INVIVO THERAPEUTICS HOLDINGS CORP.
Form 424B3
March 13, 2018
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Filed pursuant to Rule 424(b)(3)
Registration Statement No. 333-222738

PROSPECTUS SUPPLEMENT NO. 1

(TO PROSPECTUS DATED FEBRUARY 12, 2018)

INVIVO THERAPEUTICS HOLDINGS CORP.

Up to 10,700,000 shares of Common Stock

This prospectus supplement No. 1 supplements and amends the prospectus dated February 12, 2018 related to the sale or other disposition from time to time of up to 10,700,000 shares of common stock, par value $0.00001 per share, of InVivo Therapeutics Holdings Corp., a Nevada corporation (the “Company,” “we,” “us” or “our”), issued and issuable to Lincoln Park Capital Fund, LLC, the selling stockholder named in the prospectus, also referred to as Lincoln Park, pursuant to a purchase agreement dated January 25, 2018 that we entered into with Lincoln Park. We are not selling any shares of common stock under this prospectus and will not receive any of the proceeds from the sale of the shares of common stock by the selling stockholder.

This prospectus supplement should be read in conjunction with the prospectus dated February 12, 2018, which is to be delivered with this prospectus supplement. This prospectus supplement is qualified by reference to the prospectus except to the extent that the information in this prospectus supplement supersedes the information contained in the prospectus. This prospectus supplement is not complete without, and may not be delivered or utilized except in connection with, the prospectus, including any amendments or supplements to it.

Our common stock is currently quoted on The Nasdaq Global Market under the symbol “NVIV.” On March 12, 2018, the last reported sale price of our common stock on The Nasdaq Global Market was $0.67 per share.

This prospectus supplement incorporates into our prospectus the information contained in our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, filed with the Securities and Exchange Commission on March 12, 2018 and attached hereto.

EXPERTS

The financial statements of InVivo Therapeutics Holdings Corp. as of December 31, 2017 and December 31, 2016 included in this prospectus supplement, have been so included in reliance on the audit report of RSM US LLP, an independent registered public accounting firm, given the authority of that firm as experts in accounting and auditing. The audit report of RSM US LLP included in this prospectus supplement includes an explanatory paragraph related to InVivo Therapeutics Holdings Corp. and its Subsidiary's ability to continue as a going concern.

Investing in our common stock involves risks. See "Risk Factors" beginning on page 8 of the prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the prospectus to which it relates are truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus supplement is March 13, 2018.

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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10 K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
FOR THE FISCAL YEAR ENDED DECEMBER 31, 2017
TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
FOR THE TRANSITION PERIOD FROM TO

COMMISSION FILE NUMBER 001 37350

INVIVO THERAPEUTICS HOLDINGS CORP.

(Exact name of registrant as specified in its charter)

Nevada	36 4528166
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
One Kendall Square, Suite B14402, Cambridge, Massachusetts	02139
(Address of principal executive offices)	(Zip Code)

(617) 863 5500

Registrant's telephone number, including area code

Securities registered pursuant to Section 12(b) of the Act:

Title of each class to be so registered	Name of exchange on which registered
Common Stock, $0.00001 par value	The Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act: None.

Indicate by check mark if the registrant is a well known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S K is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10 K or any amendment to this Form 10 K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b 2 of the Exchange Act. (Check one):

Large accelerated filer	Accelerated filer	Non accelerated filer (Do not check if a smaller reporting company)	Smaller reporting company
Emerging growth company			

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b 2 of the Act). Yes No

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant as of June 30, 2017, the last business day of the registrant's most recently completed second fiscal quarter, was $86,007,844 based on a per share price of $2.70, which was the closing price of the registrant's common stock on the Nasdaq Global Market on such date.

As of March 9, 2018, the number of shares outstanding of the registrant's common stock, $0.00001 par value per share, was 38,054,036.

DOCUMENTS INCORPORATED BY REFERENCE

None.

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INVIVO THERAPEUTICS HOLDINGS CORP.

