Zacks Small-Cap Research

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InVivo Therapeutics (NVIV-OTC)

NVIV: Waiting For The IDE Trial To Start…

Current Recommendation	**Neutral**
Prior Recommendation	Buy
Date of Last Change	07/23/2013
Current Price (11/08/13)	$1.13
Target Price	**$2.00**

UPDATE

Last month we had a 30-minute conversation with InVivo Therapeutics' new CEO, Michael J. Astrue. Mr. Astrue took over as head of InVivo back in late August 2013 when former CEO, CFO, and Chairman, Francis M. Reynolds, resigned for an undisclosed medical condition. What exactly the medical condition was that caused Mr. Reynolds to resign, or whether or not he was effectively forced out by the board and disgruntled shareholders, remains a mystery to outsiders. However, worth noting, only a few weeks later, acting CFO, Sean F. Moran, also resigned.

We came away from the conversation with Mr. Astrue encouraged by the change in tone of the company and the focused effort on driving the scaffolding forward. The company has 4+ quarters worth of cash on hand. We remain 'Neutral' while we wait for future updates, but the valuation is now very attractive for long-term holders.

SUMMARY DATA

52-Week High	**$5.67**
52-Week Low	**$1.13**
One-Year Return (%)	**-23.65**
Beta	**0.83**
Average Daily Volume (sh)	**207,458**
Shares Outstanding (mil)	**79**
Market Capitalization ($mil)	**$89**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**0**
Insider Ownership (%)	**28**
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 A	0 A	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	$0.05 A	$0.03 A	$0.12 A	-$0.13 E	$0.07 E
2013	-$0.20 A	-$0.20 A	-$0.07 A	-$0.08 E	-$0.25 E
2014					-$0.27 E
2015					-$0.34 E

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WHAT'S NEW

Waiting For Signs Of Clinical Life

In October 2013, we had a 30-minute conversation with InVivo Therapeutics' new CEO, Michael J. Astrue. Mr. Astrue took over as head of InVivo back in late August 2013 when former CEO, CFO, and Chairman, Francis M. Reynolds, resigned for an undisclosed medical condition. What exactly the medical condition was that caused Mr. Reynolds to resign, or whether or not he was effectively forced out by the board and disgruntled shareholders, remains a mystery to outsiders. However, worth noting, only a few weeks later, acting CFO, Sean F. Moran, also resigned. Gregory D. Perry was appointed interim CFO in mid-September 2013. Below we provide a brief background for both Mr. Astrue and Mr. Perry:

- Mr. Astrue is currently the non-executive Chairman of the Board at Vivus, Inc. (VVUS). He brings over a decade of experience in the biopharmaceutical and biotechnology industries to InVivo, as well as a proven track record of success with advancing products through the FDA process. Mr. Astrue served as the interim CEO of Epix Pharmaceuticals, Inc. from 2005 to 2006 and previously served as the President and CEO of Transkaryotic Therapies, Inc. from 2003 to 2005. Mr. Astrue has also served in a number of government positions, including as Commissioner of the Social Security Administration from 2007 to 2013.

- Mr. Perry was most recently the Executive Vice President and CFO of Immunogen, Inc. Prior to joining Immunogen, Mr. Perry served as CFO of Elixir Pharmaceuticals, Inc. from 2007 to 2009. Prior to Elixir, he was CFO of Domantis Ltd., which was acquired by GlaxoSmithKline in 2006. Previously, Mr. Perry was Senior Vice President and CFO of Transkaryotic Therapies, Inc. until its acquisition by Shire plc in 2005. Mr. Perry is currently a member of the Board of Directors of Advanced Cell Technology, Inc.

From an outsider's point of view, the house-cleaning at InVivo is a good thing. Mr. Reynolds was very good at traveling around the country, appearing on morning talk shows, and hyping the InVivo story. What he lacked was an understanding of and the skills to navigate FDA regulations, or how to effectively communicate with Wall Street. Under Mr. Reynolds, the company generated some impressive animal data in acute spinal cord injury; but it took nearly two years for the company to be in position to file the investigation new drug (IND) application (July 2011) for the biodegradable polymer scaffold, and then another two years for the FDA to approve that application (April 2013). When Mr. Astrue took over three months ago, it became immediately obvious to him that InVivo was in no position to begin the IDE study anywhere near the guidance the previous management had laid out to investors. The updated clinical plan now pegs the initiation of this program in the first quarter of 2014.

