



Enabling the Nervous System to Repair Itself

Corporate Presentation

JULY 2023

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NervGen Highlights

Developing therapies to **revolutionize treatment** for a broad range of therapeutic indications

NVG-291, a first-in-class drug candidate under development with potential to **repair nervous system damage**

Demonstrated functional improvement in six **different models** of nervous system damage

Targeting indications of **high unmet medical need** beginning with spinal cord injury (SCI)

Proof of concept (Phase 1b/2a) spinal cord injury clinical trial enrolling in 2023 with results expected in 2024

Leadership



Mike Kelly, MBA, BSBA
Chief Executive Officer

Mike brings three decades of pharmaceutical industry experience in creation, development and strengthening of both private and public companies.



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 experience in the pharmaceutical industry and as a practicing physician conducting clinical research in the field of neurology.



Matvey Lukashev, PhD
VP, Research & Preclinical Devt.

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



Nana Collett, MS, MBA
VP, Program Management

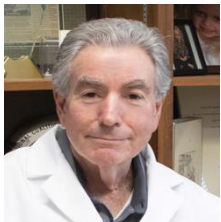
Nana has over 20 years experience managing biopharma product development programs from preclinical stage to Phase 3 across a range of therapeutic areas.



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

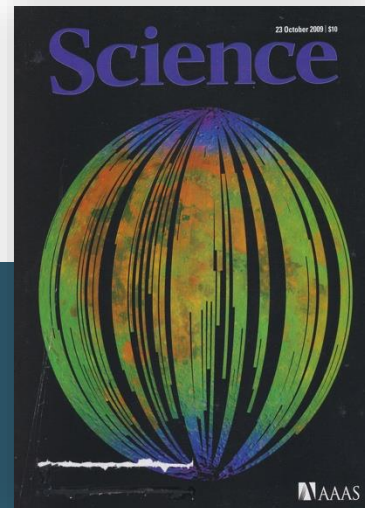


Jerry Silver, PhD



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

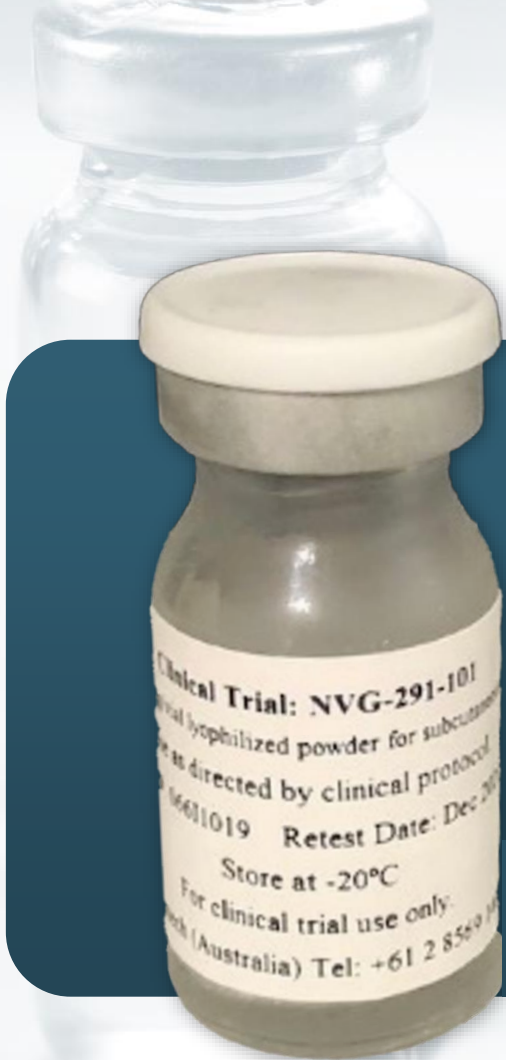


2018