ANNUAL REPORT ON FORM 10 K

FOR THE YEAR ENDED DECEMBER 31, 2017

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PART I

SPECIAL NOTE REGARDING FORWARD LOOKING STATEMENTS

This Annual Report on Form 10 K contains “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These statements include statements made regarding our commercialization strategy, future operations, cash requirements and liquidity, capital requirements, and other statements on our business plans and strategy, financial position, and market trends. In some cases, you can identify forward-looking statements by terms such as “may,” “might,” “will,” “should,” “believe,” “plan,” “intend,” “anticipate,” “target,” “estimate,” “expect,” and ot expressions. These forward-looking statements are subject to risks and uncertainties that could cause actual results or events to differ materially from those expressed or implied by the forward-looking statements in this Form 10-K, including factors such as our ability to raise substantial additional capital to finance our planned operations and to continue as a going concern; our ability to execute our strategy and business plan; our ability to obtain regulatory approvals for our products, including the Neuro-Spinal Scaffold™; our ability to successfully commercialize our current and future product candidates, including the Neuro-Spinal Scaffold; the progress and timing of our development programs; market acceptance of our products; our ability to retain management and other key personnel; our ability to promote, manufacture, and sell our products, either directly or through collaborative and other arrangements with third parties; and other factors detailed under “Risk Factors” in Part I, Item 1A of this Form 10-K. These forward looking statements are only predictions, are uncertain, and involve substantial known and unknown risks, uncertainties, and other factors which may cause our actual results, levels of activity, or performance to be materially different from any future results, levels of activity, or performance expressed or implied by these forward looking statements. Such factors include, among others, the following:

- our limited operating history and history of net losses;
- our ability to raise substantial additional capital to finance our planned operations and to continue as a going concern;
- our ability to initiate and complete the INSPIRE 2.0 Study to support our existing Humanitarian Device Exemption application;
- our ability to execute our strategy and business plan;
- our ability to obtain regulatory approvals for our current and future product candidates, including our Neuro-Spinal Scaffold implant;
- our ability to successfully commercialize our current and future product candidates, including our Neuro-Spinal Scaffold implant;

- the progress and timing of our current and future development programs;

- our ability to successfully open, enroll and complete clinical trials and obtain and maintain regulatory approval of our current and future product candidates;

- our ability to protect and maintain our intellectual property and licensing arrangements;

- our reliance on third parties to conduct testing and clinical trials;

- market acceptance and adoption of our current and future technology and products;

- our ability to promote, manufacture and sell our current and future products, either directly or through collaborative and other arrangements with third parties; and

- our ability to attract and retain key personnel.

We cannot guarantee future results, levels of activity, or performance. You should not place undue reliance on these forward looking statements, which speak only as of the date of this Annual Report on Form 10 K. These cautionary

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statements should be considered with any written or oral forward looking statements that we may issue in the future. Except as required by applicable law, including the securities laws of the United States, we do not intend to update any of the forward looking statements to conform these statements to reflect actual results, later events or circumstances, or to reflect the occurrence of unanticipated events.

As used herein, “we,” “us,” “our,” or the “Company” means InVivo Therapeutics Holdings Corp., together with its consolidated subsidiaries, unless otherwise noted.

Item 1. BUSINESS

Overview

We are a research and clinical-stage biomaterials and biotechnology company with a focus on treatment of spinal cord injuries, or SCIs. Our mission is to redefine the life of the SCI patient, and we seek to develop treatment options intended to provide meaningful improvement in patient outcomes following SCI. Our approach to treating acute SCIs is based on our investigational Neuro-Spinal Scaffold implant, a bioresorbable polymer scaffold that is designed for implantation at the site of injury within a spinal cord and is intended to treat acute SCI. The Neuro-Spinal Scaffold implant incorporates intellectual property licensed under an exclusive, worldwide license from Boston Children’s Hospital and the Massachusetts Institute of Technology. We also plan to evaluate other technologies and therapeutics that may be complementary to our development of the Neuro-Spinal Scaffold implant or offer the potential to bring us closer to our goal of redefining the life of the SCI patient.

