High ASIA Impairment Scale Conversion Rate Following Scaffold Implantation in Acute Thoracic Complete AIS A Spinal Cord Injury (SCI): Potential Mechanisms

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Novel Clinical Approach for Acute SCI Treatment: Intraparenchymal Scaffold Implantation

- Designed to act as a physical substrate to promote neural repair
  - Porous, bioresorbable device
  - \textit{In vivo} residence time \( \sim 4-8 \) weeks
- Intraparenchymal implantation within acute cavity following durotomy and often myelotomy
- Investigational device currently being evaluated in INSPIRE clinical trial: \textbf{NCT02138110} – Currently enrolling baseline T2-T12/L1 AIS A injuries <96hrs
The Scaffold Preserves Spinal Cord Architecture in Pre-Clinical Models

Rat Acute Spinal Cord Contusion Injury (at 12 weeks)

Cyst Reduction

Remodeled Tissue

Cavity Volume (mm$^3$)

Control Scaffold

0
2
4
6
*

Remodeled Tissue Volume (mm$^3$)

Control Scaffold

0.0
0.5
1.0
1.5
2.0
*

Laminin

Remodeled Tissue

P<0.05
Neural Regeneration and Remyelination with Schwann Cells after Scaffold Implantation

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

**Epicenter**
Inset: Schwann cells ensheathing axons

**White Matter**

Rat Acute Spinal Cord Contusion Injury (at 12 weeks)

Oligodendrocytes  Schwann Cells
The INSPIRE Study - Promising Neurologic Outcomes and Favorable Safety Profile

*All Subjects were AIS A at Baseline

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age</th>
<th>Sex</th>
<th>NLI</th>
<th>Time to Implant (hr)</th>
<th>Neurologic Outcome to Date</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>25</td>
<td>M</td>
<td>T11</td>
<td>9.2</td>
<td>Converted to AIS C at 1 month</td>
</tr>
<tr>
<td>2</td>
<td>22</td>
<td>F</td>
<td>T7</td>
<td>45.6</td>
<td>Remains AIS A at 12 months</td>
</tr>
<tr>
<td>3</td>
<td>56</td>
<td>M</td>
<td>T4</td>
<td>82.6</td>
<td>Converted to AIS B at 1 month</td>
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<tr>
<td>4</td>
<td>28</td>
<td>M</td>
<td>T3</td>
<td>52.9</td>
<td>Remains AIS A at 12 months</td>
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<tr>
<td>5</td>
<td>18</td>
<td>F</td>
<td>T8</td>
<td>69.1</td>
<td>Converted to AIS B at 6 months</td>
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<tr>
<td>6</td>
<td>21</td>
<td>M</td>
<td>T10</td>
<td>8.8</td>
<td>Converted to AIS B at 2 months</td>
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<tr>
<td>7</td>
<td>25</td>
<td>M</td>
<td>T4</td>
<td>21.3</td>
<td>Remains AIS A at 3 months</td>
</tr>
<tr>
<td>9</td>
<td>37</td>
<td>M</td>
<td>T3</td>
<td>40.4</td>
<td>Converted to AIS B at 3 months</td>
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</tbody>
</table>

- 5 of 8 evaluable subjects converted from complete to incomplete injuries within 6 months
- Natural history reports ~14-16% conversion rate in this patient population
Clinical Benefit of Scaffold Implantation: Potential Mechanisms

- Scaffold implantation permits:
  - Intra-dural decompression
  - Evacuation of necro-hemorrhagic tissue
- Scaffold promotes endogenous tissue remodeling:
  - Potential cyst reduction – Follow-up MRI’s being assessed (clinical)
  - Neural regeneration (pre-clinical)
  - Promotion of remyelination by Schwann cells (pre-clinical)
Conclusion and Future Clinical Plans for Scaffold Device

• **Conclusion**
  • The Scaffold device has demonstrated a favorable safety profile to date in the limited subject population
  • Preliminary neurological recovery is promising and warrants further clinical investigation
  • Various clinical mechanisms of action are presented and future advanced studies would be needed to confirm these hypotheses

• **Future Plans**
  • Continue to enroll acute T2-T12/L1 AIS A to reach 20 evaluable subjects (12 more needed)
    • 23 clinical sites throughout the U.S. and Canada are currently open
  • Plan to initiate acute cervical AIS A trial in coming months
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