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



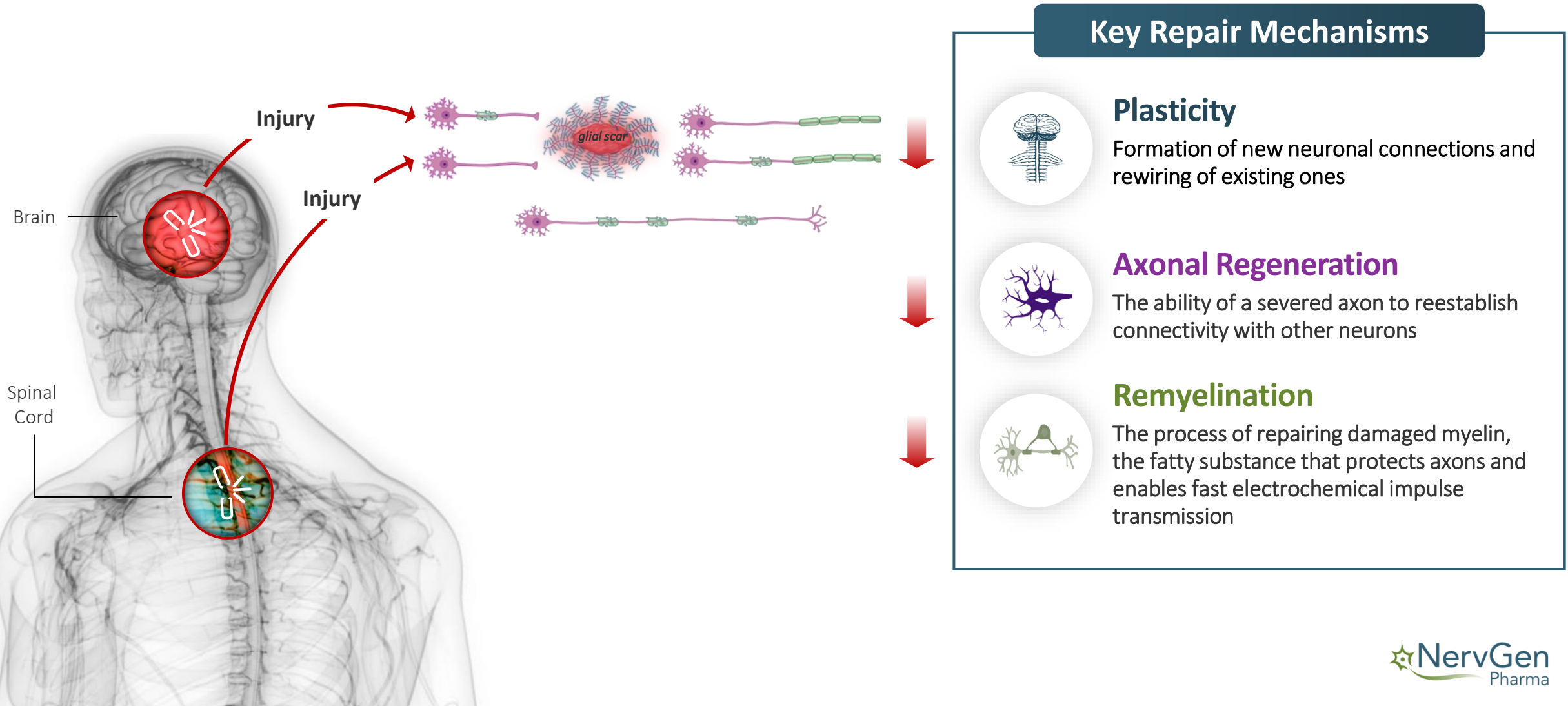
NVG-291: Product Candidate Overview



- 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

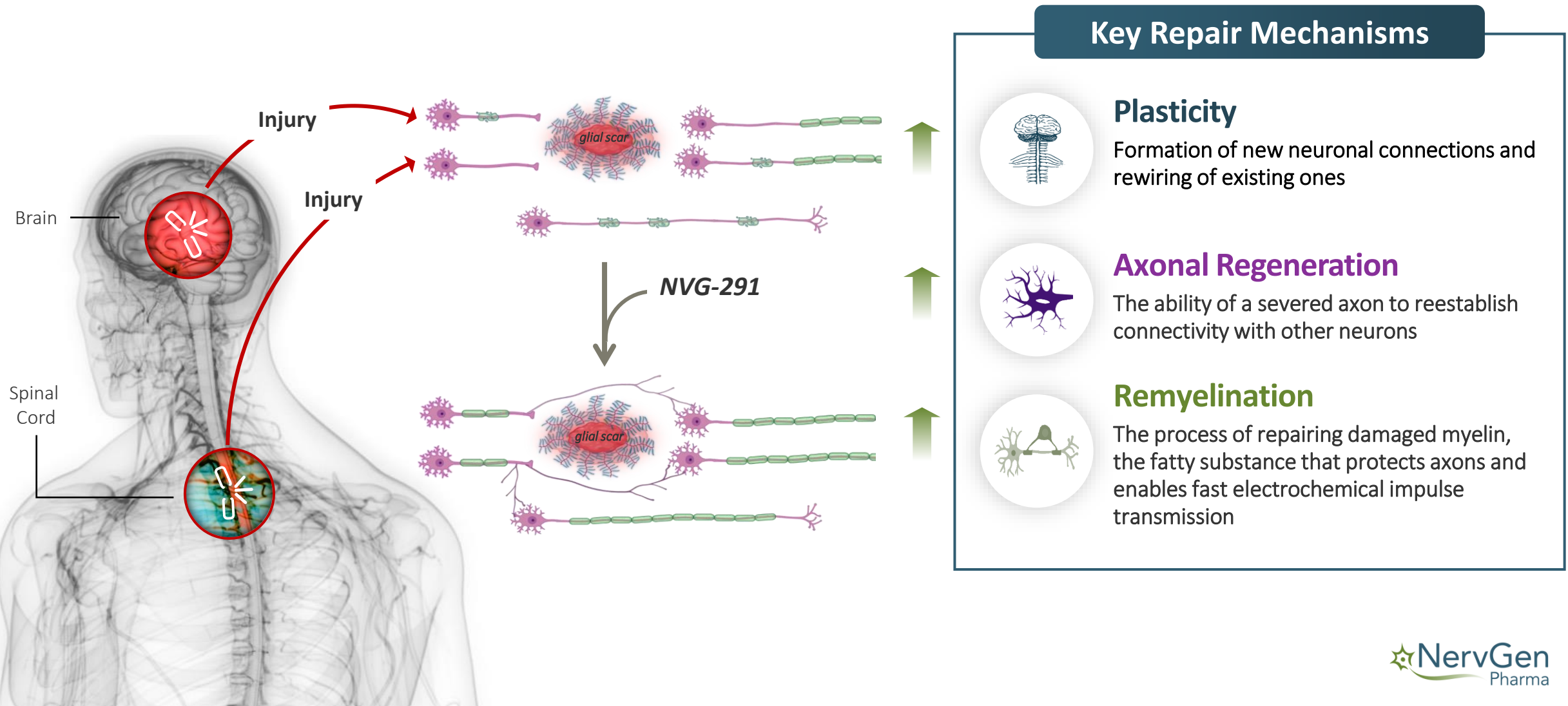
Nervous System Damage Has Limited Treatment Alternatives

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

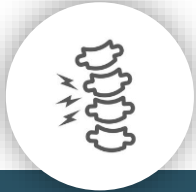


Multiple Preclinical Studies Using NVG-291-R* Report Improved CNS/PNS Repair

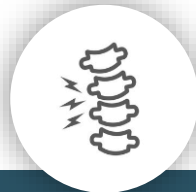
Enhanced Plasticity, Repair (Axonal, Myelination), and Recovery of Function

Conditions Modeled

ACUTE SPINAL CORD INJURY



CHRONIC SPINAL CORD INJURY



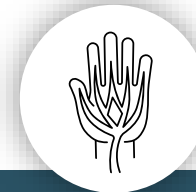
STROKE
(Ischemic, Hemorrhagic)



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., bioRxiv, doi:10.1101/2022.08.01.502398 (not peer-reviewed)

