ISCoS 2016 Annual Scientific Meeting
Clinical Trials Update for 2016

The INSPIRE Study:
Neuro-Spinal Scaffold™

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Agenda

1. Neuro-Spinal Scaffold™
2. Summary of Preclinical Studies
3. The INSPIRE Study
   A. Study Design
   B. Eligibility Criteria
   C. Results to Date
4. Next Steps
Neuro-Spinal Scaffold™ – Designed to Act as a Physical Substrate to Promote Neural Repair

Highly porous biopolymer composition:
- PLGA is the biodegradable cylindrical skeleton along which cells can grow
- Positively charged Poly-L-Lysine promotes cellular adhesion
Innovative Approach to Promote Spinal Cord Healing by *Neuro-Spinal Scaffold™*

Butterfly Bandage

2D Wound Healing

Neuro-Spinal Scaffold

Internal 3D Wound Healing
The *Neuro Spinal Scaffold™* Increases Remodeled Tissue Supporting Neural Regeneration

- Remodeled tissue at site of Scaffold implantation contains abundant laminin (green) and new axons (red) versus large cyst when untreated.
- Infiltrating Schwann cells (red) surrounding axons (green).

Rat Acute Spinal Cord Contusion Injury (at 12 weeks)
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

Slotkin JR et al., manuscript submitted
The INSPIRE Study – Study Design

**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**

- **Primary Objective:** To evaluate whether the Scaffold is safe and demonstrates probable benefit for the treatment of complete T2-T12/L1 spinal cord injury

- **Primary Endpoint:** AIS conversion by 6 month follow-up visit

- **Objective Performance Criterion:** At least 25% of subjects convert from complete paraplegia (AIS A) to partial paralysis by 6 months
  
  - Large, multinational, natural history databases consistently indicate that only 12-16% of subjects with complete (AIS A) thoracic injury will convert to an improved AIS grade within 6 months after injury

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

- **Plan to enroll 20 subjects**

- **Currently 23 active sites in the US and Canada, with sites in the UK planned**
The INSPIRE Study – Key Eligibility Criteria

**INCLUSION**
- Neurological level of injury T2 to T12/L1
- AIS A classification
- 16-70 years of age, inclusive
- Must implant Scaffold within 96 hours from injury
- Non-penetrating SCI (contusion injury) that is no less than approximately 4 mm in diameter by MRI
- Informed consent obtained

**EXCLUSION**
- Terminally ill subjects
- Significant TBI, coma, or unreliable ISNCSCI
- Penetrating SCI
- Radiographic or visual evidence of parenchymal dissociation or anatomic transection where the contusion completely bridges a full cross-section of the spinal cord
- Requiring long-term ongoing mechanical ventilation
- Clinically significant pre-existing neurological comorbidities, respiratory disease, or infection; documented immune deficiency disorders; recent significant substance abuse or severe mental illness

**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**
The INSPIRE Study - Promising Neurologic Outcomes and Favorable Safety Profile

<table>
<thead>
<tr>
<th>Subject</th>
<th>Date of Implantation</th>
<th>NLI</th>
<th>Neurologic Outcome to Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>October 2014</td>
<td>T11</td>
<td>Converted to AIS C at 1 month</td>
</tr>
<tr>
<td>2</td>
<td>January 2015</td>
<td>T7</td>
<td>Remains AIS A at 12 months</td>
</tr>
<tr>
<td>3</td>
<td>June 2015</td>
<td>T4</td>
<td>Converted to AIS B at 1 month</td>
</tr>
<tr>
<td>4</td>
<td>August 2015</td>
<td>T3</td>
<td>Remains AIS A at 12 months</td>
</tr>
<tr>
<td>5</td>
<td>September 2015</td>
<td>T8</td>
<td>Converted to AIS B at 6 months</td>
</tr>
<tr>
<td>6</td>
<td>February 2016</td>
<td>T10</td>
<td>Converted to AIS B at 2 months</td>
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<tr>
<td>7</td>
<td>March 2016</td>
<td>T4</td>
<td>Remains AIS A at 3 months</td>
</tr>
<tr>
<td>9</td>
<td>May 2016</td>
<td>T3</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 Serious Safety Events related to either the Scaffold or the procedure to implant the Scaffold
Neuro-Spinal Scaffold™ for Treatment of Acute Thoracic Complete Spinal Cord Injury

- Designed to promote the formation of neuro-permissive remodeled tissue that supports neural regeneration and re-myelination of denuded axons
- Scaffold implant into spinal cord contusion cavity feasible 9 - 83 hours after injury
- Preliminary results demonstrate 5 of 8 subjects with AIS conversion occurring 1 to 6 months post injury
- Excellent safety profile
InVivo Therapeutics - Next Steps

**Acute SCI: Neuro-Spinal Scaffold™**

1. The INSPIRE Study
   - Complete subject enrollment
   - Results available late 2017
2. Investigate the safety and feasibility of the Neuro-Spinal Scaffold™ in cervical SCI

**Chronic SCI: Bioengineered Neural Trails™** - Novel neural stem cell product for chronic SCI
Thank you!

➢ Subject 1 walking with aid 12 months after Scaffold implant