Market Opportunity

Our clinical program is intended to address the lack of successful treatments for SCIs, which can lead to permanent paralysis, sensory impairment, and autonomic (bowel, bladder, and sexual) dysfunction. The current management of acute SCI is a surgical approach consisting of spine stabilization and an external decompression procedure of uncertain value. We believe the market opportunity for our Neuro-Spinal Scaffold implant is significant. It is estimated that approximately 285,000 people are currently living in the United States with paralysis due to SCI (chronic SCI), and approximately 15,000 individuals in the United States will become fully or partially paralyzed each year (acute SCI). We are pursuing regulatory approval from the U.S. Food and Drug Administration, or FDA, through the Humanitarian Device Exemption, or HDE, pathway. When this pathway was initiated for the Neuro-Spinal Scaffold implant, it was limited to populations of 4,000 or less patients per year. We were granted a Humanitarian Use Device, or HUD, designation for the Neuro-Spinal Scaffold implant, which includes thoracic and cervical patients afflicted with complete (no motor or sensory function in the lowest sacral segments) SCI, such as paraplegia or tetraplegia, and excludes gunshot or other penetrating wounds. Recently, the 21st Century Cures Act increased the upper population limit for an HDE from 4,000 to 8,000, which allows us to potentially request an expansion of our

current HUD to include additional SCI patients, i.e., incomplete (partial sensory or sensory/motor function below the injury site, including the lowest sacral segments) SCI patients. Future products, which may include use of stem cells or drug ingredients, may enable the treatment of a broader population such as patients with chronic paralysis and would require separate regulatory approval.

Since 1973, the National Spinal Cord Injury Statistical Center, or NSCISC, at the University of Alabama has been commissioned by the U.S. government to maintain a national database of SCI statistics. The financial impact of SCIs, as reported by the NSCISC, is substantial. Direct costs, which include hospital and medical expenses, modification of the home, and personal assistance, are highest in the first year after injury. According to the fact sheet published in 2017 by NSCISC titled “Spinal Cord Injury—Facts and Figures at a Glance”, (i) during the first year, average cost of care ranges from $352,279 to $1,079,412, depending on the severity of the injury, (ii) the net present value, or NPV, to maintain a quadriplegic injured at age 25 for life is $4,789,384, and (iii) the NPV to maintain a paraplegic injured at age 25 for life is $2,341,988. These costs place a tremendous financial burden on families, insurance providers, and government agencies. Moreover, despite such a significant financial investment, the patient often remains disabled for life because current medical interventions address only the symptoms of SCI rather than the underlying neurological cause. We believe our approach could represent an important advance in the treatment of SCIs.

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The American Spinal Injury Association, or ASIA, in collaboration with the International Spinal Cord Society, or ISCoS, has developed a neurologic examination tool for assessing SCI known as the International Standards for Neurological Classification of Spinal Cord Injury, or ISNCSCI. Results of the ISNCSCI examination are used to determine the ASIA Impairment Scale, or AIS, classification.

Patients with complete SCI are classified as AIS A. Patients with incomplete SCI, who have partial sensory and/or motor function below the level of injury, including the lowest sacral segments, are classified as AIS B (partial sensory function), AIS C (partial sensory and motor function), or AIS D (partial sensory and increased motor function, i.e., can move at least half of the muscles against gravity). Patients who have a complete return of sensory and motor function are classified as AIS E.

These classifications are based upon the ISNCSCI examination in which an examiner performs a neurologic examination to assess sensory function of the entire body and motor function of the upper and lower extremities.

Our Clinical Program

We currently have one clinical development program for the treatment of acute SCI.

