Zacks Small-Cap Research

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John D. Vandermosten, CFA
312-265-9588 / jvandermosten@zacks.com
Brian Marckx, CFA
312-265-9474 / bmarckx@zacks.com

scr.zacks.com
10 S. Riverside Plaza, Chicago, IL 60606

InVivo Therapeutics (NVIV-NASDAQ)

Releases 2015 results, reports continued patient conversion and raises sufficient funds to support operations until 2018.

Based on our DCF model and a 15% discount rate, NVIV is valued at approximately $18.00 per share. We apply a 65% probability of FDA approval for the Neuro-Spinal Scaffold. The model does not reflect any revenue benefit from the Neural Trails initiative or potential market expansion into the incomplete AIS B or lower market.

Current Price (4/29/2016)	$6.00
Valuation	**$18.00**

OUTLOOK

In January 2016, InVivo Therapeutics received approval of its protocol amendment from the FDA, which converted its ongoing NSS pilot study into a pivotal probable benefit study. The company plans to use this single study as the basis for a HDE application with planned submission in late 2017. In April, NVIV reported that a fourth patient reported improvement to AIS B or better leaving only one additional conversion before the study achieves its primary endpoint.

In December, NVIV announced its treatment for chronic spinal cord injury (SCI) through its Bioengineered Neural Trails Program which may restore neuronal connectivity and promote neurological recovery in patients with chronic SCI. Although currently in a pre-clinical stage, this program may take the baton from the NSS into chronic SCI and address the nearly 300,000 Americans currently suffer from this condition and currently have only limited therapeutic options.

At the current price, we view InVivo shares as meaningfully undervalued, and feel they provide significant long-term upside potential. With sufficient cash to support two more years of operations, we believe the current share price presents investors with an attractive long-term buying opportunity. Our price target reflects material market penetration into the complete AIS A thoracic and cervical market.

SUMMARY DATA

52-Week High	**$17.87**
52-Week Low	**$3.66**
One-Year Return (%)	**-50.5**
Beta	**3.23**
Average Daily Volume (sh)	**432,759**
Shares Outstanding (mil)	**31.9**
Market Capitalization ($mil)	**$191**
Short Interest Ratio (days)	**7.6**
Institutional Ownership (%)	**16**
Insider Ownership (%)	**18**
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 2015 Estimate	**N/A**
P/E using 2016 Estimate	**N/A**
Zacks Rank	**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)
2015	$0.0 A	$0.0 A	$0.0 A	$0.0 A	$0.0 A
2016	$0.0 E	$0.0 E	$0.0 E	$0.0 E	$0.0 E
2017					$0.0 E
2018					$51.5 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2015	-$0.64 A	-$0.39 A	-$0.09 A	-$0.17 A	-$1.26 A
2016	-$0.19 E	-$0.20 E	-$0.19 E	-$0.20 E	-$0.78 E
2017					-$0.86 E
2018					$0.44 E

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WHAT'S NEW

InVivo Reports Fiscal Year 2015 Financial Results

InVivo Therapeutics Holdings Corp. (NASDAQ: NVIV) reported financial results for its 2015 fiscal year for the period ending December 31, 2015. During this period, no revenues were reported. Operating expenses for the twelve month period were $22.4 million, which was higher than the $17.8 million spent in the prior year. Research and development expenses were $10.1 million and general and administrative expenses were $12.3 million with R&D falling slightly over the prior year and G&A rising over 60%.

Research and development expenses fell by $0.2 million, but the decline would have been greater ($0.8 million) if $0.6 million of insurance proceeds were added back in 2014 that offset R&D expenses. Year over year, R&D fell due to lower consulting costs, testing costs, packaging and lab supplies and lower compensation expense. Some other expenses offset the overall decline and NVIV experienced an increase in clinical trial costs, stock compensation expense and bonuses.

General and administrative expenses rose 63% or $4.8 million in 2015 due to higher legal costs and other costs related to the class action lawsuit regarding the alleged false and misleading statements regarding the timing and completion of the clinical study of the Neuro-Spinal Scaffold.[1] Other expenses that added to the year over year increase include greater stock compensation, investor relations, NASDAQ listing, board and audit and consulting expenses and fees.

Interest income increased fractionally and interest expense grew slightly to $0.2 million due to the amortization of the debt discount. Derivative loss, due to stock price appreciation and the exercise of warrants was $10.8 million.

Estimates

We anticipate that InVivo will launch the Neuro-Spinal Scaffold (NSS) in 2018 following a successful approval of the device in 2017. The company, concurrent with the approval process for the complete thoracic indication, has announced an intention to begin pivotal trials for a complete cervical indication as well, which we forecast will be completed by 2020. We believe that sales will rise from $51 million in 2018 rising to $600 million over the next ten years. These estimates do not include any revenues from approval of the device for incomplete thoracic or cervical indications nor do they include any revenues for the Bioengineered Neural Trails initiative.

Public Offering of Shares

On March 14, 2016, NVIV announced that it would offer common shares and warrants through Raymond James & Associates to fund the current and forthcoming clinical trials and support general corporate expenses. The offering, which included 0.5 warrant for every share, was priced at $7.50 per unit for 4.29 million units, which included the 15% over allotment of 0.56 million shares. The 2.15 million separable warrants have an exercise price of $10 and expire after a 5-year term. Gross proceeds are expected to be $32.2 million.

Other Material Events Year to Date 2016

- On February 29, the company received a protocol amendment approval from the FDA to establish the Objective Performance Criterion (OPC) for the INSPIRE study. The OPC was defined as a 25% or higher proportion of the study participants demonstrating a one ASIA Impairment Scale (AIS) grade improvement six months following the procedure. This compares to historical six-month improvement rates in the 12% to 16% range. This is a very positive event for InVivo given their strong conversion rate thus far. We believe that InVivo will be able to surpass the 25% hurdle, providing strong support for eventual approval.