We asked Mr. Astrue what exactly has the company been focusing on since he took over, and what still needs to be done before that first patient can be enrolled in the pilot study. Although he was hesitant to give us a direct answer, we got the sense that most of the work is clinical and regulatory. We think the animal model data is solid and the scaffolding works in-line with how it was designed – to support and protect the damaged spinal cord from the secondary inflammation that the company believes is responsible for up to 90% of paralysis following an acute injury. Data generated by the company over the past several years shows consistent results between motor scores and kinematic/EMG analysis, no adverse histopathology, confirmed biocompatibility, significant remodeling and promotion of new tissue generation in the lesions of scaffold implanted subjects. What InVivo needs to spend the next few months on is the logistics of actually running a multi-center clinical trial in this potential breakthrough indication.

From a design standpoint, the pilot study looks to be similar to what the company previously communicated. The study will seek to enroll 5 patients in an open-label, staggered enrollment format. The first patient will be enrolled at either the Massachusetts General Hospital (MGH) or the Geisinger Medical Center (GMC). This first patient will be treated and followed for three months after surgery. Assuming no serious adverse events occurred in this first patient, InVivo will be allowed to expand enrollment to the second patient. The second patient will follow a similar treatment and three-month follow-up period before the third patient is enrolled. This will proceed as such until all five patients have been enrolled. All five patients will have acute thoracic injuries deemed to be neurologically complete (ASIA-A classification) at time of enrollment. Enrolled should take at least 21 months to complete, but given the open-label design of the study, data from the first patient should become available as soon as three or four months after the study begins, followed by more data from each additional patient on a rolling 3-4 month basis.

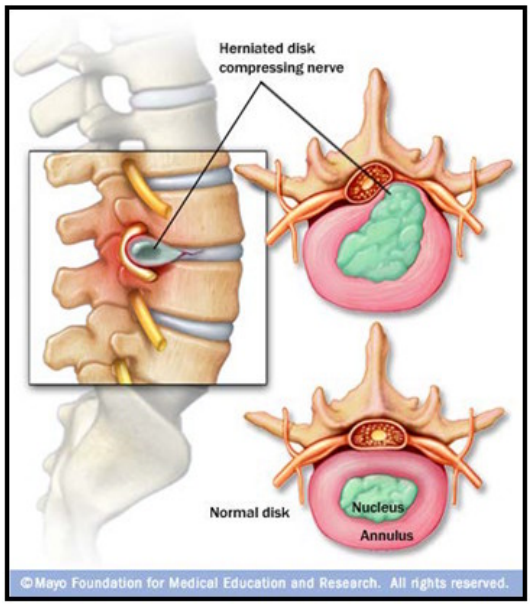
From the FDA's viewpoint, the pilot study remains squarely a safety assessment. Given that the company saw no serious adverse events in animal studies, we are confident enrollment will proceed on plan once the study begins in the first quarter of 2014. That makes for an interesting flow of news from InVivo throughout 2014 and 2015. However, gone is InVivo talking about FDA approval after the pilot study under the FDA's Humanitarian Use Device (HUD) pathway. The previous management seemed intent on finding the quickest route to market, and that was through a Humanitarian Device Exemption (HDE). The FDA actually approved the HUD in April 2013, but with a lack of a human pivotal efficacy study uptake would have been limited. New CEO, Michael Astrue, believes the best and most effective path to market is to follow the traditional PMA pathway for medical devices. That means conducting a larger, controlled human pivotal study after the 5-person pilot study completes. We saw significant investor confusion of HUD, so although the first approval of the scaffolding won't be in 2014 or 2015 as Mr. Reynolds emphatically promised, once cleared by the FDA in 2017 or 2018, InVivo's scaffolding will have adequate data and labeling to drive sales to the potential blockbuster level we believe the device could achieve.

The company has also recently shed some light on the potential commercialization of the scaffolding. According to industry statistics, nearly 80% of all spinal cord injuries are treated at 75 Level 1 trauma centers around the U.S. Management believes they can effectively target these 75 centers with 10 to 20 direct representatives. InVivo's scaffolding is designed to complement the current standard of care for an acute spinal cord injury, not replace it. The sales forced, armed with pivotal human efficacy data and promoting the product under that type of marketing message, should have enormous success. We've written in the past about the market opportunity here for InVivo.

