



# Enabling the Nervous System to Repair Itself

Corporate Presentation

May 2024

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# NervGen Highlights

NVG-291, a novel first-in-class drug candidate with potential to **repair nervous system damage and restore motor, sensory and cognitive function**

Demonstrated functional improvement in **six different preclinical models** in several independent labs

**Phase 1b/2a** in spinal cord injury underway

Our pipeline of indications includes **ALS, stroke, multiple sclerosis, and Alzheimer's disease**

# Leadership



**Mike Kelly, MBA**  
**Chief Executive Officer**

Mike has over 30 years of pharmaceutical experience. Most recently, as President of US Operations for Adapt Pharma, Inc., which developed and commercialized NARCAN (naloxone HCl) Nasal Spray in the US and Canada and was sold to Emergent BioSolutions for US\$735 million.



**Bill Adams, CPA, CA**  
**Chief Financial Officer**

Bill has over 25 years of strategic financial management experience that includes mergers and acquisitions, operations and capital markets in Canada and the US.



**Dan Mikol, MD, PhD**  
**Chief Medical Officer**

Dan has over 25 years of pharmaceutical experience as a practicing physician conducting clinical research in the field of neurology. Most recently, at Amgen he served as the Head of clinical development in neuroscience and nephrology and was instrumental in the approval of Aimovig. Dan was also the development lead for Tysabri at Biogen and supported the Japan approval of Tysabri for relapsing multiple sclerosis.



**Matvey Lukashev, PhD**  
**VP, Research & Preclinical Dev.**

Matvey has over 30 years of experience in academia, industry and biotech settings focused on translational research and drug discovery.



# History of NervGen Technology

## 1990s

Dr. Silver discovered that glial scars contains chondroitin sulfate proteoglycans (**CSPG**), a group of molecules known to inhibit cellular events central to neural tissue repair

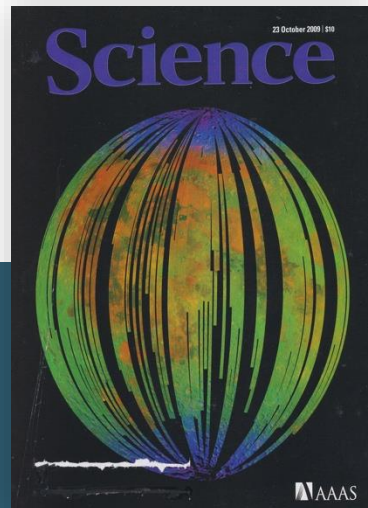


Jerry Silver, PhD



## 2009

Dr. Silver and collaborators from Harvard co-discovered that CSPGs bind to protein tyrosine phosphatase sigma (**PTPσ**), a receptor present in the brain and spinal cord and involved in CSPG-dependent inhibition of neuroplasticity



## 2015

Dr. Silver's team designed a peptide (NVG-291-R) derived from PTPσ shown to relieve CSPG-mediated inhibition of nervous system repair. **NVG-291** is the humanized version of NVG-291-R



## 2018

NervGen licensed NVG-291 **global rights for development and commercialization** in all indications from Case Western with intellectual property protection until 2037



## 2023

NervGen has initiated a **Phase 1b/2a** placebo-controlled proof-of-concept trial (NCT05965700) to evaluate the efficacy of NVG-291