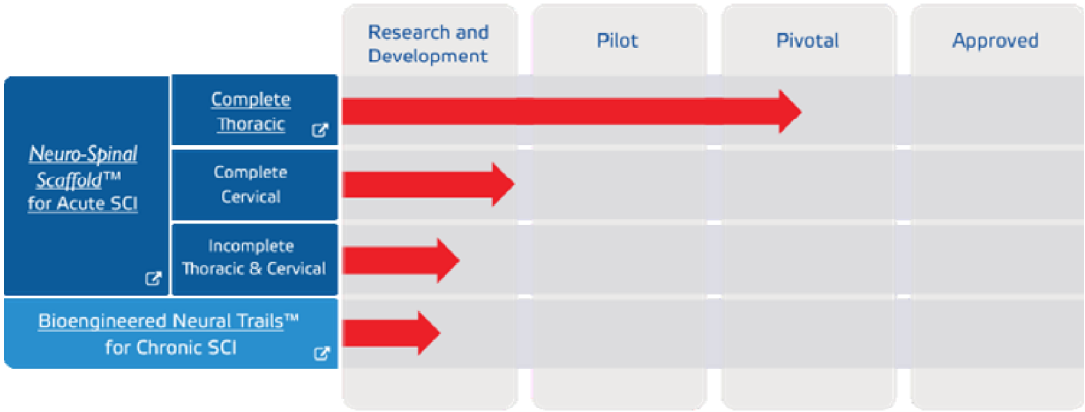
- The company has been fortunate to attend and announce attendance at a number of conferences, presenting to both investors and practitioners. So far in 2016, this includes the Biotech Showcase, the Cowen Health Care Conference, the Spine Summit, American Spinal Injury Association (ASIA) Annual Scientific Meeting, the Committee Roundtable on Biomedical Engineering Materials and Applications (BEMA) and the American Association for Neurological Surgeons (AANS).

[1] A lawsuit was filed in July 2014 and was dismissed with prejudice in April 2015. Following the dismissal, the plaintiff filed an appeal which will be heard in 2016.

- InVivo has added several new clinical trial locations so far this year and now has 19 sites that are participating in the INSPIRE study. Over the next few quarters we anticipate some additional sites to be opened. Below we list the sites added year to date.

    - February 3, UCSD Medical Center, San Diego, California
    - March 2, Vidant Medical Center in Greenville, North Carolina
    - March 3, University of Louisville Hospital in Louisville, Kentucky
    - March 8, Thomas Jefferson University Hospital in Philadelphia, Pennsylvania
    - April 5, University of Virginia Health System in Charlottesville, Virginia

- NVIV has also updated their pipeline chart, illustrating the current and planned programs for SCI. Currently, we anticipate that the complete thoracic program (the INSPIRE study) will wrap up sometime in early 2017, followed soon after by a filing with the FDA and, if successful, FDA approval in early 2018 and a launch of the NSS shortly after. InVivo plans to begin with the complete cervical trial in the next couple months, which we anticipate will commence as a pivotal trial also using the Humanitarian Device Exemption (HDE) pathway. The population size for the cervical group is similar to the thoracic group at about 2,000 patients and we believe that NVIV will be able to take advantage of the HDE due to the population size and only be required to show probable benefit. No announcement regarding timing for the incomplete thoracic and cervical trial has been made, but we foresee clinical trials beginning in the next few years. However, we note that due to the addressable population size in excess of 12,000 patients annually, the Premarket Approval (PMA) pathway must be used for this group, requiring a statistically significant study to support evidence of effectiveness, which will require a larger trial and potentially greater duration as compared to the complete thoracic and complete cervical efforts. InVivo has not provided detail regarding the clinical development program for the Bioengineered Neural Trails initiative, but has indicated that they are targeting a pre-IND meeting with the FDA by year end 2016. See below for a graphic summary of the current programs.



- NVIV performed three implantations since the beginning of the year; unfortunately one of the patients died due to the injuries sustained in the vehicle accident that damaged their spine. The patient who died will not be included as part of the study as there was no opportunity to observe the outcome of the implantation procedure. We discuss each of the eight patients in more detail later in our report.

Neuro-Spinal Scaffold Background

InVivo Therapeutics conducted an early pilot study of the Neuro-Spinal Scaffold (NSS) under an approved Investigational Device Exemption (IDE) application for the treatment of complete traumatic acute spinal cord injury (SCI). In April 2013, InVivo received a Humanitarian Use Device (HUD) designation for the NSS. The goal of the FDA-approved pilot study was to capture data on the safety and feasibility of the NSS and to gather preliminary evidence of clinical effectiveness. The pilot study was initially approved to enroll five patients, but InVivo announced that the FDA approved expansion of the study to permit enrollment to ten patients in October 2015. We believe that expansion of the pilot study set the stage for transition into the pivotal probable benefit study, and to use this single study as the basis for a Humanitarian Device Exemption (HDE) application will reduce clinical trial timelines and time to potential approval and commercialization.

Currently, there are 19 clinical sites open, and 7 patients are currently enrolled in the study and implanted with the NSS. We believe that additional trial sites will be added this year and InVivo has authorization to open up to 40 domestically and internationally. While the majority of these sites should be in the U.S., there is also the opportunity to open trial sites in both Canada and the United Kingdom.

FDA Approves *INSPIRE* Probable Benefit Study of the Neuro-Spinal Scaffold

On January 4, 2016, InVivo received approval of a protocol amendment from the FDA, which converted its ongoing pilot study into a pivotal probable benefit study. As a reminder, on December 3, 2015, InVivo announced that it has received conditional approval of the protocol amendment, and the approval was conditional solely upon a minor change to the informed consent form. We were expecting full approval of the amendment within 30 days of the conditional approval announcement, and this occurred within the expected timeframe. We see the approval by the FDA for the conversion of the pilot study into a pivotal probable benefit study as good news and as a major milestone for InVivo. It is important to understand that the original pilot study has been converted into the probable benefit study, and that the probable benefit study will not be a new study. We think that InVivo was able to receive approval for the probable benefit study largely due to the fact that both studies have similar outcome measures, and thus rolling the pilot study into the probable benefit study was much easier for the FDA to accept and approve. The company expects completing enrollment of the pivotal probable benefit study and submitting an application for Humanitarian Device Exemption (HDE) approval in late 2017. If all goes well, we believe this supports obtaining FDA approval to commence commercialization under an HDE.

Going forward, the study will be known as "***The INSPIRE Study: InVivo Study of Probable Benefit of the Neuro-Spinal Scaffold for Safety and Neurologic Recovery in Subjects with Complete Thoracic AIS A Spinal Cord Injury***," and is designed to enroll 20 implanted patients, which includes the 7 patients currently enrolled from the original pilot study. The primary objective of INSPIRE is to evaluate whether the NSS is safe and demonstrates probable benefit for the treatment of patients with complete T2-T12/L1 SCI. The primary endpoint is defined as the proportion of patients achieving an improvement of at least one American Spinal Injury Association (ASIA) impairment scale (AIS) grade at 6 months post-implantation. The AIS grade improvement represents regained sensory function, and/or motor and sensory function. Additional endpoints of the trial are various measures of neurological function, and include: ISNCSCI sensory and motor scores, bladder and bowel function, Spinal Cord Independence Measure (SCIM III), pain, Quality of Life and MRI measures (mainly to see cyst formation, which often happens in patients that are untreated).