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

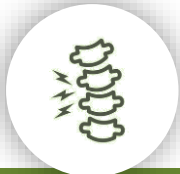




1. Luo, F. et al., Nature Communications, 9, 1–16. (2018).

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
Incidence*	18,000	795,000	~7,000	10,000	500,000
Prevalence*	291,000	9.4M	~25K-30K	~1M	6.7M
Lifetime Cost*	\$1M-\$4M+	\$140,000+	\$1.4M	\$4M+	\$400,000
System Cost*	\$50B+	\$57B	\$250M-\$1.0B	\$85B	\$320B-\$345B
Current Treatment*	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
Unmet Needs*	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

A man with a beard, wearing a white t-shirt and grey pants, is sitting in a wheelchair. He is looking out a large window on the left side of the frame. The room has a light-colored floor and a white wall. A diagonal beam of light or a structural element is visible in the upper right.

Spinal Cord Injury

No FDA approved drug to enable sustained functional recovery

- Goal is improved motor, bladder, bowel, sexual and/or sensory function
- NVG-291 has shown positive preclinical results
- Significant unmet medical need



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

TREATMENT

Surgery
(decompression)

Rehabilitation
(regain function)

SCI Facts and Figures

Incidence and Prevalence

There are approximately **18,000 spinal cord injuries** every year in the US¹

In 2019, there were just under **300,000 people living in the US** who have suffered a spinal cord injury¹

Worldwide, the **annual incidence** is estimated to be **250,000 to 500,000**²

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 patient³

Each individual with SCI faces an expected **lifetime cost of care between \$1M and \$4M**, depending on severity and age at injury⁴