Neuro-Spinal Scaffold Implant for acute SCI

Our Neuro-Spinal Scaffold implant is an investigational bioresorbable polymer scaffold that is designed for implantation at the site of injury within a spinal cord. The Neuro-Spinal Scaffold implant is intended to promote appositional, or side-by-side, healing by supporting the surrounding tissue after injury, minimizing expansion of areas of necrosis, and providing a biomaterial substrate for the body’s own healing/repair processes following injury. We believe this form of appositional healing may spare white matter, increase neural sprouting, and diminish post-traumatic cyst formation.

The Neuro-Spinal Scaffold implant is composed of two biocompatible and bioresorbable polymers that are cast to form a highly porous investigational product:

· Poly lactic-co-glycolic acid, a polymer that is widely used in resorbable sutures and provides the biocompatible support for Neuro-Spinal Scaffold implant; and

· Poly-L-Lysine, a positively charged polymer commonly used to coat surfaces in order to promote cellular attachment.

Because of the complexity of SCIs, it is likely that multi-modal therapies will be required to maximize positive outcomes in SCI patients. In the future, we may attempt to further enhance the performance of our Neuro-Spinal Scaffold implant by multiple combination strategies involving electrostimulation devices, additional biomaterials, drugs approved by the FDA, or growth factors. We expect the Neuro-Spinal Scaffold implant to be regulated by the FDA as a Class III medical device.

Preclinical and Non-clinical Studies relating to the Neuro-Spinal Scaffold

SCI can result in permanent paralysis, sensory impairment, and autonomic (bowel, bladder, and sexual) dysfunction. These functional deficits result from damage to or loss of cells (neurons and glia) in the affected region of the spinal cord, either from the initial mechanical trauma or through secondary mechanisms that persist for several weeks. The ability of potential treatments for SCI to mitigate loss of function or promote recovery can be evaluated with non-clinical models using different species and different methods of inducing SCI. In our preclinical studies, we utilized rat, non-human primate, and pig models because each exhibits a pattern of neuropathology following SCI that is similar to human SCI. Hemicordectomy injury models, in which sections of spinal cord are surgically removed, are useful in the evaluation of treatment strategies that involve device implantation. Unilateral hemicordectomy models preserve function on one side of the cord, resulting in improved recovery of bladder and bowel function. We, therefore, evaluated the bioresorbable polymer scaffold device in both rats and non-human primates with unilateral hemicordectomy injury. Because most human SCIs are non-penetrating contusion injuries resulting from rapid compression of spinal tissue by intrusion of bone or disc material following mechanical disruption of the vertebral column, we also evaluated the bioresorbable polymer scaffold device in rat and pig models of spinal contusion injury.

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Our first non-clinical study was conducted by founding scientists of our wholly-owned subsidiary in rats with surgically induced unilateral spinal cord hemicordectomy injury. This study (see Teng, Y. D., et al., Functional recovery following traumatic spinal cord injury mediated by a unique polymer scaffold seeded with neural stem cells, Proceedings of the National Academy of Sciences 99, pg. 3024-3029, 2002) demonstrated the baseline safety and efficacy of porous, biodegradable scaffolds fabricated from PLGA-PLL polymer. Subsequently, the safety and efficacy of implantation of the bioresorbable polymer scaffold device was evaluated in rats with spinal cord contusion injury. Initial studies suggest that 24 hours after contusion injury was an appropriate time for device implantation based on both histological evaluation and ex vivo Magnetic Resonance Imaging, or MRI, techniques. Based on these results, we conducted larger rat contusion studies in our laboratory. We evaluated functional recovery with the 21-point Basso, Beattie, and Bresnahan, or BBB, locomotor rating scale to assess open field locomotion. In the first model, the BBB score was not improved by the scaffold device. However, implantation of the bioresorbable polymer scaffold device into the necrotic zone of the injured spinal cord resulted in appositional healing and tissue remodeling that preserved spinal cord architecture. Morphometric analysis of spinal sections stained with hematoxylin & eosin revealed that non-implanted rats with contusion injury developed large cavities surrounded by a thin rim of spared white matter. In contrast, rats treated with the implanted bioresorbable polymer scaffold device demonstrated decreased cavity volume along with increased amounts of spared and remodeled tissue at the lesion epicenter. Immunofluorescence labeling within the remodeled tissue identified high levels of laminin, an absence of GFAP-positive astrocytes, as well as beta-3 tubulin positive axons. This indicated that the bioresorbable polymer scaffold device supports tissue formation and remodeling favorable for axon regrowth. Following spinal contusion injury, myelin-producing nerve cells called Schwann cells arise from either injured nerve roots or endogenous sources within the central nervous system. The Schwann cells migrate into the injury region, promoting axonal growth and remyelinating segmentally demyelinated axons. In rats implanted with the bioresorbable polymer scaffold device, we observed that Schwann cell myelination was extensive within preserved penumbra white matter and also that Schwann cell myelination was detected within the remodeled tissue. These results indicate that implantation of the bioresorbable polymer scaffold device in the acutely injured rat spinal cord can provide the benefit of preserving spinal cord architecture through reduced cavitation, and promotion
of white matter sparing and tissue remodeling supportive to axon sprouting and spinal cord activity.