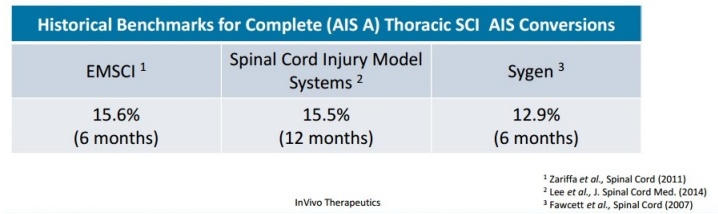
The inclusion criteria for the trial were expanded from their initial criteria to include patients with T2 injuries (new range: T2-T12/L1; original range: T3-T12/L1) and ages 16-17 (new range: ages 16-70; original range: ages 18-70). We believe that lowering the age limit is logical, as there are many cases of motor vehicle accidents involving inexperienced adolescent drivers. Additionally, including more thoracic segment injuries allows for more potential patients to qualify for the study. The FDA has also agreed to increase the total number of allowable U.S. sites to 40. In addition to the U.S. sites, the company plans to initiate the study in Canada as well as the United Kingdom. Full inclusion criteria can be found on ClinicalTrials.gov. Other inclusion criteria include: (1) Recent injury: Must receive NSS within 96 hours from injury, and (2): Non-penetrating contusion injury no less than approximately 4 mm diameter by MRI. We think that widening the criteria makes sense, and anticipate it will allow for more patients to qualify for the trial (and also bring on more neurosurgeons/investigators).

The Objective Performance Criterion (OPC)

As a reminder, obtaining marketing approval for the NSS is very different as compared to other devices as InVivo is pursuing the accelerated regulatory Humanitarian Device Exemption (HDE) pathway. An HDE only requires the demonstration of safety and probable benefit, which is a lower regulatory hurdle. InVivo is able to pursue the HDE pathway, due to the significant unmet medical need for SCI as there are currently no approved treatments for these types of SCI patients and the population is relatively small. As such, InVivo only needs to demonstrate probable benefit of the NSS device in order to get it approved.

As per the FDA and the FD&C Act Section 520(m), probable benefit under an HDE is defined as, "The device will not expose patients to an unreasonable or significant risk of illness or injury and the probable benefit to health from the use of the device outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment." We think the definition of probable benefit is vaguely defined to allow for the FDA to adapt to varying circumstances.

To assess probable benefit, InVivo along with the FDA will establish the OPC to define success in this uncontrolled study, which is primarily based on AIS conversion rates. The OPC has been set at 25% or more of the patients in the INSPIRE study achieving an improvement of at least one AIS grade by six months post-implantation. The level was set largely based on data from longitudinal, natural history databases. In large European and U.S. databases [European Multicenter Study about Spinal Cord Injury (EMSCI) - Zaffira *et al*., 2011; Spinal Cord Injury Model System (U.S. database) – Lee *et al*., 2014; Sygen clinical trial in spinal cord injury – Fawcett *et al*., 2007], the published rates of spontaneous improvement of at least one AIS grade for complete (AIS-A), thoracic SCI patients at six months are less than 16% (*below*). In other words, when looking across the large European/U.S. databases, as well as the newer and older databases, patients with thoracic complete injuries typically do not have favorable outcomes, and less than 16% of those patients can be expected to have any type of improvement in AIS scores by six or twelve months. Over the last ten years, the percentages have remained relatively constant in terms of neurological outcome.



As discussed above, the adopted OPC seeks a minimum of 25% of the study participants to show an improvement of at least one AIS grade by six months post-implantation. The study seeks to enroll 20 patients. The determination of the OPC is a key milestone that will allow the company to plot the path to eventual commercialization. We remind investors that HDE approval is not guaranteed if the 25% hurdle is met, as there is also a safety component that needs to be considered.

It is very likely that InVivo will be able to surpass the historical benchmark range mentioned above (12.9% to 15.6%) given its current success rate of a one level improvement in AIS score for four of the seven enrolled patients. We do think the OPC will end up being some percentage or range above 25%. At this point, it could potentially range from 20% to 45% which is from four to nine conversions.

Below, we review each patient enrolled in the trial.

Patient #1 (Jordan):

The first patient to enroll in the NSS study was involved in a dirt bike accident on October 13, 2014. The injury was classified as AIS-A and graded as complete (total paralysis) at T11 and below. On October 16, 2014, InVivo announced the NSS was successfully implanted in the patient (the surgery took place approximately 8 hours following the accident).

On January 21, 2015 InVivo announced a positive safety update at 3 months post-injury. At that time the injury was graded as "incomplete" and Jordan was reclassified to AIS-C from AIS-A, with motor, sensory, bowel, and bladder functional improvements compared to baseline.

On May 14, 2015 InVivo announced that between the 3-month and 6-month post-injury assessment Jordan had regained partial function of knee extensors and remained classified as AIS-C with a motor incomplete spinal cord injury.

On October 23, 2015, InVivo announced that between the 6-month and 12-month post-injury assessment, Jordan continued to demonstrate motor improvement with an additional 8 points gained on the AISA impairment scale. He demonstrated further bilateral improvements in the motor function of hip flexors and knee extensors, and also demonstrated first time bilateral contractions of the ankle dorsiflexors and ankle plantar flexors. Jordan remains classified as AIS-C. As per the company, a large natural history database shows that patients with similar T10-T12 level injuries have an average increase of lower extremity motor scores between 6 and 12 months of fewer than 2 points.

Patient #2 (Jesi):

The second patient to enroll in the NSS was struck by a car while riding on the back of a motorcycle on January 18, 2015. Her injury was classified as AIS-A impairment and graded as complete at T6 with total paralysis at T8 and

below. On January 22, 2015, InVivo announced that the NSS was successfully implanted, however due to the severity of the patient's injuries the doctors had to wait two days after her accident to perform the surgery.

On March 26, 2015, InVivo announced re-opening of enrollment in the pilot study, signifying success with respect to the safety endpoint at 30 days post-surgery for Jesi.

On May 14, 2015, InVivo announced a positive safety and efficacy update on Jesi at 3 months post-injury. Despite a return of some sensory and motor function, including appreciable improvement in trunk stability, self-care, mobility, and bowel and bladder function at the 3-month post-implant assessment, Jesi remained classified as AIS-A on the impairment scale due to a lack of consistent and profound sensory and motor function at the sacral S4-S5 region.