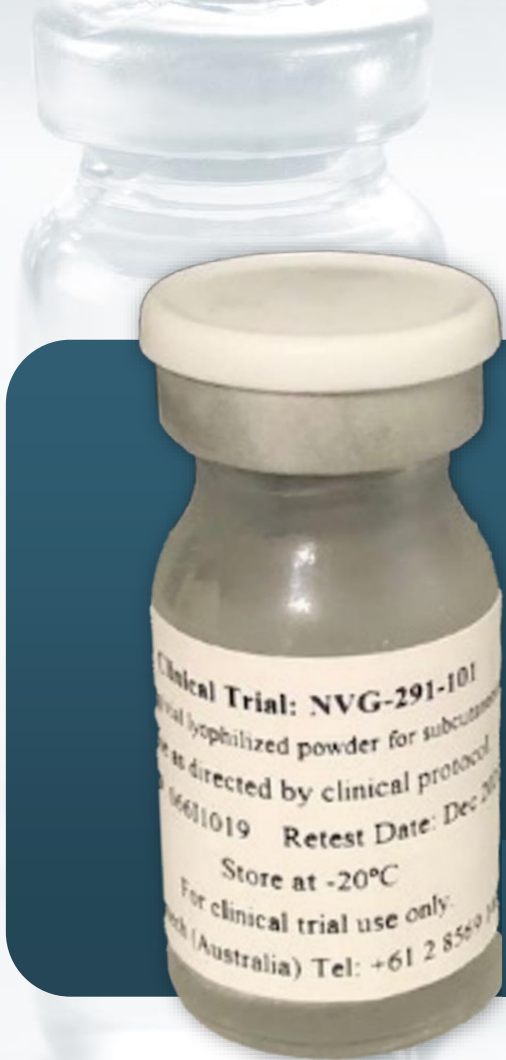
Phase 1b/2a Trial

Shirley Ryan  
**Abilitylab.**





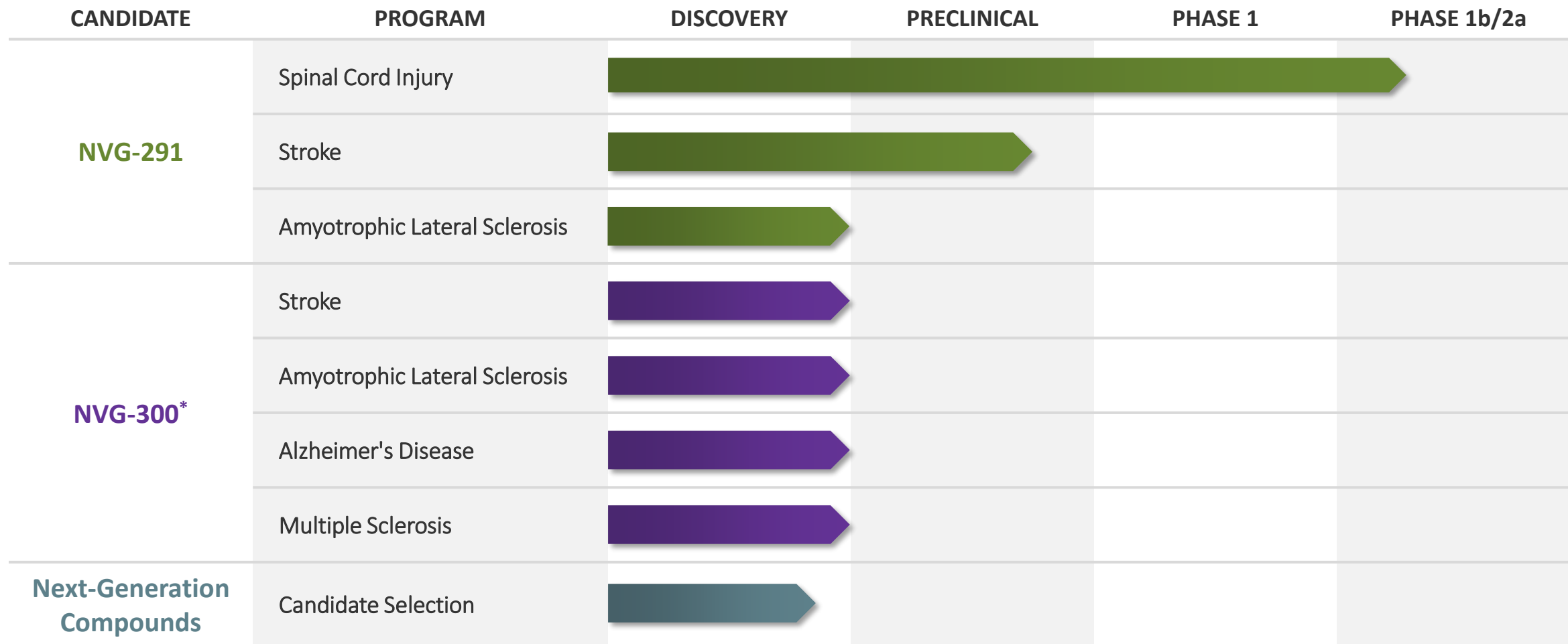
# NVG-291: Product Candidate Overview



- Cell-penetrating peptide, 35 amino acids in length
- Designed to cross cell membranes for enhanced cellular uptake of the drug
- Route of administration is subcutaneous injection
- Manufactured by chemical synthesis
- Discovery focused on analogs with new composition of matter IP, improvements in pharmacology and cost of manufacturing

