InVivo Therapeutics
Developing Innovative Products for Spinal Cord Injury
Forward-Looking Statements

Before we begin, we would like to remind everyone that during our presentation, we will be making forward-looking statements about our business, plans, and objectives. These statements are based on how we see things today. These statements can be identified by words such as believes, estimates, expects, or similar references to the future, and include statements we may make regarding our product development strategy, business prospects, and clinical and operational milestones. We wish to caution you that actual events or results may differ materially from those expressed in forward-looking statements made by us or on our behalf. For more information on the many factors that can result in actual performance differing from our forward-looking statements, please see our filings made with the SEC, including our 2015 Annual Report on Form 10-K filed on March 4, 2016 and our Quarterly Reports on Form 10-Q filed on May 6, 2016 and August 4, 2016.
Neuro-Spinal Scaffold™ for Acute SCI
Designed to Promote Healing in Spinal Cord Injury
InVivo’s Pioneering Clinical Approach for Acute SCI: The *Neuro-Spinal Scaffold™*

- Highly porous biopolymer *Neuro-Spinal Scaffold*
- Composition:
  - PLGA is the biodegradable skeleton along which cells can grow
  - Poly-L-Lysine promotes cellular adhesion
Two Types of Spinal Cord Injury: Closed (Contusion) vs Open (Compound) Injury

**Closed (Contusion) Injury**
- Outer region of cord is preserved and cord appears intact externally
- Injury leads to cavity filled with necrotic material
- Pressure builds inside the cord, which may lead to further injury
- Preclinical model: contusion injury

**Open (Compound) Injury**
- Outer region of cord is breached and injury is visible externally
- Myelotomy (cutting into the cord) may not be required
- Minimal added pressure inside cord
- Preclinical model: hemicordectomy
Progression of Acute SCI to Post-Traumatic Cavity in Contusion Injuries

- Spinal Cord Injury
- Hemorrhage & Spinal Cord Swelling
- Reduced Blood Flow & Ischemic Necrosis
- Cavity Development & White Matter Reduction
- Chronic injury and mature cavity formation

### Time

- **Normal**
  - Highly vascularized gray matter
  - White matter

- **2 hours after SCI**
  - Acute hemorrhage & necrosis

- **24 hours after SCI**
  - Liquefactive necrosis

- **12 weeks after SCI**
  - Mature cavity

*Histology from rat contusion model of SCI*
First *Neuro-Spinal Scaffold™* Implantation in Human Contusion Injury
The **Neuro-Spinal Scaffold™** Preserves Macroscopic Spinal Cord Architecture

**Rat Acute Spinal Cord Contusion Injury (at 12 weeks)**

**Cyst Reduction**

**White Matter Sparing**

**Remodeled Tissue**

*Cyst Reduction*

*Cavity Volume (mm³)*

**Control**

**Neuro-Spinal Scaffold**

*P<0.05*

**White Matter Width (mm)**

**Control**

**Neuro-Spinal Scaffold**

*P<0.05*

**Remodeled Tissue Volume (mm³)**

**Control**

**Neuro-Spinal Scaffold**

*P<0.05*
The **Neuro Spinal Scaffold™** Increases Remodeled Tissue Supporting Neural Regeneration

Rat Acute Spinal Cord Contusion Injury (at 12 weeks)

**Control**

- Minimal neuro-permissive matrix

**Neuro-Spinal Scaffold**

- Remodeled tissue with extensive neuro-permissive matrix

- Neuro-permissive matrix supports neural regeneration

Company images
Neural Regeneration and Remyelination with Schwann Cells after *Neuro-Spinal Scaffold™* Implantation

**Contusion Injury**
Central epicenter (a) and white matter (b)

**Epicenter**
Schwann Cells aid neural regeneration

**White Matter**
Schwann Cells restore signal transduction

Inset: Schwann cells ensheathing axons

Rat Acute Spinal Cord Contusion Injury (at 12 weeks)

Oligodendrocytes  Schwann Cells
Neuro-Spinal Scaffold™ Promotes Neural Regeneration and Functional Recovery

Primate Hemicordectomy Model (at 3 Months)

- Increased remodeled tissue
- Neural regeneration: Myelin basic protein stained axons in remodeled tissue
- Improved functional recovery

Hemicordectomy Model

Slotkin JR et al., manuscript submitted
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**

- Designed as 20-patient pivotal study to be used for HDE application
  - Endpoint: improvement in ASIA Impairment Scale (AIS) grade by 6 months

- Objective Performance Criterion (study success definition) – at least 25% of patients improve AIS grade by 6 months