On July 6, 2015, InVivo announced a 6-month post-implant assessment that showed Jesi had marked improvement in sensory function with partial sensation present 5 dermatome levels lower on the right side compared to the 3-month assessment. This translates to regaining partial sensation from the lower ribs to the hip on the right. In addition, Jesi continues to make meaningful progress in activities of daily living.

Although Jesi remains at AIS A, the company reports that she continued bowel and bladder improvement through month 12.

Patient #3 (Roger):

On June 4, 2015, InVivo announced that the third patient was enrolled in the pilot study. The NSS was implanted three and a half days after the high-level T4 injury occurred at Carolinas Medical Center in Charlotte, NC. Roger, a 55-year-old construction worker, fell out of a deer stand and was left with a damaged spinal cord with no sensation from the middle of his chest down.

On July 6, 2015, InVivo announced that in the time between implantation and the 1-month post-injury assessment, the third patient improved from a complete AIS-A spinal cord injury to an incomplete AIS-B spinal cord injury and that the patient regained sacral sensation with improved bladder function. In addition, there were no reported serious adverse events associated with the NSS.

As per the company presentation at the 2015 Stem Cell Meeting on the Mesa, InVivo fact sheet, and updated January 2016 corporate presentation, we gather that Roger had regained partial sensation from the mid-chest to mid-abdomen at the 3-month and 6-month assessments.

Patient #4

On August 20, 2015, InVivo announced that the fourth patient was enrolled in the pilot study. The NSS was implanted 53 hours after the T3 injury occurred at the UC Davis Medical Center in Sacramento, CA. The patient remains ASI-A at month 6. No other follow-up data has been reported to date.

Patient #5

On September 8, 2015, InVivo announced that the fifth patient was enrolled in the pilot study. The NSS was implanted 69 hours after the T8 injury occurred at Keck Hospital of University of Southern California (USC) in Los Angeles. The patient remains ASI-A at month 3. No other follow-up data has been reported to date.

Patient #6

On February 23, 2016, InVivo enrolled a sixth patient into the INSPIRE study. The NSS was implanted at Barnes-Jewish Hospital at Washington University Medical Center in St. Louis, Missouri. The implantation was performed approximately 10 hours after the injury by Dr. Wilson Ray, M.D.

Patient #7

On March 24, 2016, InVivo added a seventh patient to the study. Neurosurgeon Dr. Domagoj Coric, M.D. performed the implantation at the Carolinas Medical Center in Charlotte, North Carolina. The procedure was performed approximately 21 hours after the SCI. This was the third implantation Dr. Coric performed.

Patient #8

On April 19, 2016, InVivo announced that the eighth patient in the study had died from injuries sustained from a serious motor vehicle accident. Dr. Travis Dumont, M.D. implanted the NSS 71 hours after the injury, and the patient died two days later. The principal investigator determined that the death was unrelated to the NSS or the implantation procedure and the death will be further reviewed by the Data and Safety Monitoring Board (DSMB) and the FDA. We remind investors that many times the patients who have suffered thoracic spinal cord injury also have other injuries that can be life threatening.

InVivo will continue to follow all of the patients enrolled in the INSPIRE trial for 10 years. Jordan and Jesi have completed their 12-month assessments. Patient #3 has completed his 6-month exam, and Patients #4 and #5 have completed their 3-month assessments. We believe that the study will continue to enroll patients until it has reached the full 20 individuals. We look forward to hearing updates as they are made available.

Policy Change on Patient Updates

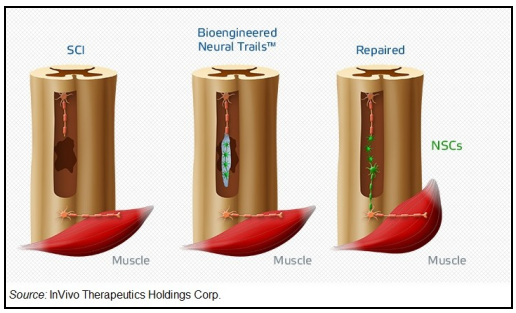
On September 30, 2015, InVivo filed a Form 8-K stating that it would only provide updates on patients enrolled if the results were dramatically positive or negative and as per industry standards (*below*).

> *"**Item 7.01. Regulation FD Disclosure:** On September 30, 2015, InVivo Therapeutics Holdings Corp. (the "Company") posted an updated investor presentation including updated patient information, in the "Investor Relations" section of its website at www.invivotherapeutics.com. As previously communicated, with the exception of dramatically positive or negative results, the Company expects to communicate any interim information according to industry standards. The Company does not consider a patient's unchanged [AIS] classification or a medically insignificant adverse event to be material."*

The company will continue to announce the enrollment of each patient and any conversions of AIS classification as well as any other dramatically positive or negative events.

Addressing Chronic Spinal Cord Injury: Bioengineered Neural Trails™ Program

On December 2, 2015, InVivo announced a strategy for the treatment of chronic spinal cord injury (SCI) through its Bioengineered Neural Trails Program in order to restore neuronal connectivity and promote neurological recovery in patients with chronic SCI. Although it is in the pre-clinical stage, we believe it is important to offer some insight into chronic SCI program.

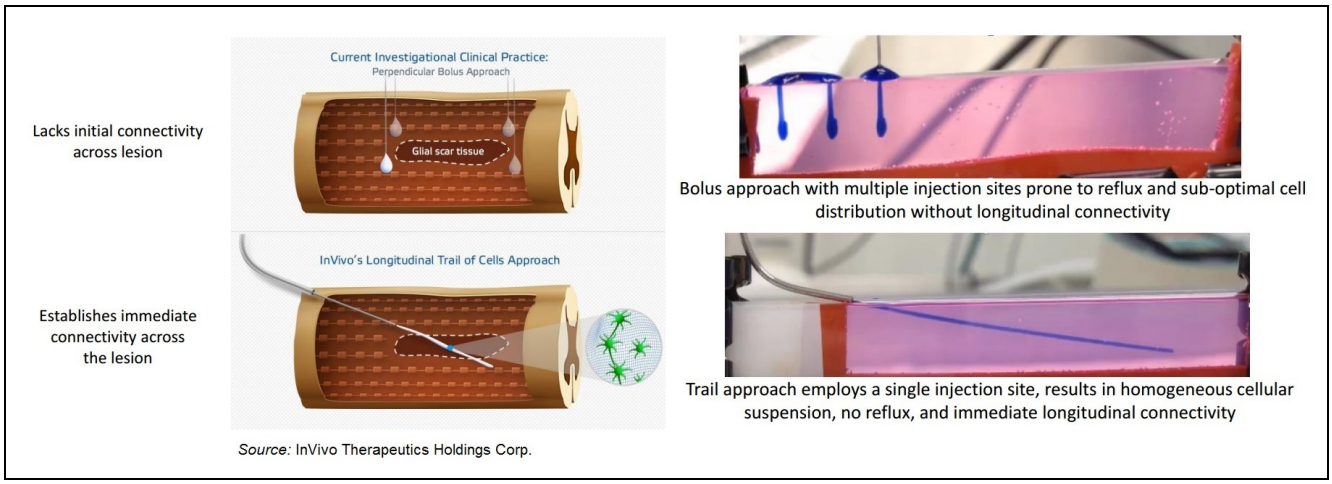


Source: InVivo Therapeutics Holdings Corp.