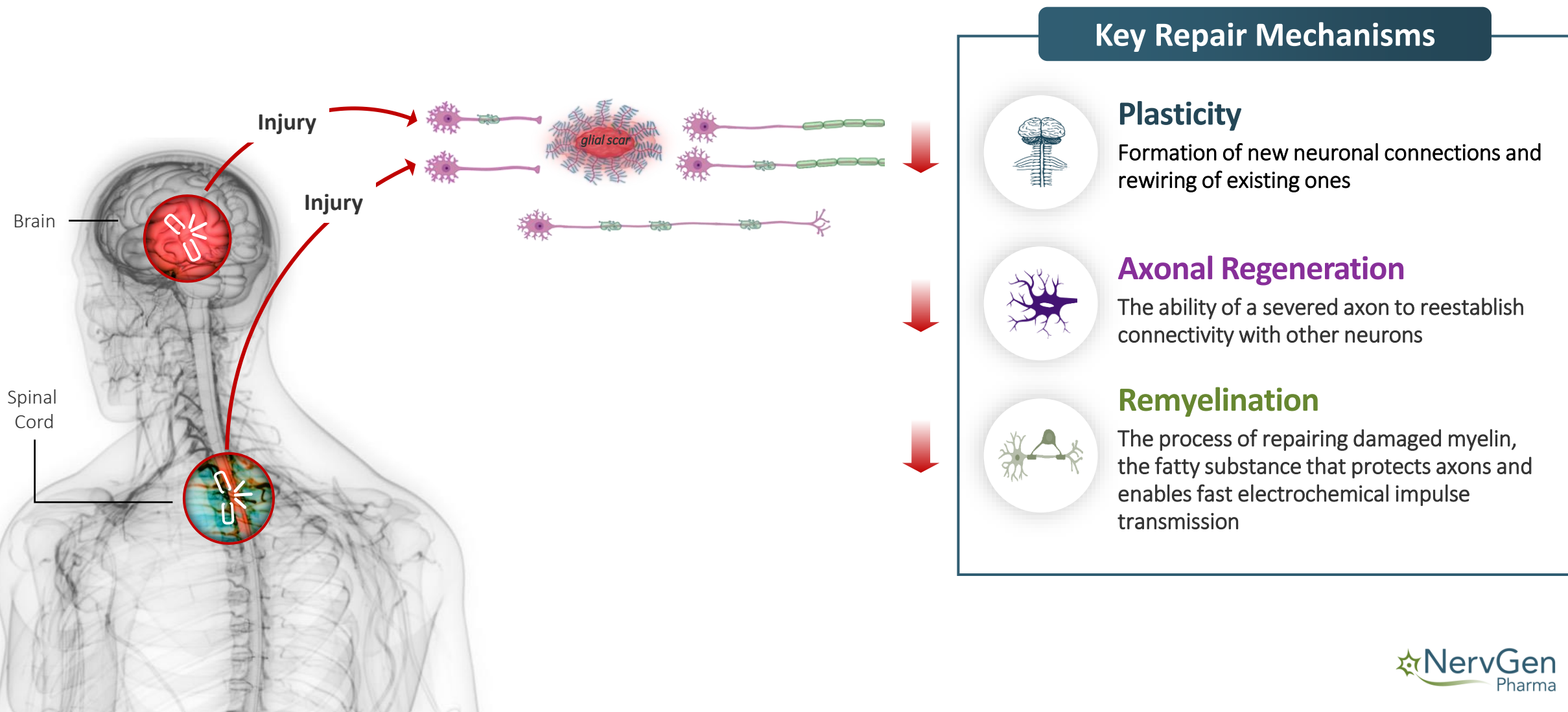
# Product Pipeline

## Multiple development opportunities



# Nervous System Damage Has Limited Treatment Alternatives

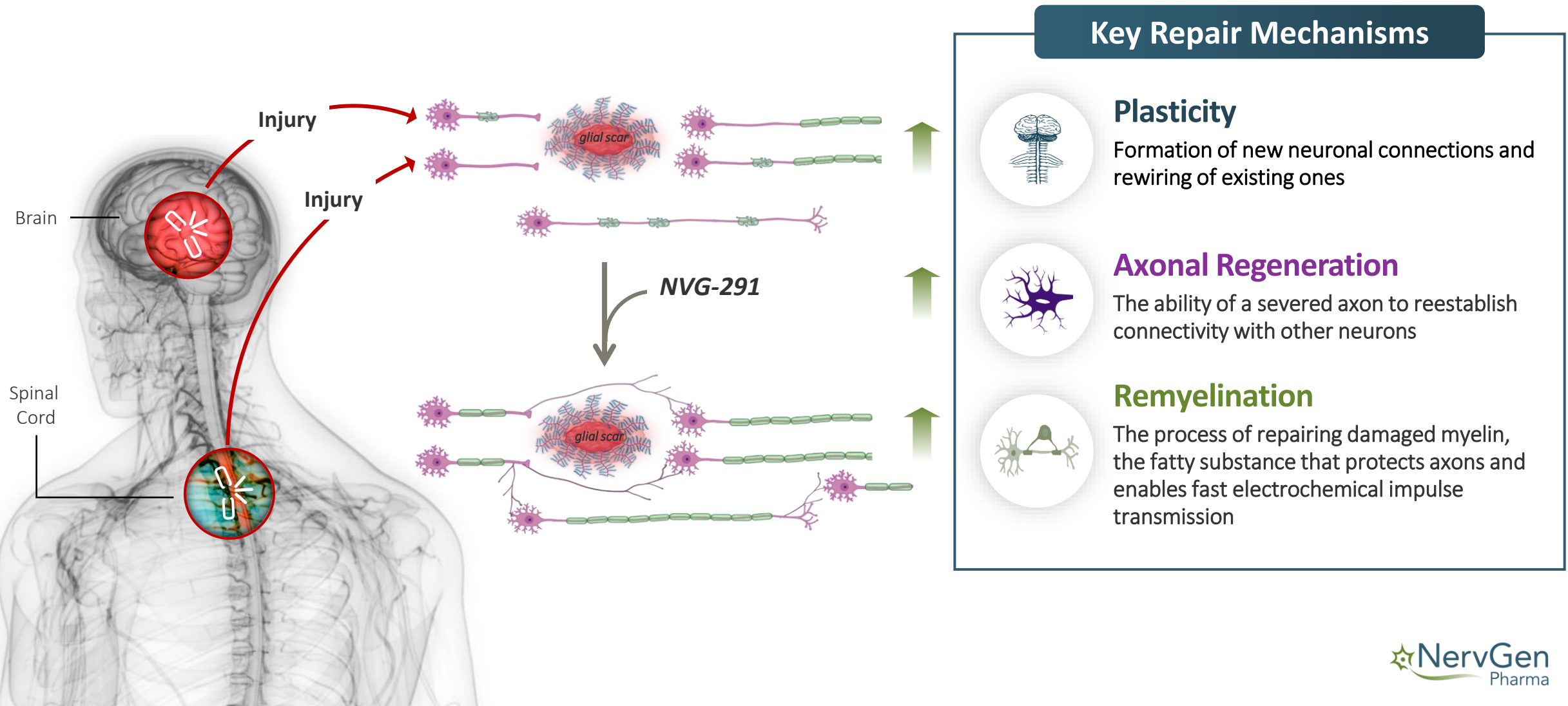
Glial scars and accumulation of CSPGs suppress CNS repair