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

(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

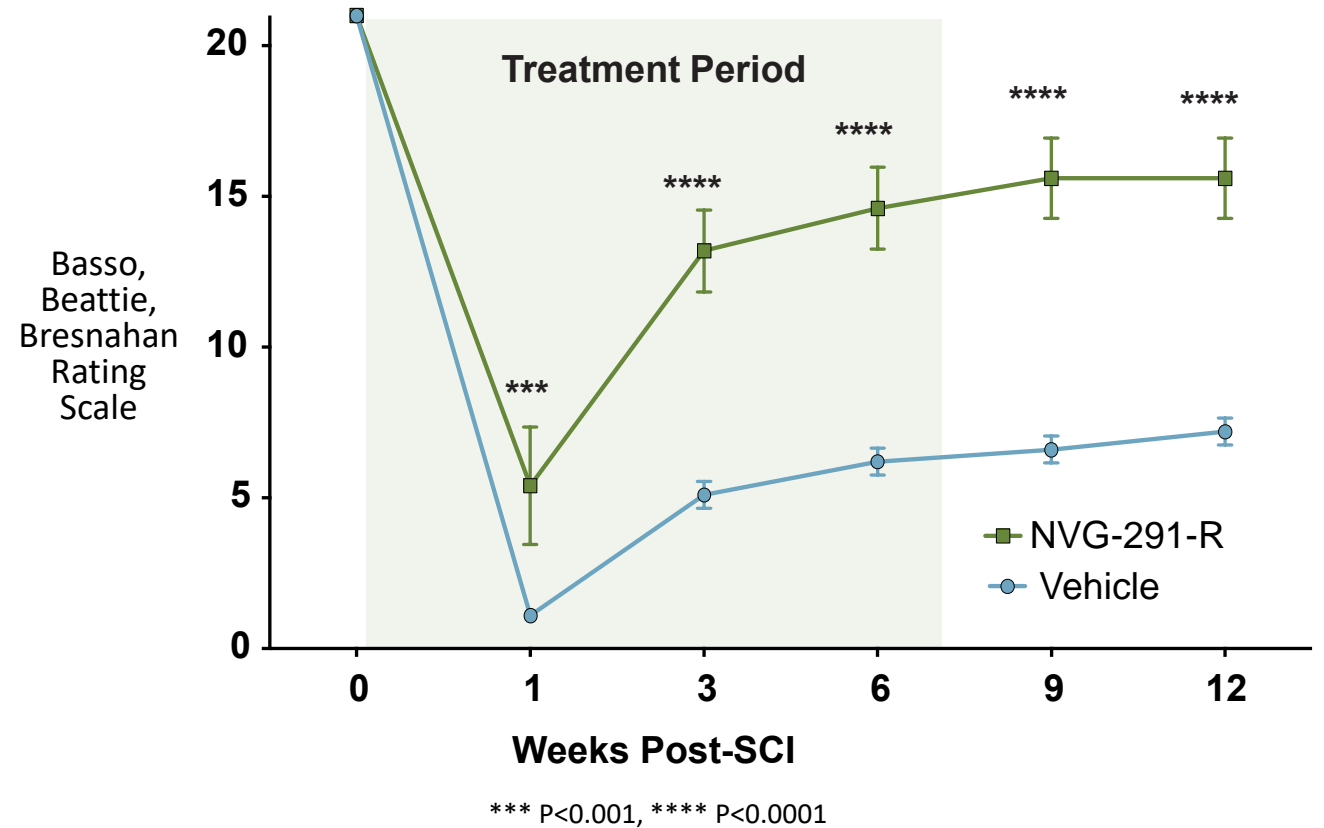
Acute SCI Preclinical Study

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



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

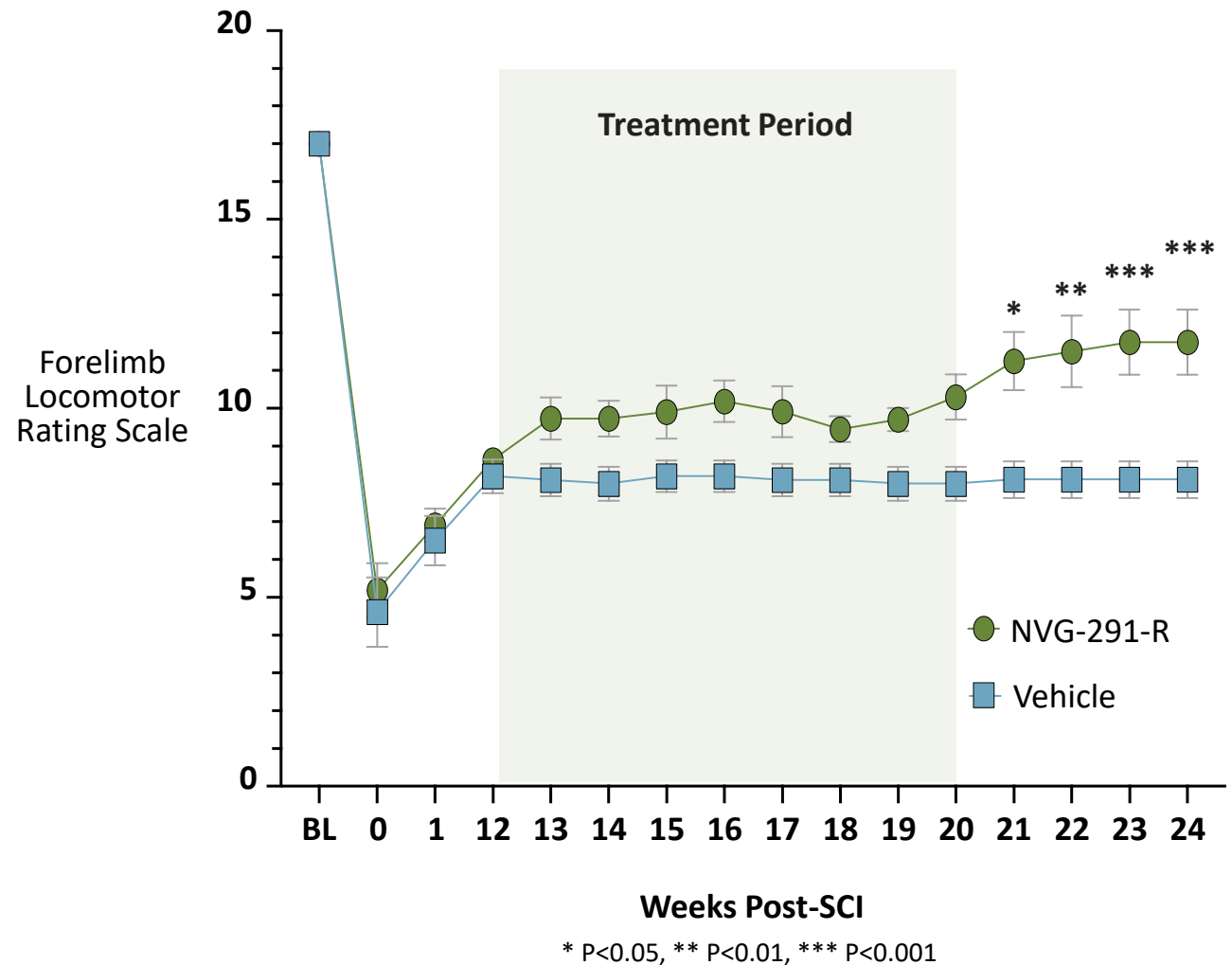
Chronic SCI Preclinical Study

Overview

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

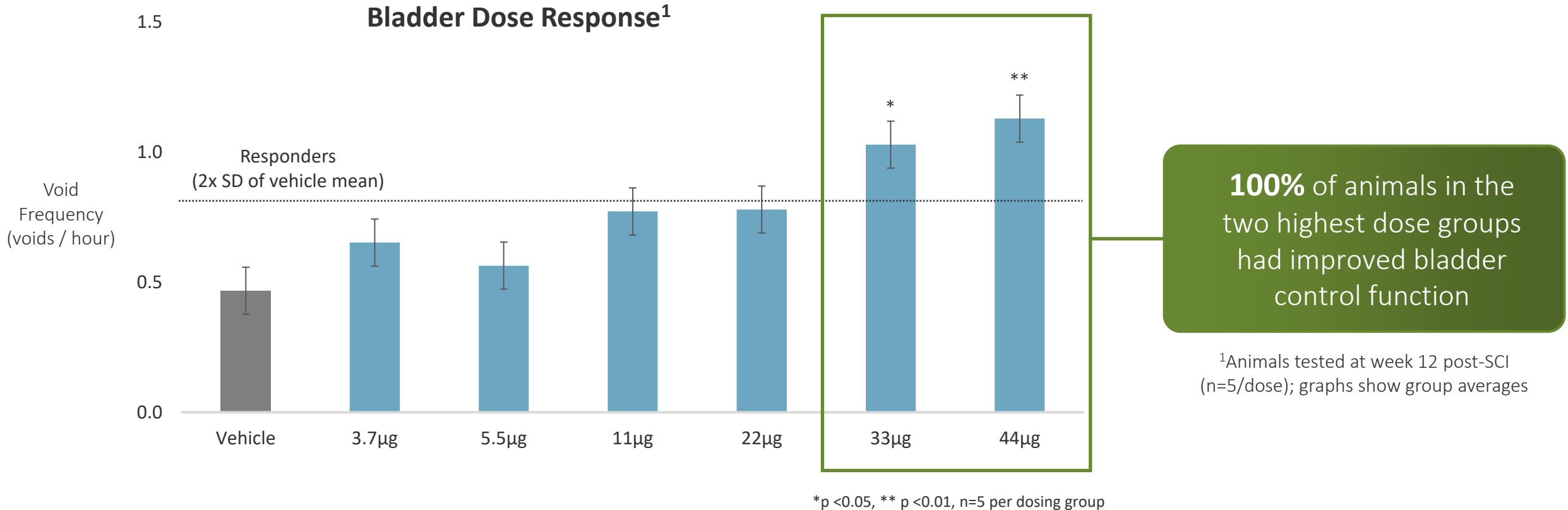
Results

- 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

Two Cohorts

- Randomized 1:1 to NVG-291 and placebo

Chronic SCI

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

Subacute SCI

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

Administration / Trial

- Once daily subcutaneous injection
- 16-week trial (12-wk treatment, 4-wk noninterventional period)
- Exercise over 16 weeks
- Single center, Shirley Ryan AbilityLab (Chicago, IL)
 - Decrease variability of electrophysiological assessments
 - Ensure standardized exercise program



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
- Plasma 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)