- Additional Endpoints: sensory and motor scores, bladder and bowel function, Spinal Cord Independence Measure, pain, quality of life

- 23 clinical sites (US and Canada)
  - Plan also to include United Kingdom clinical sites in 2016

**NOTE:** FDA has recommended inclusion of a control arm in the study as part of a Study Design Consideration (SDC). As is typical of the regulatory process, InVivo has previously addressed a number of SDCs regarding the study. InVivo is engaged in a discussion with the FDA regarding this SDC and will provide an update if substantial changes are made to the study protocol. InVivo continues to believe that the current study design is sufficient to demonstrate safety and probable benefit in support of an HDE application for marketing approval.
Promising Neurologic Outcomes and Favorable Safety Profile in The INSPIRE Study

<table>
<thead>
<tr>
<th>Subject</th>
<th>Neurologic Level of Injury</th>
<th>Injury Type</th>
<th>Time to Implant</th>
<th>Neurologic Outcome to Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>T11</td>
<td>Closed</td>
<td>9 hrs.</td>
<td>Converted to AIS C at 1 month</td>
</tr>
<tr>
<td>2</td>
<td>T7</td>
<td>Open</td>
<td>46 hrs.</td>
<td>Remains AIS A at 12 months</td>
</tr>
<tr>
<td>3</td>
<td>T4</td>
<td>Closed</td>
<td>83 hrs.</td>
<td>Converted to AIS B at 1 month</td>
</tr>
<tr>
<td>4</td>
<td>T3</td>
<td>Closed</td>
<td>53 hrs.</td>
<td>Remains AIS A at 6 months</td>
</tr>
<tr>
<td>5</td>
<td>T8</td>
<td>Open</td>
<td>69 hrs.</td>
<td>Converted to AIS B at 6 months</td>
</tr>
<tr>
<td>6</td>
<td>T10</td>
<td>Open</td>
<td>9 hrs.</td>
<td>Converted to AIS B at 2 months</td>
</tr>
<tr>
<td>7</td>
<td>T3</td>
<td>Closed</td>
<td>21 hrs.</td>
<td>Remains AIS A at 3 months</td>
</tr>
<tr>
<td>9</td>
<td>T4</td>
<td>Open</td>
<td>40 hrs.</td>
<td>Converted to AIS B at 3 months</td>
</tr>
</tbody>
</table>

Note: Subjects 8 and 10 passed away with the cause of death deemed unrelated to Neuro-Spinal Scaffold™ or implantation

- No obvious correlations between AIS conversions and injury level or type or time to implant
- Conversions observed with open injuries unlikely to benefit from surgical decompression alone
- Delayed and prolonged recoveries indicate that neural regeneration may be taking place beyond the acute injury period
Marked Long-term Improvement in First Patient

- Improved from T11 complete AIS A to AIS C at 1 month
  - <5% of AIS A patients with a T10-T12 injury progress to AIS C or D at 1 month \(^1\)
- Regained bowel function and improved bladder function
- Continued significant motor improvement from months 6 to 12

\(^1\) Zariffa et al., Spinal Cord (2011)
InVivo’s Chronic SCI Product: Bioengineered Neural Trails™

Neural Stem Cells Incorporated into an Injectable Scaffold for Minimally-Invasive Delivery
Bioengineered Neural Trails™: InVivo’s Novel Neural Stem Cell Product for Chronic SCI

- Neural stem cells incorporated into an injectable scaffold for minimally-invasive delivery designed to:
  - Bridge the site of injury to create neuronal detour circuits
  - Activate the resting potential of network below injury site
Bioengineered Neural Trails Provide Many Advantages Over Conventional Bolus Injections

**Bolus approach**
- Reflux at multiple injection sites
- Sub-optimal cell distribution
- No longitudinal connectivity

**Trail approach**
- No reflux at single injection site
- Homogeneous cellular suspension
- Immediate longitudinal connectivity
Feasibility of Proprietary Device Demonstrated in Pilot Porcine Study
The Bioengineered Neural Trail Creates a Continuous Neural Plexus Bridging the Injury

3D MRI reconstruction demonstrating continuous Bioengineered Neural Trail in a pig spinal cord

Histology demonstrating interconnected human cells in a pig spinal cord
Next Steps for Bioengineered Neural Trails™

• Optimize all aspects of product profile in preparation for IND: instrumentation, biomaterial, and NSCs
• Strengthen and broaden intellectual property portfolio
• Partner with a stem cell company to accelerate project timelines

Human Cells (STEM121) and Neural Progenitors (DCX)