# Novel Therapy Under Development to Repair Nervous System Damage

NVG-291 targets negative effects of CSPGs on CNS repair

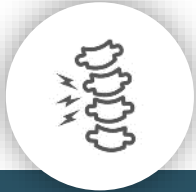


# Multiple Preclinical Studies Using NVG-291-R\* Report Improved CNS/PNS Repair

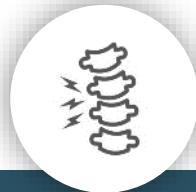
Enhanced Plasticity, Repair (Axonal, Myelination), and Recovery of Function

Conditions Modeled

**ACUTE SPINAL CORD INJURY**



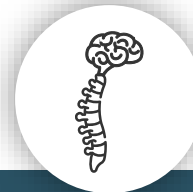
**CHRONIC SPINAL CORD INJURY**



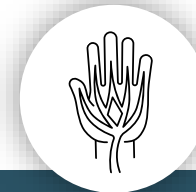
**STROKE**  
(Ischemic, Hemorrhagic)



**MULTIPLE SCLEROSIS (EAE)**



**PERIPHERAL NERVE INJURY**



**OPTIC NERVE DEMYELINATION**



Functional Endpoints

Motor  
Sensory  
Bladder

Motor

Motor  
Sensory  
Object recognition

Motor

Motor  
Sensory

Visual  
Behavioral

1. Lang, B.T. et al., Nature, 518, 404–408. (2015).
2. Rink, S. et al., Experimental Neurology, 309, 148–159. (2018).
3. Ham, T.R. et al., Ann Biomed Eng, 47, 744–753. (2019).
4. Ham, T.R. et al., Materials Science and Engineering: C, 110, 110656. (2020).

1. Milton et al, Journal of Neurotrauma, (2023)  
doi:[10.1089/neu.2023.0117](https://doi.org/10.1089/neu.2023.0117)

1. Luo et al., Cell Reports Volume 40, Issue 4, 111137, 2022
2. Yao et al., Journal of Neuroinflammation 19:207, 2022

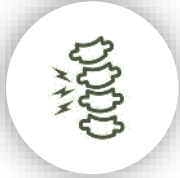
1. Luo, F. et al., Nature Communications, 9, 1–16. (2018).

1. Li, H. et al., Scientific Reports, 5, 1–14. (2015).
2. Yao, M. et al., Neuropharmacology, 144, 208–218. (2019).

1. Niknam, P. et al., Molecular and Cellular Neuroscience, 99, 103391. (2019).

# Nervous System Damage Markets and Opportunity

## Significant medical costs and morbidity



	SCI	Ischemic Stroke	ALS	MS	AD
<b>Incidence*</b>	18,000	~690,000	~7,000	10,000	500,000
<b>Prevalence*</b>	291,000	9.4M	~25K-30K	~1M	6.7M
<b>Lifetime Cost*</b>	\$1M-\$4M+	\$140,000+	\$1.4M	\$4M+	\$400,000
<b>System Cost*</b>	\$50B+	\$57B	\$250M-\$1.0B	\$85B	\$320B-\$345B
<b>Current Treatment*</b>	Decompressive surgery and rehabilitation	TPA must be given within hours of stroke; rehabilitation	Disease modifying agents (e.g. riluzole, edaravone) to slow progression – none stop progression	Immunomodulatory/ immunosuppressive therapies to reduce relapses and/or slow progression	Symptomatic therapies (e.g. cholinesterase inhibitors) to temporarily improve cognition; anti-beta mAbs to slow progression
<b>Unmet Needs*</b>	Effective treatments to enhance recovery	Effective treatments to enhance recovery	Treatment that improve function	Treatments to remyelinate axons and improve function	Treatments to effect enduring improvements

