Translation of Biomaterial-based Therapies for the Treatment of Spinal Cord Injury: The *Neuro-Spinal Scaffold™* and Bioengineered Neural Trails™

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Agenda

• Spinal cord injury background
  – Science of natural progression & modern day standard of care

• Neuro-Spinal Scaffold™: Our approach to acute SCI
  – Technology & mechanism of action
  – Translation to the clinic
  – Clinical results to date and future clinical development plans

• Bioengineered Neural Trails: Our approach to chronic SCI
  – Rationale
  – Pre-clinical development and results to date
Spinal Cord Injury: An Unmet Clinical Need

- Unserved patient population
  - 12,500 new cases of acute SCI per year in US\(^1\)
  - 276,000 currently live with chronic SCI in US\(^1\)
  - Only small percentage of patients ever regain function\(^2\)

- Acute SCI clinical trials using drugs/biologics/cells have all been unsuccessful in showing clinically meaningful improvement

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Progression of Acute SCI to Post-Traumatic Cavity in Contusion Injuries

Hemorrhage & Spinal Cord Swelling
Reduced Blood Flow & Ischemic Necrosis
Cavity Development & White Matter Reduction

Chronic injury and mature cavity formation

Acute SCI:
Neuro-Spinal Scaffold™

Chronic SCI:
Bioengineered Neural Trails™

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
Standard of Care Following Acute Injury

• Extradural bony decompression and spine stabilization using mechanical hardware

• Rehabilitation is recommended however no specific regimens are proven to improve neurologic recovery (i.e. no SOC rehab)

• Surgical access to the injured spinal cord (intradural/intraparenchymal) is not currently practiced
Neuro-Spinal Scaffold™ for Acute SCI
Designed to Promote Healing in Spinal Cord Injury
Novel Clinical Approach for Acute SCI: The **Neuro-Spinal Scaffold™**

poly(lactic-co-glycolic acid)-b-poly(L-lysine)
First **Neuro-Spinal Scaffold™** Implantation in Human Contusion Injury
Neuro-Spinal Scaffold™ Mechanism of Action

- Promotes the formation of neuro-permissive remodeled tissue that supports neural regeneration
- Provides structural support to surrounding viable tissue
- Serves as a locus for 3-dimensional appositional healing
- Preserves macroscopic spinal cord architecture and decreases cyst volume
- Increases spared white matter and promotes remyelination of denuded axons
The Neuro-Spinal Scaffold™ Preserves Macroscopic Spinal Cord Architecture

Rat Acute Spinal Cord Contusion Injury (at 12 weeks)

Control

Neuro-Spinal Scaffold

Cyst Reduction

White Matter Sparing

Remodeled Tissue

Cyst Volume (mm³)

Control

Neuro-Spinal Scaffold

White Matter Width (mm)

Control

Neuro-Spinal Scaffold

Remodeled Tissue Volume (mm³)

Control

Neuro-Spinal Scaffold

*P<0.05

Poster D8-06; National Neurotrauma Society 2015 Symposium; Santa Fe, NM.
Neural Sprouting Within Remodeled Tissue Contains Laminin and Sparse Collagen
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

Oligodendrocytes    Schwann Cells

Rat Acute Spinal Cord Contusion Injury (at 12 weeks)
InVivo’s Chronic SCI Product: Bioengineered Neural Trails™
Neural Stem Cells Incorporated into an Injectable Scaffold for Minimally-Invasive Delivery
Disruption of Motor Control within the Spinal Cord Following Injury

Motor Output

No Motor Output
Trails of Transplanted Cells May Provide a Preferred Delivery Approach to Bridge the Injury

Multi-modal therapy includes:
1. Neural stem cells
2. Biomaterial matrix
3. Novel Injection device/method

Conventional Bolus Injections Rostral/Caudal

Bioengineered Neural Trials™ “neuronal relay”
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

Collagen matrix to simulate spinal cord
Development of a Novel Device to Inject Therapeutic Trails within the Spinal Cord

The TrailMaker™ Injection Device

Positioning Arm

Cart

Control Panel
Bioengineered Neural Trails™: InVivo’s Novel Neural Stem Cell Product for Chronic SCI

Porcine Model (1 week after injection)  Rat Model (1 month after injection)

3D MRI of Bioengineered Neural Trail

Histology demonstrating interconnected human cells (STEM121) and neural precursors (rat only) (DCX)