The program was further highlighted on December 3, 2015 during the Key Opinion Leader (KOL) Event and Company Update in New York City at the Palace Hotel. The event included presentations by Bob Langer, ScD, the David H. Koch Institute Professor at Massachusetts Institute of Technology and co-founder of InVivo; and Nick Theodore, MD, Chief of Spinal Surgery at the Barrow Neurosurgical Institute and the neurosurgeon who performed the first Neuro-Spinal Scaffold implantation. Dr. Langer discussed his contributions to the development of the field of biomaterials and InVivo's product candidates that evolved from work performed in his laboratory. Dr. Theodore presented on current state-of-the-art surgical treatment of spinal cord injury patients and a case study of the first patient in InVivo's ongoing Neuro-Spinal Scaffold study. Additionally, management also provided several company updates including introduction of its chronic spinal cord injury Bioengineered Neural Trails™ Program during the event.

Bioengineered Neural Trails™ are injectable combinations of biomaterials and neural stem cells (NSCs) delivered using minimally invasive surgical instrumentation and techniques to create trails across the chronic injury site. Another way to look at the program is to think of it as the NSS device with stem cells. The multimodal approach

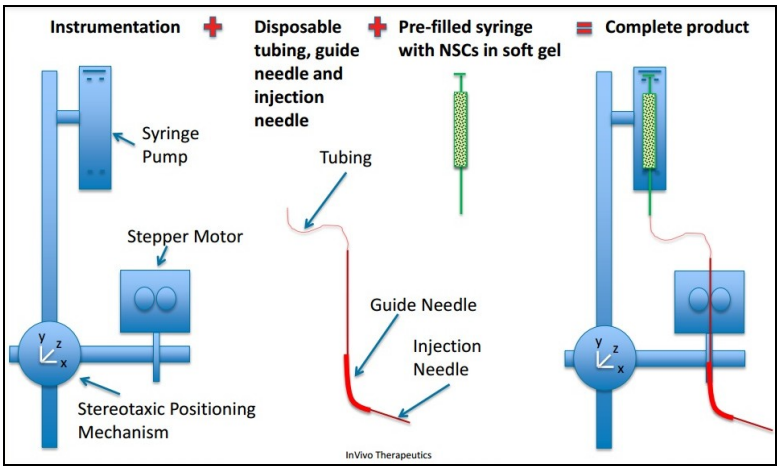
aims to bridge the spinal cord lesion at the time of implantation with a trail of neural stem cells (NSCs) delivered in a soft, gel-like scaffold that is both injectable and biodegradable.



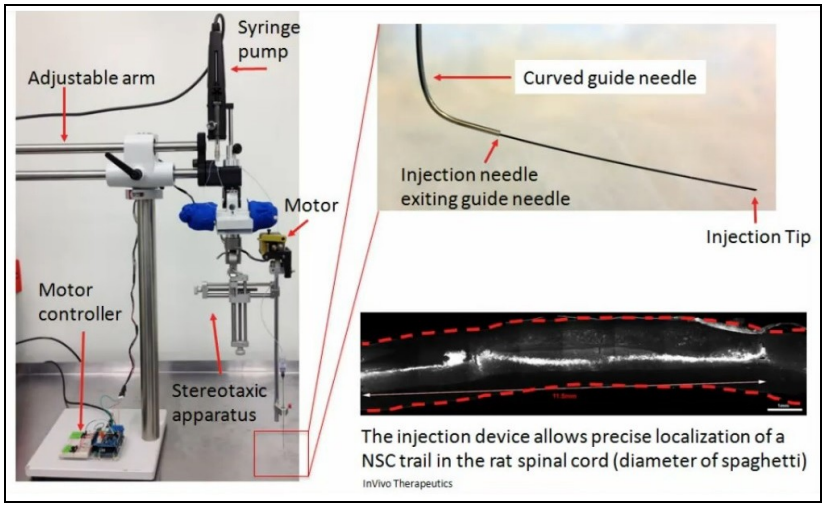
As per InVivo, the current practice is to inject boluses of stem cells in a perpendicular fashion via a needle, which lacks connectivity across the injury site, and can result in pressure/reflux issues as well as multiple injection sites and cell settling. InVivo is proposing to use a guide needle with a shape retaining injection needle in order to create a trail of stem cells across the lesion (*above*). The injected material is a soft, biomatrix containing neural stem cells that differentiate into neurons. InVivo's technique involves advancing the injection needle through a guide needle (with the assistance of fluoroscopy and ultrasound), and once fully extended, it is retracted with a motor. Subsequently, a syringe pump ejects the stem cells that create the neural trail. As the needles are retracted, a trail of cells is left behind, which InVivo believes will establishes immediate connectivity across the lesion site. As per InVivo, the injectable scaffold is a soft, biomaterial aimed to improve the viability, delivery and differentiation of the NSCs. The biomaterial is formed of a polymer, and serves as a scaffold with attachment sites for receptors on NSCs, which promotes migration of the cells. The biomaterial maintains homogenous cell suspension during shipment, and has the unique property of liquefying as it is injected, to only return back to a gel state in the body.

We believe what sets InVivo apart is that the company is focused on using neural stem cells that create neural connections as opposed to just injecting mesenchymal stem cells that give trophic support to existing cells within the spinal cord or just injecting cells that will turn into myelinating cells/axons. NSCs are able to differentiate into the 3 main cell types of the central nervous system (CNS): astrocytes, oligodendrocytes, and neurons, and these NSCs can help to repair the spinal cord via regeneration by secreting trophic factors, remyelinating bare axons, and/or establishing new neuronal connections.