\* US only

█ Depicts current market opportunity of lead indication



## SCI Demographics

- Average age: ~43
- Male (78%), female (22%)
- Cause: vehicle (38%); fall (33%); violence (15%); sports (8%)
- Annual hospitalization (30%): UTI, pneumonia, decubitus ulcer
- Duration of hospitalization and rehabilitation: 2 to 3 months
- Chance of depression: 25%
- Significant urinary and sexual dysfunction

**Surgery**  
(decompression)

**TREATMENT**

**Rehabilitation**  
(regain function)

No FDA approved drugs to enable sustained functional recovery

# SCI Facts and Figures

## Incidence and Prevalence

**~18,000**

**Spinal cord injuries** every year in the US<sup>1</sup>

**~300,000**

**People living in the US** who have suffered a spinal cord injury in 2019<sup>1</sup>

up to  
**500,000**

Worldwide, the estimated **annual incidence** of spinal cord injury<sup>2</sup>

## Economic Impact

Individuals with SCI face a difficult and expensive journey through the healthcare system; that journey begins with **2-3 months in rehabilitation** and **costs \$200,000 or more per patient**<sup>3</sup>

Each individual with SCI faces an expected **lifetime cost of care between \$1M and \$4M**, depending on severity and age at injury<sup>4</sup>

In addition to the enormous economic costs, individuals with SCI face a **shorter expected lifespan, higher unemployment, higher chance of bankruptcy**<sup>5</sup>

(1) NSCSC: SCI Facts and Figures at a Glance; 2019 SCI Data Sheet Accessed May 11, 2023. (2) World Health Organization, Key Facts on Spinal Cord Injury, 2013; <https://www.who.int/news-room/fact-sheets/detail/spinal-cord-injury>. (3) DeVivo MJ, et. Al. Costs of Care Following Spinal Cord Injury, Top. Spinal Cord Inj. Rehab. 2011;16(4):1-9. (4) Cao Y, Chen Y, DeVivo MJ, Lifetime Direct Costs After Spinal Cord Injury, Top. Spinal Cord Inj. Rehab. 2011;16(4):10-16 (5) Merritt CH, Taylor MA, Yelton CJ, Ray SK Economic impact of traumatic spinal cord injuries in the US, Neuroimmunol. Neuroinflammation 2019;6:9