The spinal cord anatomy of non-human primates is very similar to that of humans. We performed a series of studies in African green monkeys to evaluate the bioresorbable polymer scaffold device in a non-human primate. Our first study in African green monkeys established that unilateral thoracic hemicordectomy SCI (a new model in this species) produced a consistent functional deficit, and we observed a consistently positive response to scaffold implantation (see Pritchard, et al., Establishing a model spinal cord injury in the African green monkey for the preclinical evaluation of biodegradable polymer scaffolds seeded with human neural stem cells, Journal of Neuroscience Methods 188, pg. 258- 269, 2010). We then conducted two larger studies evaluating the safety and efficacy of the bioresorbable polymer scaffold device in the African green monkey (see Slotkin, J.R., Pritchard, et al., Biodegradable scaffolds promote tissue remodeling and functional improvement in non-human primates with acute spinal cord injury. Biomaterials, 123, pp. 63-76). The extent and time course of functional recovery in biopolymer implant-treated primates was assessed with video capture and KinemaTracer evaluation of locomotor behavior with synchronous electromyography recording along with locomotor observation rating. When the results of these two studies were combined and analyzed together, we found that implantation of the bioresorbable polymer scaffold device resulted in an increase in remodeled tissue in the region of the hemicordectomy compared to non-implant controls, and improved recovery of locomotion in subjects with full unilateral hemicordectomy lesions (see Slotkin, J.R., et al., Biodegradable scaffolds promote tissue remodeling and functional improvement in non-human primates with acute spinal cord injury, Biomaterials, 123, pg. 63-76, 2017).

The pig has been used as a large animal model of spinal cord contusion injury due to similarities in size and structure to the human spinal cord. We evaluated the surgical feasibility of implanting the bioresorbable polymer scaffold device in a spinal cord after a contusion injury in a pig model. Severe contusion injuries were created in Gottingen pigs with a weight drop apparatus. At approximately 4, 6, and 24 hours after contusion injury, the pigs underwent the bioresorbable polymer scaffold device surgical implantation procedure. At each time point, a large volume of necro-hemorrhagic fluid and debris rapidly effluxed from the injury site, releasing built-up pressure and resulting in a substantial cavity in the center of the spinal cord. Increased spinal tissue pressure after contusion injury results in reduced blood perfusion and ischemia in damaged spinal tissue, and is an important contributor to the pathophysiology of SCI. As part of our study, we placed bioresorbable polymer scaffold devices into the resulting contusion-induced spinal cord cavity. We measured intraspinal pressure (using catheter pressure probes) at the contusion epicenter in the pigs before, during, and after the surgical procedure. As expected, contusion injury elevated intraspinal

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tissue pressure compared to normal values. Surgical implantation of the bioresorbable polymer scaffold device resulted in a return of intraspinal tissue pressure to physiologically normal levels.