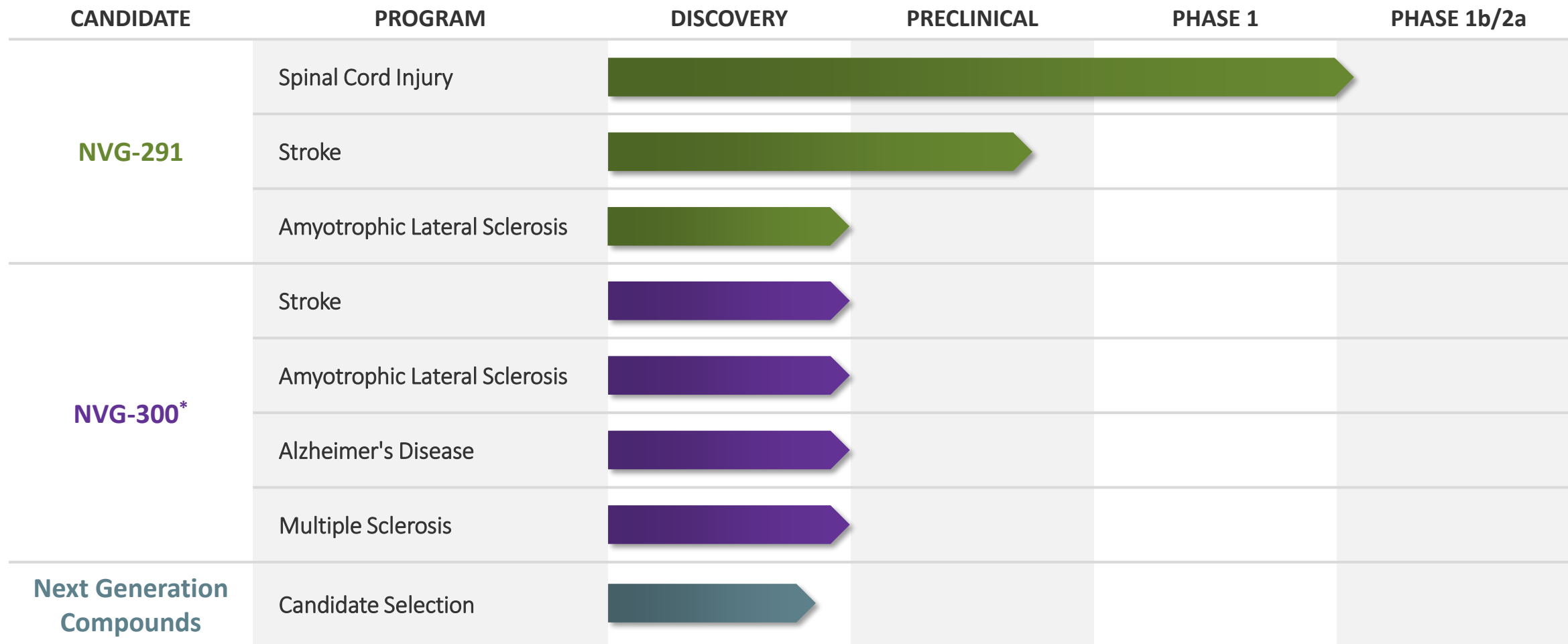
Daniel Lammertse, MD

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

Emeritus Clinical Scientist at Craig Hospital in Englewood Colorado

Product Pipeline

Multiple development opportunities



Board and Key Partnerships



Bill Radvak

Chairman & Co-Founder



Glenn Ives

Former Partner, Deloitte LLP



Krista McKerracher

Former Global Franchise Head, Novartis



Harold Punnett, DMD

Co-Founder



Randall Kaye, MD

CMO, Longboard Pharmaceuticals



Adam Rogers, MD

Former CEO & Co-Founder, Hemera



Brian Bayley

Director, Earlston Investments



Mike Kelly

President & CEO, NervGen



Craig Thompson

CEO, Cerevance

KEY PARTNERS



Key Value Drivers

Phase 1b/2a clinical trial: IRB approval and first patient dosed (2023)

Preclinical data in multiple indications (2023/24)

Next generation compound progress (2023/24)

Proof of concept readout in chronic SCI (mid-2024)



Enabling the Nervous System to Repair Itself

www.nervgen.com

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