# Acute SCI Preclinical Study

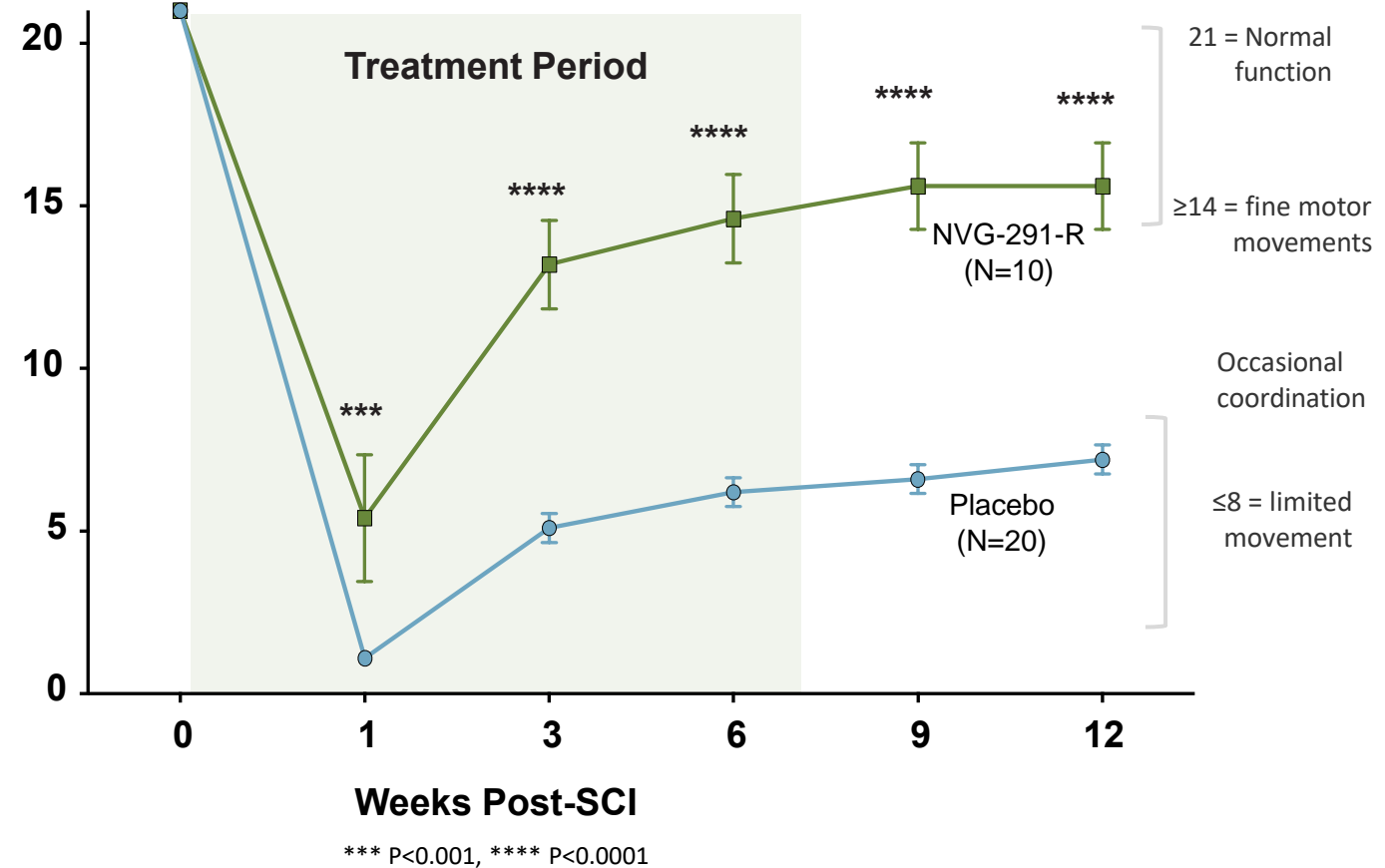
## Overview

- T8 compression injury
- 500 µg/day x 7 weeks
- Treatment began 1 day post injury

## Results

- Significant recovery of locomotor and bladder function
- Enhanced neuroplasticity (i.e. axonal sprouting) near and far from injury
- Functional improvements persist after treatment
- NVG-291-R can promote recovery in acute SCI

Basso, Beattie, Bresnahan  
Rating Scale



# NVG-291-R: Severe Spinal Cord Injury Model

## Representative of Placebo Group

(Back Legs and Tail Dragging)



[Click here to play video](#)

## Representative of NVG-291-R Group

(Back Legs and Tail Active)



Remarkable and robust repair across multiple models

# NVG-291-R: Severe Spinal Cord Injury Model

Representative of Placebo Group



Hind legs are immobile



[Click here to play video](#)

Representative of NVG-291 Group



Significant motor recovery: consistent coordination, toe clearance, tail held high consistently