The Hydrogel Looms Large

Before we hung-up with Mr. Astrue, we had to get an update on the company's Hydrogel product – a product that seems to have captivated most investors we speak with on InVivo. True, the Hydrogel has enormous potential for the company, potentially even beyond the biodegradable scaffolding for spinal cord injury. However, besides hyping the science the market opportunity, the previous management has done very little to explain to investors what exactly the Hydrogel is and why they are so excited about its potential.

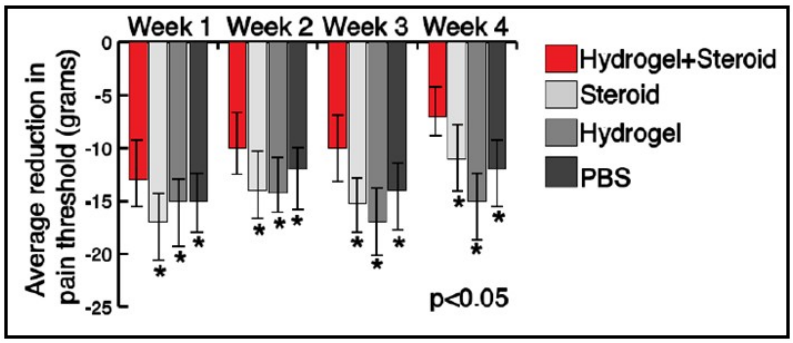
The primary indications for the Hydrogel will be in treating peripheral nerve pain and in acting as a dural sealant following spinal and cranial surgery requiring the opening of the dura mater. For peripheral nerve pain, we provide a brief glimpse at the preclinical data that shows encouraging proof-of-concept in animal models.



Disk herniation and radiculopathy are two major causes of peripheral nerve pain. In lumbar radiculopathy, pain or numbness of the buttock and leg is typically caused by compression of the lumbar spinal nerve root (sciatica). Disc herniation, stenosis, osteophyte formation, spondylolithesis, and other degenerative disorders all lead to this type of pain. Existing treatment options include NSAIDs and epidural steroid injections. However, these injections are short-lived and carry risk of side effects. The Hydrogel is designed to function as a therapeutic drug delivery depot that provides sustained local release of drugs that provide pain relief, such as glucocorticoid or corticosteroids, for weeks beyond existing depot formulations.

Lots of companies have injectable sustained release pain medications. This is not a revolutionary approach. However, InVivo believes its proprietary poly-ethylene glycol (PEG) formulation Hydrogel has a number of unique advantages over conventional sustained-release depot formulations based on control and residence time, pharmacokinetics and pharmacodynamic properties, and, most importantly, a lack of swelling post injection (more on that below). Treatment for peripheral nerve pain is a pretty sizable market opportunity in the U.S., as 3-4% of the population suffers from chronic lower back pain. InVivo estimates there were nearly 9 million epidural steroid injections in the U.S. in 2010. It's a $20 billion dollar market! Conventional injections last four to six weeks, at best. InVivo's could last 3 months.

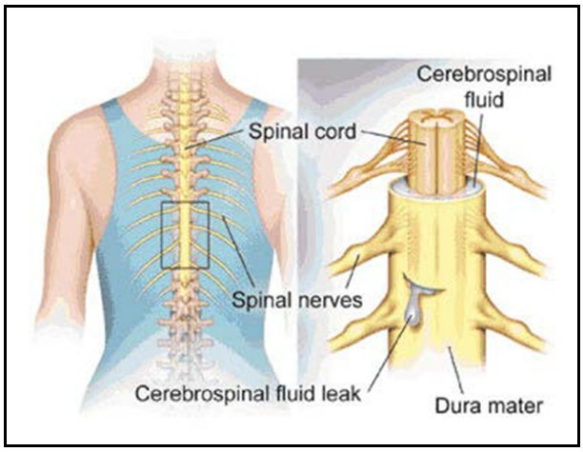
InVivo has presented preclinical data conducted by Geisinger in rodent sciatic nerve ligation model. The four week study compared InVivo's Hydrogel plus methylprednisolone to the Hydrogel alone, methylprednisolone alone, and a control (phosphate buffered saline). The data below shows the comparison for the four groups to baseline "pre-ligation". Results show a clear and statistically significant move back to baseline "no pain" for the combination Hydrogel + MPSS product vs. all other components. What's very interesting is that MPSS, the current standard of care, really offers no statistically significant difference from the PBS control. Thus investors can get a sense of the opportunity here for InVivo – the standard of care is pretty terrible but still generates billions in sales. With a clearly superior alternative, InVivo's combination Hydrogel + MPSS product could become the new standard of care and generate pretty significant sales.