The image below offers a representation of the patented surgical device and its various components:



A real-life setup of the equipment is shown below, with a visualization of injected NSCs in a rat spinal cord:



In order to support this strategy, InVivo has entered into agreements with the University of California, San Diego and James Guest, M.D., Ph.D., to expand the company's intellectual property portfolio. InVivo entered into an exclusive license agreement with UC San Diego for issued patent US 9,011,410 titled "***Spinal Multisegmental Cell and Drug Delivery System***," and into an assignment agreement with Dr. Guest for issued patent US 7,666,177 titled "***Method and System for Cellular Transplantation in the Spinal Cord***." InVivo also has filed a provisional application in support of the Bioengineered Neural Trails™ Program titled "***Methods and Systems for Delivery of a Trail of a Therapeutic Substance***." We believe that the patents in addition to the provisional patent application help solidify the IP portfolio for the Bioengineered Neural Trails for InVivo.

Next Steps for Bioengineered Neural Trails

According to the National Spinal Cord Injury Statistical Center, approximately 276,000 patients currently live with spinal cord injury in the U.S. with limited therapeutic options. Neural stem cell transplantation offers some promise, and we believe InVivo aims to tackle a huge unmet clinical need with its Bioengineered Neural Trails™ Program. The goal of the program is to improve neurological function in chronically injured patients.

We think it is a rational approach for the company to pursue this chronic SCI strategy, and in our opinion, is a natural next step for the company. Although it is too early for us to include sales of this product in our current model, the Bioengineered Neural Trails Program presents enormous potential upside to the InVivo story as the chronic SCI market is approximately 25x that of the acute SCI market.

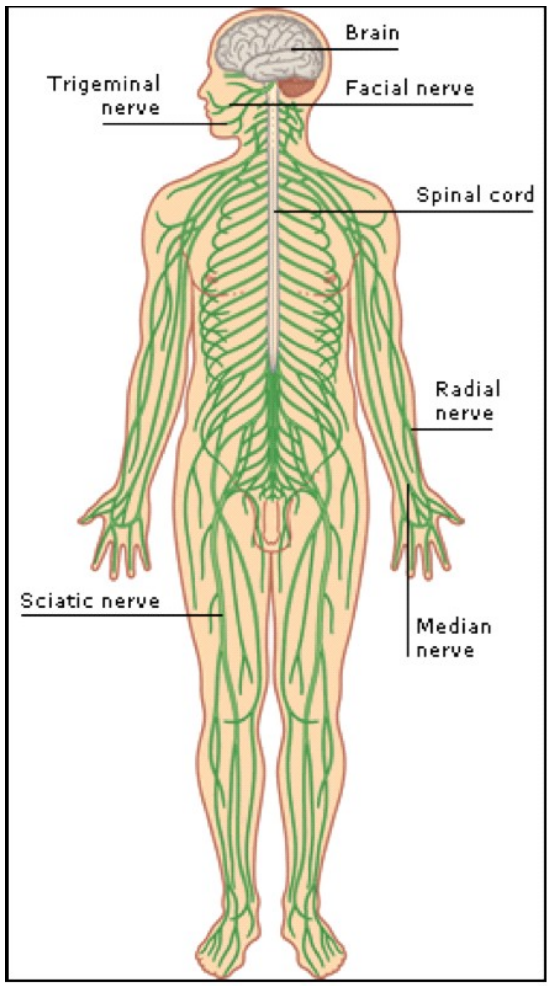
We will proceed to highlight some of the next steps for InViVo as it pertains to the chronic SCI program:

- Optimize all aspects of product profile in preparation for IND: instrumentation, biomaterial, and NSCs
- Strengthen and broaden intellectual property portfolio
- Aim to partner with a stem cell company to accelerate project timelines
- Target pre-IND meeting with the FDA by the end of 2016

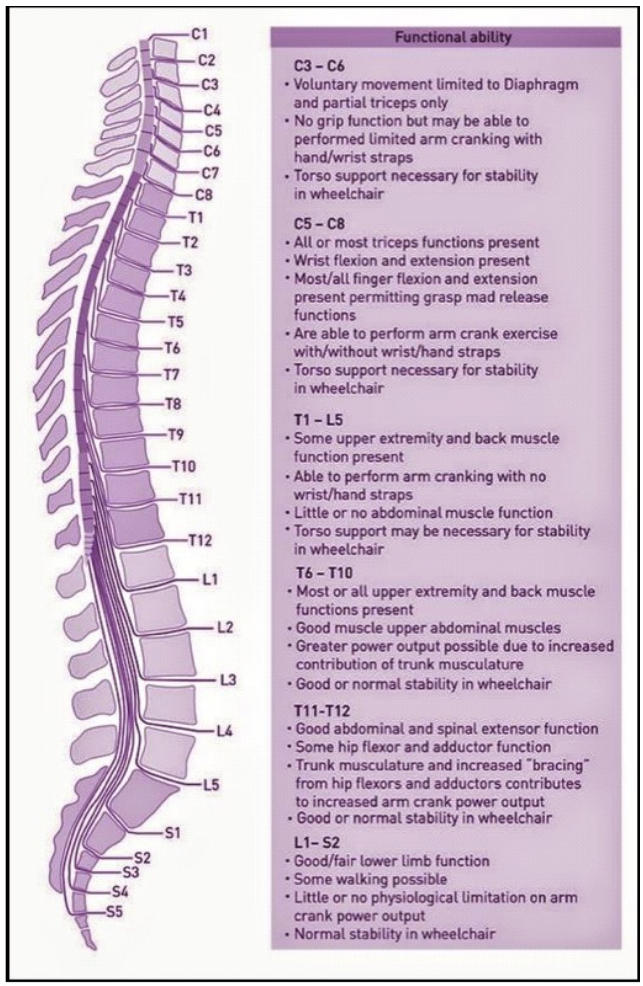
Combining the NSS device with neural stem cells is a sensible approach for treating chronic SCI patients and InVivo anticipates conducting a pre-IND meeting with the FDA by the end of 2016.

Review of Spinal Cord Anatomy

In order to understand spinal cord injuries in humans, it is important to understand how the spinal cord functions with the peripheral nerves in the body. The site of a spinal cord injury is not geographically associated with physiological control because there are sensory root ganglion that branch off from the central canal containing peripheral nerve cells that travel down the body to the pelvis, hips, legs, and feet. There are peripheral nerves that travel down the legs and attach to the central cord at regions all along the spine. The figures provided below depict the peripheral nerves and the different groups of vertebrae that control various regions of the body. For example, an injury at the C8 level just below the base of the neck will cause a loss of sensory and motor control to the chest, abdomen, pelvis, legs, and feet. However, the patient may still be able to move their fingers because this is controlled by peripheral nerves and dorsal root ganglia that attach at the C7 region of the spine.