Taken together, these non-clinical studies in two rat SCI models, the African green monkey unilateral hemicordectomy injury model, and the pig contusion injury model demonstrate that the bioresorbable polymer scaffold device, surgically implanted at the epicenter of the wound after an acute SCI, acts by appositional healing to help spare spinal cord tissue, decrease post-traumatic cyst formation, decrease spinal cord tissue pressure, and promote tissue remodeling supportive to axon sprouting and spinal cord activity.

Completed Pilot Study

We conducted an early feasibility human pilot study, as the initial phase of a larger pivotal study, of our Neuro-Spinal Scaffold under our approved Investigational Device Exemption, or IDE, application for the treatment of complete, traumatic acute SCI. The study was intended to assess the safety and feasibility of the Neuro-Spinal Scaffold for the treatment of complete thoracic functional SCI, as well as to gather preliminary evidence of the clinical effectiveness of the Neuro-Spinal Scaffold.

The pilot study was initially approved for five subjects in up to six clinical sites across the United States, and was later modified to increase the number of allowable clinical sites to up to 20 and to permit enrollment of up to 10 subjects. The pilot study was initially staggered such that each patient that met the eligibility criteria would be followed for three months prior to enrolling the next patient in the study. In December 2014, the FDA approved an expedited enrollment plan that allowed us to continue enrolling patients more rapidly barring any significant safety issues. We enrolled five subjects in the pilot study between October 2014 and September 2015. The FDA approved conversion of this pilot study to a pivotal probable benefit study, which we refer to as The INSPIRE Study, that includes data from the patients enrolled in the pilot study.

The INSPIRE Study

Our Neuro-Spinal Scaffold implant has been studied in 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, under an Investigational Device Exemption application for the treatment of neurologically complete thoracic traumatic acute SCI. We commenced an FDA-approved pilot study in 2014 that the FDA approved converting into The INSPIRE Study in January 2016. As of December 31, 2017, we had implanted our Neuro-Spinal Scaffold implant in a total of 19 patients in The INSPIRE Study, 16 of whom reached the six month primary endpoint visit, and three of whom died. In July 2017, after the third patient death, enrollment of patients in The INSPIRE Study was placed on hold as we engaged with the FDA to address the patient deaths. We subsequently closed enrollment in The INSPIRE Study and will follow the remaining active subjects until completion. Following discussions with the FDA, in March

2018, we received FDA approval for a randomized controlled trial to supplement the existing clinical evidence for the Neuro-Spinal Scaffold implant that we obtained from The INSPIRE Study. We refer to this herein as the INSPIRE 2.0 Study.

The purpose of The INSPIRE Study, which was the original study, was to evaluate whether the Neuro-Spinal Scaffold implant is safe and demonstrates probable benefit for the treatment of complete T2-T12 neurological level of injury (NLI) SCI. The primary endpoint was defined as the proportion of patients achieving an improvement of at least one AIS grade at six months' post-implantation. Additional endpoints included measurements of pain, sensory and motor scores, bladder and bowel function, Spinal Cord Independence Measure (a disability scale for patients with SCI), and quality of life. The INSPIRE Study included an Objective Performance Criterion, or OPC, which is a measure of study success used in clinical studies designed to demonstrate safety and probable benefit in support of an HDE approval. At the time enrollment of patients in The INSPIRE Study was placed on hold, the OPC was defined as 25% or more of the patients in the study demonstrating an improvement of at least one AIS grade at the six month post-implantation visit.

The FDA approved the enrollment of up to 30 patients in The INSPIRE Study so that there would be at least 20 evaluable patients at the primary endpoint analysis, accounting for events such as screen failures or deaths that would prevent a patient from reaching the primary endpoint visit. Of the 19 patients implanted in The INSPIRE Study, 16 patients have reached the six-month primary endpoint visit. Of these 16, seven had improved from complete AIS A SCI to incomplete SCI (two patients to AIS C and five patients to AIS B) at the six-month primary endpoint visit and nine had not demonstrated improvement at that visit. Three of the seven patients who improved were assessed to have AIS B SCI at the six-month primary endpoint and were later assessed to have improved to AIS C SCI at the 12 or 24-month

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visits. Two of the 16 patients were initially assessed to have improved from complete AIS A SCI to incomplete AIS B SCI, but each was later assessed to have reverted to complete AIS A SCI prior to the six-month examination. One of these two was then assessed at the six-month visit to have improved again to AIS B and the other remained AIS A. Since we have closed enrollment, the target of enrolling 20 evaluable patients into The INSPIRE Study will not be reached.