The next steps for InVivo in lumbar radicular pain are to meet with the U.S. FDA for a pre-IND meeting and agree upon a clinical pathway for the pilot study. Unlike spinal cord injury, which is a fairly concentrated market allowing for InVivo to market and promote the scaffolding in-house, the opportunity with the Hydrogel is large and fragmented. Thus, we expect the company to look to partner this indication after the pilot study. Besides MPSS, there are dozens of other pain medications that could allow for delivery through InVivo's Hydrogel technology.

In use of the Hydrogel as a dural sealant, InVivo would be going squarely up against existing dural sealant products, for example Covidien's DuraSeal. During neurosurgical procedures, preventing the leakage of cerebrospinal fluid (CSF) is essential to reduce potential adverse events such as infection and to ensure positive patient outcomes. To achieve a watertight closure, surgeons can use a product like DuraSeal. The product is approved as an adjunct to suturing – and it's approved as a medical device (not a therapeutic). Covidien describe the product as an innovative synthetic (PEG) absorbable hydrogel sealant that lasts 4 to 8 weeks. CSF leak is a major complication following spinal or cranial surgeries. According to Covidien, there are 1.5 million spinal surgeries performed in the U.S. each year, about 10% of which require a dural sealant. This complicating alone can add $15,000 in additional costs to the healthcare system.

An issue with DuraSeal is potential swelling of the gel post-injection. This is a very tricky situation given the tight location of the spinal cord and potential neurological or physical impact that swelling or added pressure could have on the patient. InVivo believes their proprietary formulation of PEG could offer similar efficacy to DuraSeal but with less risk of complications resulting from swelling. We were unable to peg an exact sales number for DuraSeal at Covidien, but with an estimated 150,000 spinal surgeries with CSF leak per year, we see a pretty meaningful opportunity here.



What's Next From InVivo

The company exited the third quarter, ended September 30, 2013, with roughly $19 million in total cash on hand. That's about 4-5 quarters worth of burn assuming burn stays around $4 million per quarter. Although this number could increase once the IDE trial starts next year. Over the next few weeks we expect the company to provide an update on the development timelines for the scaffolding and Hydrogel products. We think that could drive the shares higher given the current reset and low expectations from investors. Mr. Reynolds suffered from "irrational exuberance" with respect to InVivo's potential. That's not to say InVivo does not have enormous potential over the long-term, but we hung up the phone refreshed to hear a far more even-keeled, straightforward, and realistic tone from Mr. Astrue. History tells us Mr. Astrue knows what he's doing, and perhaps no small biotech company out there has a more impressive scientific advisory board than InVivo. Going forward, Mr. Astrue's job will be to manage the exciting science and potential significant leap forward in standard of care that InVivo's technology allows with realistic and obtainable clinical and regulatory goals for investors to feel comfortable and return to the story. A $1.15 per share, we think the stock is looking attractive assuming the ship is now heading in the right direction.

