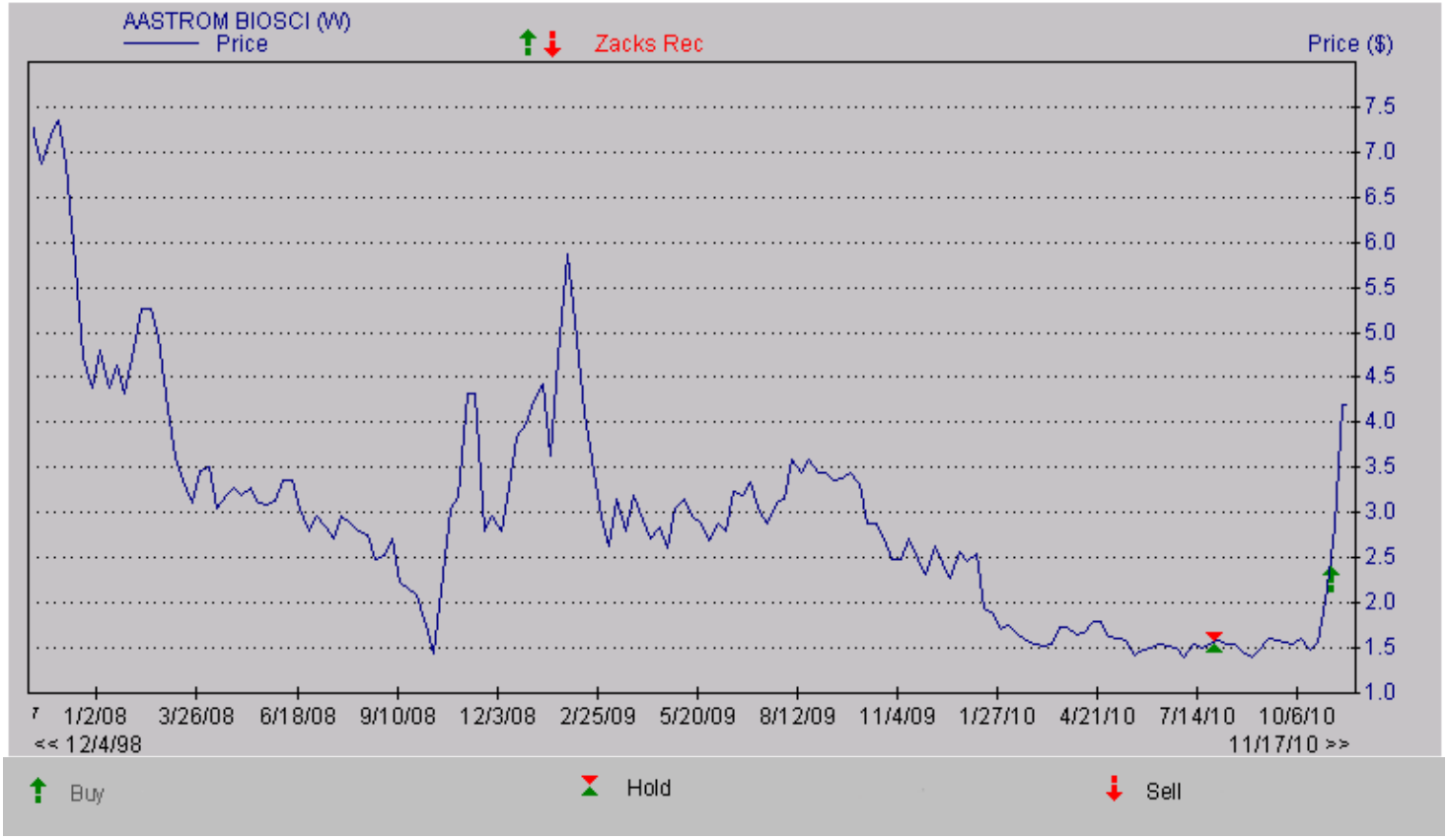
Aastrom Biosciences
Income Statement

Aastrom Biosciences	Jun-10	Sep-10	Dec-10	Mar-11	Jun-11	Jun-11	Jun-12	Jun-13	Jun-14
	2010 A	Q1 A	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**
YOY Growth	*0%*	-	-	-	-	*0%*	*0%*	*0%*	*0%*
Product Sales & Rentals	**$0.089**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	*0.0%*	*0.0%*	*0.0%*
Total Revenues	**$0.089**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	*-51.1%*	-	-	-	-	*-100.0%*	-	-	-
Cost of Product Sales & Rentals	$0.034	$0	$0	$0	$0	$0	$0	$0	$0
Product Gross Margin	*0%*	-	-	-	-	-	-	-	-
Research & Development	$12.658	$4.167	$4.250	$5.000	$6.000	$19.417	$25.000	$25.000	$20.000
% R&D	*14222.5%*	-	-	-	-	-	-	-	-
Selling, General, and Admin	$5.201	$1.686	$1.700	$1.750	$1.800	$6.936	$7.250	$8.000	$9.000
% SG&A	*5843.8%*	-	-	-	-	-	-	-	-
Operating Income	($17.804)	($5.853)	($5.950)	($6.750)	($7.800)	($26.353)	($32.250)	($33.000)	($29.000)
Operating Margin	-	-	-	-	-	-	-	-	-
Other Income (Expenses)	$0.075	$0.020	$0.026	$0.055	$0.045	$0.146	$0.120	$0.130	$0.200
Pre-Tax Income	($17.729)	($5.833)	($5.924)	($6.695)	($7.755)	($26.207)	($32.130)	($32.870)	($28.800)
Taxes & Other Charges	$0	$0	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	($17.729)	($5.833)	($5.924)	($6.695)	($7.755)	($26.207)	($32.130)	($32.870)	($28.800)
Net Margin	-	-	-	-	-	-	-	-	-
Reported EPS	**($0.72)**	**($0.21)**	**($0.21)**	**($0.23)**	**($0.27)**	**($0.92)**	**($1.00)**	**($0.97)**	**($0.80)**
YOY Growth	-	-	-	-	-	-	-	-	-
FAS-123R Expense	$0.7	$0.2	$0.2	$0.2	$0.3	$0.9	$1.1	$1.5	$2.0
Weighted Ave. Shares Out	24.7	28.3	28.5	28.7	28.9	28.6	32.0	34.0	36.0

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

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HISTORICAL ZACKS RECOMMENDATIONS



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