The FDA had previously recommended that we include a randomized, concurrent control arm in The INSPIRE Study. Acting on the FDA's recommendation, we proposed and received approval for the INSPIRE 2.0 Study (described below) to supplement the existing clinical evidence for the Neuro-Spinal Scaffold implant. In addition, as one source of comparator data, we initiated the Contemporary Thoracic SCI Registry Study, or the CONTEMPO Registry Study. The CONTEMPO Registry Study will utilize existing databases and registries to develop a historical comparator that, to the extent possible, matches patients to those patients enrolled in The INSPIRE Study. The CONTEMPO Registry Study is designed to provide comprehensive natural history benchmarks for The INSPIRE Study results that include SCI patients with similar baseline characteristics treated since 2006. The CONTEMPO Registry Study includes data from the Christopher & Dana Reeve Foundation North American Clinical Trials Network Registry, as well as the Model Systems Registry and the European Multicenter Study about Spinal Cord Injury. We anticipate that there will be between 100 to 200 patients in the CONTEMPO Registry Study. We have submitted a protocol for the CONTEMPO Registry Study to the FDA. We cannot be certain what additional information or studies will be required by the FDA to approve our HDE submission.

INSPIRE 2.0 Study

Our Neuro-Spinal Scaffold implant has been approved to be studied under our approved IDE in the INPSIRE 2.0 Study, which is titled the "Randomized, Controlled, Single-blind Study of Probable Benefit of the Neuro-Spinal Scaffold™ for Safety and Neurologic Recovery in Subjects with Complete Thoracic AIS A Spinal Cord Injury as Compared to Standard of Care." The purpose of the INSPIRE 2.0 Study is to assess the overall safety and probable benefit of the Neuro-Spinal Scaffold for the treatment of neurologically complete thoracic traumatic acute SCI. The INSPIRE 2.0 Study is designed enroll 10 subjects into each study arm, which we refer to as the Scaffold Arm and the Comparator Arm. Patients in the Comparator Arm will receive standard of care, which is spinal stabilization without dural opening or myelotomy. The INSPIRE 2.0 Study is a single blind study, meaning that the patients and assessors are blinded to treatment assignments. The FDA approved the enrollment of up to 35 patients in this study so that there would be at least 20 evaluable patients (10 in each study arm) at the primary endpoint analysis, accounting for events such as screen failures or deaths that would prevent a patient from reaching the primary endpoint visit. We may conduct the INSPIRE 2.0 Study at up to 26 sites in the United States. Enrolling patients in the INSPIRE 2.0 Study will also require the approval of the IRBs at each clinical site. We estimate that from study initiation, enrollment will take an approximately 18 months, and the total time to completion of the INSPIRE 2.0 study is estimated to be two years from study initiation.

The primary endpoint is defined as the proportion of patients achieving an improvement of at least one AIS grade at six months post-implantation. Assessments of AIS grade are at hospital discharge, three months, six months, 12 months and 24 months. The definition of study success for INSPIRE 2.0 is that the difference in the proportion of

subjects who demonstrate an improvement of at least one grade on AIS assessment at the six-month primary endpoint follow-up visit between the Scaffold Arm and the Comparator Arm must be equal to or greater than 20%. In one example, if 50% of subjects in the Scaffold Arm have an improvement of AIS grade at the six-month primary endpoint and 30% of subjects in the Comparator Arm have an improvement, then the difference in the proportion of subjects who demonstrated an improvement is equal to 20% (50% minus 30% equals 20%) and the definition of study success would be met. In another example, if 40% of subjects in the Scaffold Arm have an improvement of AIS grade at the six-month primary endpoint and 30% of subjects in the Comparator Arm have an improvement, then the difference in the proportion of subjects who demonstrated an improvement is equal to 10% (40% minus 30% equals 10%) and the definition of study success would not be met. Additional endpoints include measurements of changes in NLI, sensory levels and motor scores, bladder, bowel and sexual function, pain, Spinal Cord Independence Measure (a disability scale for patients with SCI), and quality of life.