PROJECTED FINANCIALS

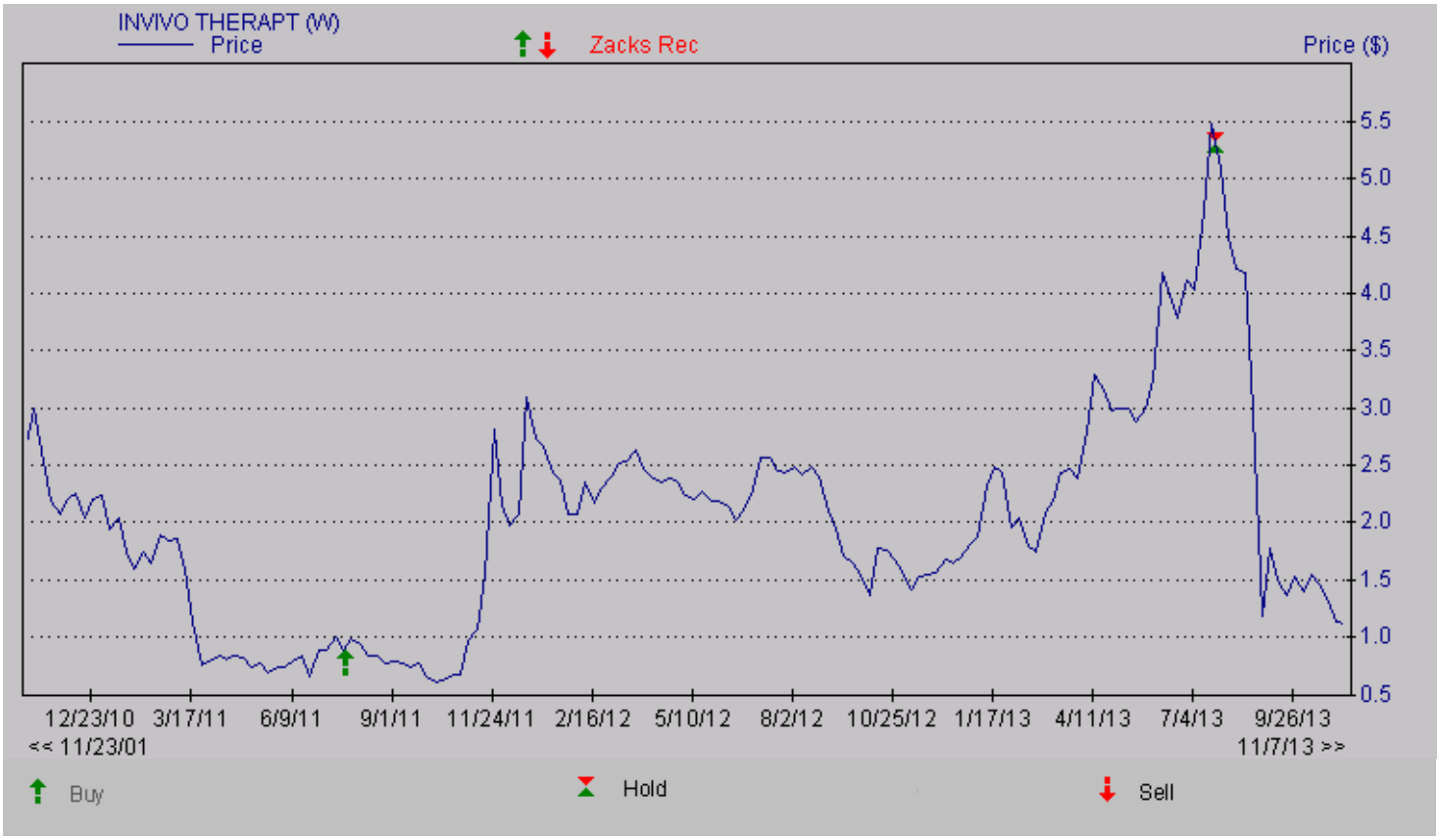
InVivo Therapeutics Holdings Corp.
Income Statement

InVivo Therapeutics	2012 A	Q1 A	Q2 A	Q3 A	Q4 E	2013 E	2014 E	2015 E
Product Sales	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	-
Collaborative & Licensing	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	-
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	-
Cost of Goods / Services	$0	$0	$0	$0	$0	$0	$0.0	$0.0
Product Gross Margin	-	-	-	-	-	-	-	-
R&D	$6.4	$1.2	$2.6	$3.0	$2.8	$9.6	$12.5	$12.5
% R&D	-	-	-	-	-	-	-	-
SG&A	$6.4	$1.6	$2.5	$2.4	$2.2	$8.7	$10.0	$16.3
% SG&A	-	-	-	-	-	-	-	-
Operating Income	($12.8)	($2.9)	($5.1)	($5.4)	($5.0)	($18.3)	($22.5)	($28.8)
Operating Margin	-	-	-	-	-	-	-	-
Net Other Income	$17.4	($10.5)	($9.2)	($0.0)	($1.0)	$0.0	$0.0	$0.0
Pre-Tax Income	$4.7	($13.3)	($14.3)	($5.4)	($6.0)	($18.3)	($22.5)	($28.8)
Taxes	$0	$0	$0	$0	$0	$0	$0.0	$0.0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0.0%*	*0.0%*
Net Income	$4.7	($13.3)	($14.3)	($5.4)	($6.0)	($18.3)	($22.5)	($28.8)
Net Margin	-	-	-	-	-	-	*#DIV/0!*	*#DIV/0!*
Reported EPS	**$0.07**	**($0.20)**	**($0.20)**	**($0.07)**	**($0.08)**	**($0.25)**	**($0.27)**	**($0.34)**
YOY Growth	-	-	-	-	-	-	-	-
Wt. Ave Shares Outstanding	63.2	66.0	72.4	78.6	79.0	74.0	82.5	85.0

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

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