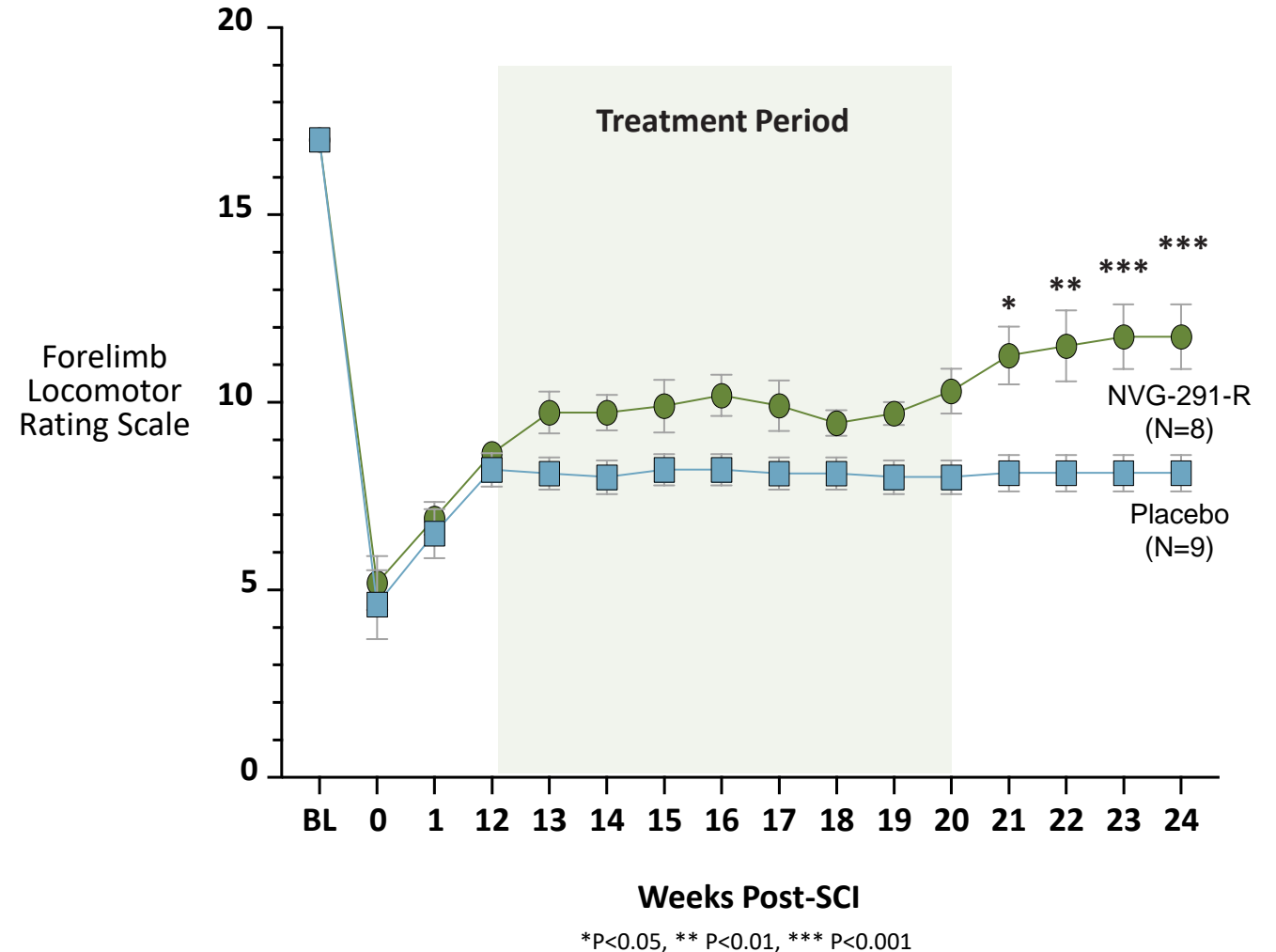
# Chronic SCI Preclinical Study

## Overview

- C2 lateral hemisection
- 500 µg/day x 8.5 weeks
- Treatment began 12 weeks post-injury

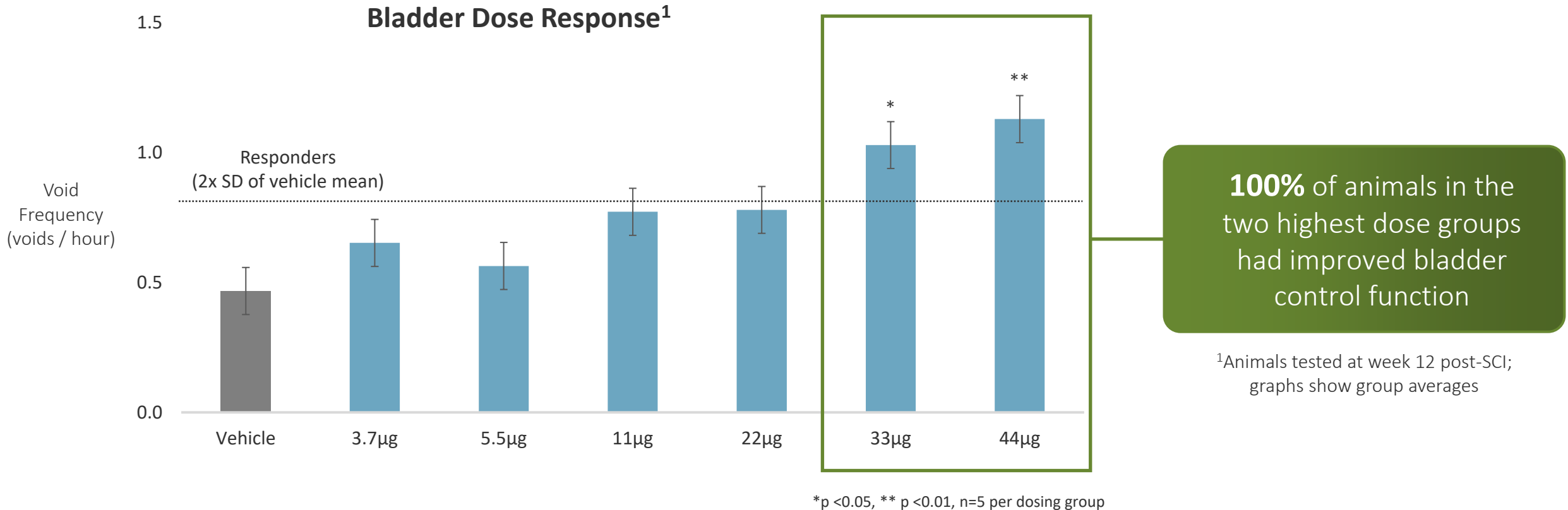
## Results

- Significant recovery of forelimb locomotor function
- Functional improvements persist after treatment
- NVG-291-R can promote recovery in chronic stages of SCI