Source: aviva.co.uk



Source: Michael Feger Paralysis Foundation

Injuries below the C8 level will likely leave arm and hand function unharmed. An injury at the L3 vertebra, located just below the belly button, will likely still allow a patient to roll their hips and contract their quadriceps muscles, as these are controlled by nerves that connect at the L1 and L2 region

Assessment of Spinal Cord Injuries

The American Spinal Injury Association (ASIA) impairment scale (AIS) describes a person's functional impairment as a result of their spinal cord injury. It is based on neurological responses, touch and pinprick sensations tested in each dermatome (area of the skin), and strength of the muscles that control ten key motions on both sides of the body, including hip flexion (L2), shoulder shrug (C4), elbow flexion (C5), wrist extension (C6), and elbow extension (C7). Traumatic spinal cord injury is classified into five categories on the ASIA Impairment Scale:

A = Complete. No sensory or motor function is preserved in the sacral segments S4-S5.

B = Sensory Incomplete. Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-S5 (light touch, pin prick at S4-S5: or deep anal pressure (DAP)), AND no motor function is preserved more than three levels below the motor level on either side of the body.

C = Motor Incomplete. Motor function is preserved below the neurological level, and more than half of key muscle functions below the single neurological level of injury (NLI) have a muscle grade less than 3 (Grades 0-2).

D = Motor Incomplete. Motor function is preserved below the neurological level, and at least half (half or more) of key muscle functions below the NLI have a muscle grade > 3.

E = Normal. If sensation and motor function are graded as normal in all segments, assuming the patient had prior deficits, then the AIS grade is E.

An individual lacking an initial SCI does not receive an AIS grade, so while AIS-E is considered "normal" sensory and motor control, this does not mean no injury is present. Also, for an individual to receive a grade of C or D, i.e. motor incomplete status, they must have either (1) voluntary anal sphincter contraction or (2) sacral sensory sparing with sparing of motor function more than three levels below the motor level for that side of the body. The standards at this time allows even non-key muscle function more than 3 levels below the motor level to be used in determining motor incomplete status (AIS-B vs. -C). When assessing the extent of motor sparing below the level for distinguishing between AIS-B and -C, the motor level on each side is used; whereas to differentiate between AIS-C and -D (based on proportion of key muscle functions with strength grade 3 or greater) the single neurological level is used.

The key takeaway from the ASIA Impairment Scale is the heavy focus on the sacral region S4-S5 in moving from AIS-A to AIS-B. As noted above, any injured subject with no sensory or motor function in the sacral segment S4-S5, which includes the sphincter muscle and region around and inside the anus, is classified as AIS-A. To move from AIS-A to AIS-B, the subject must demonstrate, at a minimum, sensory function of the S4-S5 region as assessed by light touch, pin-prick, or deep anal pressure. The key-gating factor in moving from AIS-B to AIS-C is motor control.

The Potential For the NSS is Enormous

Below we summarize the expenses for providing care to SCI patients. The first year, which is the highest cost year, represents initial hospital care and therapy, while the subsequent years largely represent ongoing home care costs. We note that the reduction in cost as a patient moves from higher levels of severity to lower levels is substantial. A one or two AIS grade improvement can have a multi-million dollar impact on lifetime patient costs and quality of life as an individual can become more independent and require less support from caregivers.

	Average Yearly Expenses (in 2014 dollars)		Estimated Lifetime Costs by Age At Injury (discounted at 2%)	
Severity of Injury	First Year	Each Subsequent Year	25 years old	50 years old
High Tetraplegia (C1–C4) AIS ABC	$1,064,716	$184,891	$4,724,181	$2,596,329
Low Tetraplegia (C5–C8) AIS ABC	$769,351	$113,423	$3,451,781	$2,123,154
Paraplegia AIS ABC	$518,904	$68,739	$2,310,104	$1,516,052
Motor Functional at Any Level AIS D	$347,484	$42,206	$1,578,274	$1,113,990

Data Source: Economic Impact of SCI published in the journal *Topics in Spinal Cord Injury Rehabilitation*, Volume 16, Number 4, in 2011.

Source: The National Spinal Cord Injury Statistical Center, Facts and Figures at a Glance. Birmingham, AL: University of Alabama at Birmingham, February 2015.

According to the NSCISC's February 2015 report "Spinal Cord Injury Facts and Figures at a Glance (*above*)," (i) during the first year, average "cost of care" ranges from around $350,000 to over $1 million, depending on the severity of the injury, and (ii) the total cost to maintain a paraplegic injured at age 25 for life is over $2.3 million. All of the patients that have been enrolled in the INSPIRE study have been paraplegia AIS-A, and so if we focus on this type of patient (Paraplegic AIS ABC on the chart below), the average yearly health care and living expense cost is over half a million dollars, with each subsequent year resulting in almost $70,000 of additional expenses. Due to the potential savings from an improvement in sensory and motor skills, we believe a cost for implantation of the NSS of $150,000 is a reasonable and conservative estimate for our financial modeling.

The potential we discuss above refers only to acute SCI under the HDE, which will serve a market size of approximately 4,000 patients. We continue to believe the NSS carries potential above the peak $600 million in product sales that we model which extends beyond acute spinal cord injury. After HDE approval, neurosurgeons may be able to use the device off-label in a large proportion of non-penetrating spinal cord injuries, regardless of the impairment level and injury location. Additionally, we feel it is a logical next step for the company to pursue the chronic SCI strategy via the Bioengineered Neural Trails Program. Although it is too early for us to include sales of this NSS seeded with NSCs product in our current model, the Bioengineered Neural Trails Program offers enormous upside if it ultimately proves successful. If the company is able to strike an alliance with a stem cell supplier and can move forward with seeding the NSS with neural-spinal stem cells in human patients, then the market opens up from approximately 12,000 acute patients per year to some 300,000 chronic patients, which represents a 25-fold increase.

Conclusion

There remains a huge unmet need in spinal cord injury as there are currently no commercially approved therapeutics (devices or drugs) to treat SCI. Currently, surgical intervention with rehabilitation is the standard-of-care in dealing with SCI patients.