We received approval for the INSPIRE 2.0 Study in early March. We believe this sets us in a direction towards a path to approval under the HDE regulatory program, and we are focused on exploring financing mechanisms to support the INSPIRE 2.0 Study.

Although The INSPIRE Study is structured with the OPC as the primary component for demonstrating probable

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benefit, the OPC is not the only variable that the FDA would evaluate when reviewing a future HDE application. Similarly, while our planned INSPIRE 2.0 Study is structured with a definition of study success requiring a minimum difference between study arms in the proportion of subjects achieving improvement, that success definition is not the only factor that the FDA would evaluate in the future HDE application. Approval is not guaranteed if the OPC is met for The INSPIRE Study or the definition of study success is met for the INSPIRE 2.0 Study, and even if the OPC or definition of study success are not met, the FDA may approve a medical device if probable benefit is supported by a comprehensive review of all clinical endpoints and preclinical results, as demonstrated by the sponsor's body of evidence.

In 2016, the FDA accepted our proposed HDE modular shell submission and review process for the Neuro-Spinal Scaffold implant. The HDE modular shell is comprised of three modules: a preclinical studies module, a manufacturing module, and a clinical data module. As part of its review process, the FDA reviews modules, which are individual sections of the HDE submission, on a rolling basis. Following the submission of each module, the FDA reviews and provides feedback, typically within 90 days, allowing the applicant to receive feedback and potentially resolve any deficiencies during the review process. Upon receipt of the final module, which constitutes the complete HDE submission, the FDA makes a filing decision that may trigger the review clock for an approval decision. We submitted the first module in March 2017 and received feedback in June 2017. We are working on responses to the FDA's questions and plan to submit an updated preclinical module in 2018. The HDE submission will not be complete until the manufacturing and clinical modules are also submitted.

Intellectual Property

We rely on a combination of patents, licenses, trade secrets, and non-disclosure agreements to develop, protect, and maintain our intellectual property. Our patent portfolio includes patents and patent applications. We seek to develop or obtain intellectual property that we believe might be useful or complementary with our products and technologies, including by way of licenses or acquisitions of other companies or intellectual property from third parties.

We hold an exclusive worldwide license to a broad suite of patents co-owned by BCH and MIT covering the use of a wide range of polymers to treat SCI, and to promote the survival and proliferation of human stem cells in the spinal cord, or the BCH License. Issued patents and pending patent applications licensed under the BCH License cover the technology underlying our Neuro- Spinal Scaffold implant and the use of a wide range of biomaterial scaffolding for treating SCI by itself or in combination with drugs, growth factors, or human stem cells. The BCH License covers eight issued United States patents and 16 issued international patents expiring between 2018 and 2027, and one pending United States patent application and seven pending international patent applications.

The BCH License has a term of 15 years from the effective date of July 2, 2007, or as long as the life of the last expiring patent right under the license, whichever is longer, unless terminated earlier by BCH. In connection with our acquisition of the BCH License, we submitted to a 5-year development plan to BCH and MIT that includes certain targets and projections related to the timing of product development and regulatory approvals. We are required to

either meet the stated targets and projections in the plan, or notify BCH and revise the plan. BCH has the right to terminate the BCH License for failure by us to either meet the targets and projections in the plan or our failure to submit an acceptable revision to the plan within a 60-day cure period after notification by BCH that we are not in compliance with the plan. We are currently in compliance with the development plan.

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