# Spinal Cord Injury

## Bladder function improved following NVG-291-R treatment in preclinical animal studies



**Bladder function is a key quality of life measure in the paralyzed population**



# NVG-291 Phase 1 Clinical Trial Results

## Study Design

### Single Dose

- 37 subjects
- 6 dose levels
- Assessed through Day 8

### Multiple Dose

- 33 subjects
- 4 dose levels
- Subjects dosed subcutaneously once/day for 14 days
- Assessed through Day 21

## Safety Results

- Well tolerated across all doses
  - Maximum tolerated dose (MTD) not reached
- No treatment discontinuations
- No serious/severe adverse events (AE) in NVG-291 group
- Most common AE was injection site related (ISR)
- No clinically significant effects related to NVG-291 treatment across all study parameters

# Phase 1b/2a Proof-of-Concept Trial in SCI

## Study Design

- 16-week trial (12-wk treatment, 4-wk noninterventional period)
  - Randomized 1:1 to NVG-291 and placebo
  - Once daily subcutaneous injection
  - Exercise over 16 weeks
- Single center, Shirley Ryan AbilityLab (Chicago, IL)
  - Ranked #1 rehabilitation hospital for >30 years
  - Monica Perez, PT, PhD – expertise in applying electrophysiology as a tool to monitor motor recovery in humans after SCI
  - Single center – decreases variability of electrophysiological assessments, ensures standardized exercise program

## Two Cohorts

### Chronic SCI

- ~20 individuals (1-10 years post-injury)

### Subacute SCI

- ~20 individuals (10-49 days post-injury)

Shirley Ryan  
**Abilitylab**



## Study Objectives

### Co-Primary Endpoints: Quantitative Measure of Motor Connectivity

- Hand muscle group
- Leg muscle group

### Secondary Endpoints

- Clinical measures based on performance tests (walking speed, hand function) and neurological assessment
- Electrophysiological measures of electrical connectivity

### Exploratory Endpoints

- Autonomic (e.g. bladder function)
- Spasticity (lower extremities)
- Mobility
- Quality of life
- Blood biomarkers

# SCI Clinical Advisory Board

**James Guest, MD, PhD, FACS**

Professor of Neurological Surgery at the University of Miami and The Miami Project to Cure

**Steven Kirshblum, MD**

Professor and Chair of the Department of Physical Medicine and Rehabilitation at Rutgers New Jersey Medical School

Chief Medical Officer for Kessler Institute for Rehabilitation and Kessler Foundation

**Brian Kwon, MD, PhD, FRCSC**

Professor in the Department of Orthopedics at the University of British Columbia, the Canada Research Chair in Spinal Cord Injury

**Linda Jones, PT, PhD**

Collaborating Investigator at Spinal Cord Outcomes Partnership Endeavor (SCOPE)

Chair of the Research Committee of the American Spinal Injury Association (ASIA)

**Daniel Lammertse, MD**

Clinical Professor of Physical Medicine and Rehabilitation at the University of Colorado School of Medicine

Emeritus Clinical Scientist at Craig Hospital in Englewood Colorado

# Board of Directors



**Bill Radvak**

Chairman & Co-Founder



**Randall Kaye, MD**

CMO, Longboard Pharmaceuticals



**Adam Rogers, MD**

Former CEO & Co-Founder, Hemera



**Harold Punnett, DMD**

Co-Founder



**Mike Kelly**

President & CEO, NervGen



**John Ruffolo**

Founder & Managing Partner, Maverix



**Brian Bayley**

Director, Earlston Investments



**Krista McKerracher**

Former Global Franchise Head, Novartis



**Craig Thompson**

CEO, Cerevance



**Glenn Ives**

Former Partner, Deloitte LLP

# Share and Capital Structure

<b>Exchange/Market: Ticker</b>	TSX: NGEN.V	OTCQB: NGENF
<b>Recent Share Price</b> (May 22, 2024)	CA \$2.16	US \$1.59
<b>Shares Outstanding</b>	69.9 million	
<b>Fully Diluted</b>	91.3 million (~11.3 million options & retention securities, ~10.1 million warrants*)	
<b>Insider Ownership</b>	23.3%	
<b>Cash &amp; Cash Equivalents</b> (March 31, 2024)	CA \$30.3 million	US \$22.4 million

\*Warrant exercise prices between US\$1.75 to CA\$3.00



# Key Value Drivers for 2024

**Phase 1b/2a clinical trial** recruitment progress

**Preclinical data** in multiple indications

**Next generation** compound progress

**Phase 1b/2a Proof-of-concept** readout in chronic SCI



# Enabling the Nervous System to Repair Itself

[www.nervgen.com](http://www.nervgen.com)

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