InVivo's news regarding the successful conversion of four of seven active patients is a strong positive for the stock. While some have postulated that this early success may indicate an early filing for approval, we remind investors that the objective of the pivotal study is to show both probable benefit (which will be supported by surpassing the 25% hurdle) and safety, which may require observation of the full 20 patients throughout the six month term. While it is possible that the company may file early, we do not incorporate this into our expectations.

Shares of InVivo are well below their 12-month high despite the story continuing to unfold in a very positive manner. We believe the current price of the shares presents substantial upside as determined by our target price. As of December 31, 3015, InVivo had $20 million in cash on hand and raised an additional $30 million from the March share offering. These funds should be sufficient to support the company's operations until 2018 assuming the anticipated $1.4 million monthly cash burn rate continues.

Our current model forecasts the completion of the pivotal probable benefit study in 2017, an application for approval under HUD in late 2017 and ultimate approval in 2018. Our financial model assumes the INSPIRE trial reaches full enrollment on time, and that approval will be contingent upon showing safety and probable benefit in a larger number of patients. Based on our estimates and 10-year DCF model, we have determined a price target of $18 which uses a 15% discount rate and a 65% probability of approval.

PROJECTED FINANCIALS

InVivo Therapeutics Holdings Corp. - Income Statement

InVivo Therapeutics	2015 A	Q1 E	Q2 E	Q3 E	Q4 E	2016 E	2017 E	2018 E
Product Sales	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$51**
YOY Growth	-	-	-	-	-	-	-	-
Collaborative & Licensing	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$51**
YOY Growth	-					-	-	-
Cost of Goods / Services	$0	$0	$0	$0	$0	$0	$0	$0
Product Gross Margin	-	-	-	-	-	-	-	-
R&D	$10.1	$2.8	$3.0	$3.0	$3.2	$12.0	$15.0	$18.0
G&A	$12.3	$3.3	$3.5	$3.5	$3.7	$14.0	$16.0	$17.0
Operating Income	($22.4)	($6.1)	($6.5)	($6.5)	($6.9)	($26.0)	($31.0)	$16.5
Operating Margin	-	-	-	-	-	-	-	-
Net Other Income	($10.9)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Pre-Tax Income	($33.3)	($6.1)	($6.5)	($6.5)	($6.9)	($26.0)	($31.0)	$16.5
Taxes	$0	$0	$0	$0	$0	$0.0	$0.0	$0.0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0.0%*	*0.0%*	*0.0%*
Net Income	($33.3)	($6.1)	($6.5)	($6.5)	($6.9)	($26.0)	($31.0)	$16.5
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($1.26)**	**($0.19)**	**($0.20)**	**($0.19)**	**($0.20)**	**($0.78)**	**($0.86)**	**$0.44**
YOY Growth	-					-	-	-
Wt. Ave Shares Outstanding	26.5	31.3	33.0	34.4	35.0	33.4	36.0	37.0

Source: Company Filing // Zacks Investment Research, Inc. Estimates

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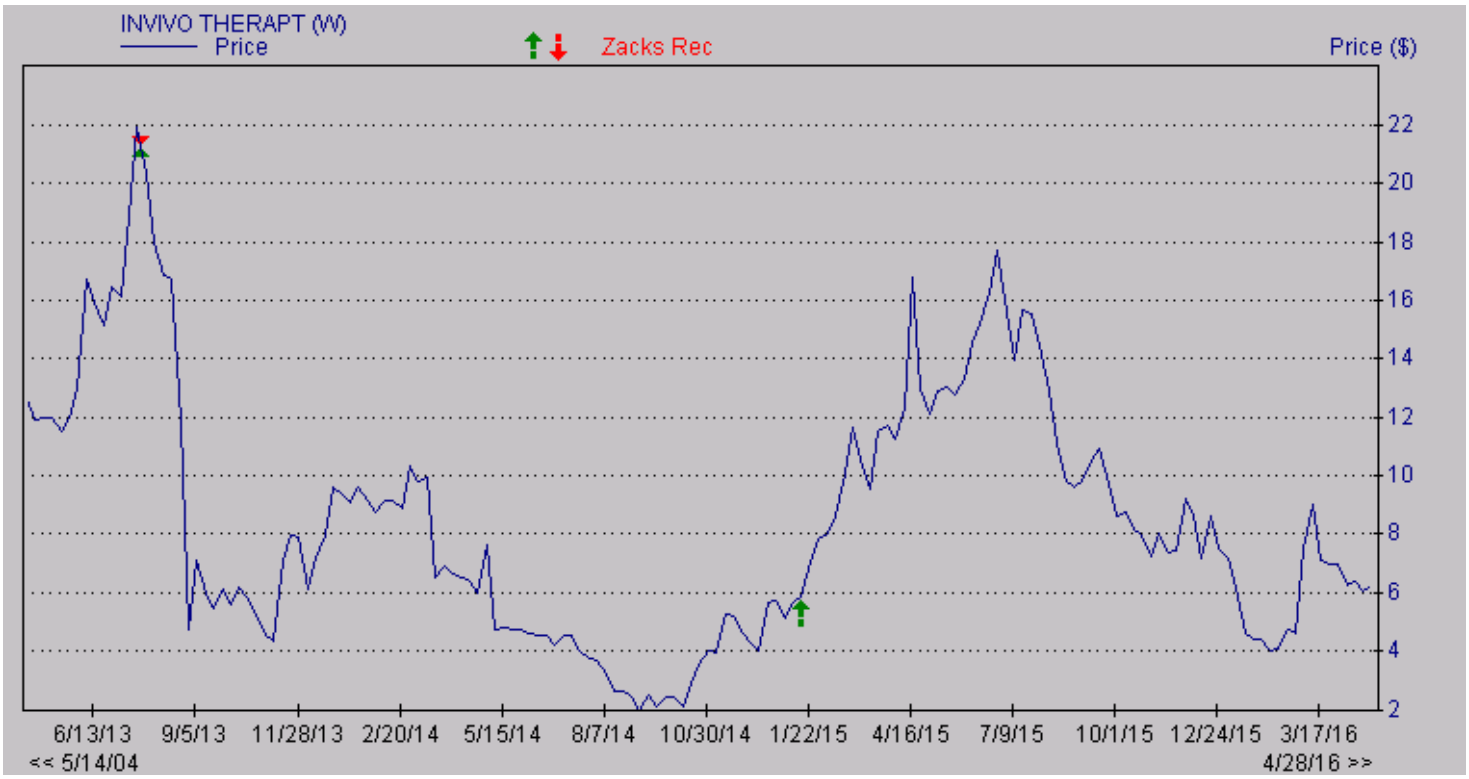
HISTORICAL STOCK PRICE



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