



Enabling the Nervous System to Repair Itself

Corporate Presentation

September 2023

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NervGen Highlights

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

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

Phase 1b/2a in spinal cord injury initiated, results expected in 2024

Advancing our pipeline in indications of **high unmet medical need**

Leadership



Mike Kelly, MBA
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, designing Phase 1-4 clinical trials, and leading clinical development teams.



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.



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

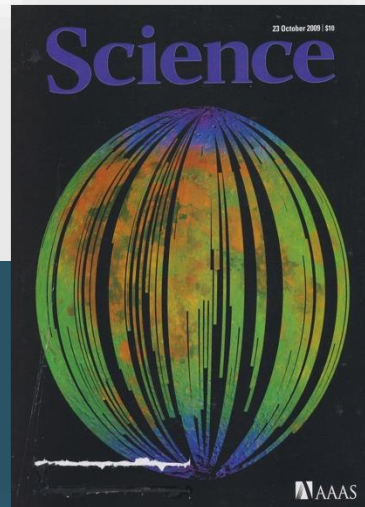


Jerry Silver, PhD



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



2023

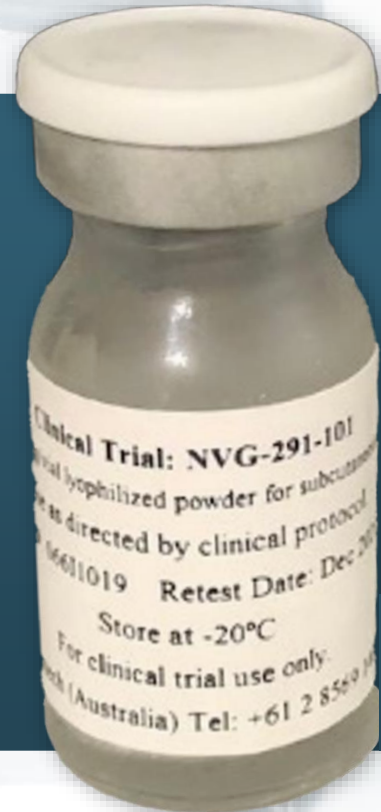
NervGen has initiated a **Phase 1b/2a** placebo-controlled proof-of-concept trial (NCT05965700) to evaluate the efficacy of NVG-291

Phase 1b/2a Trial

Shirley Ryan
Abilitylab.



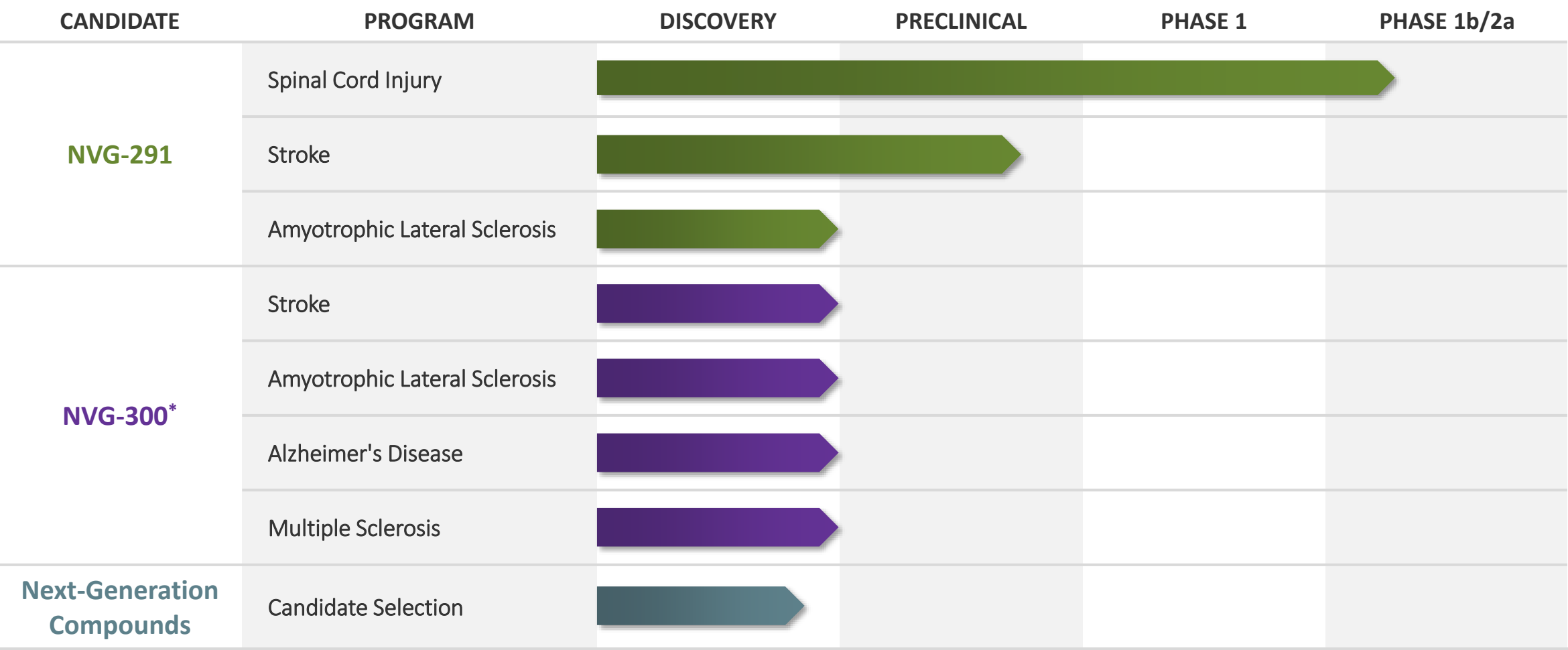
NVG-291: Product Candidate Overview



- 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

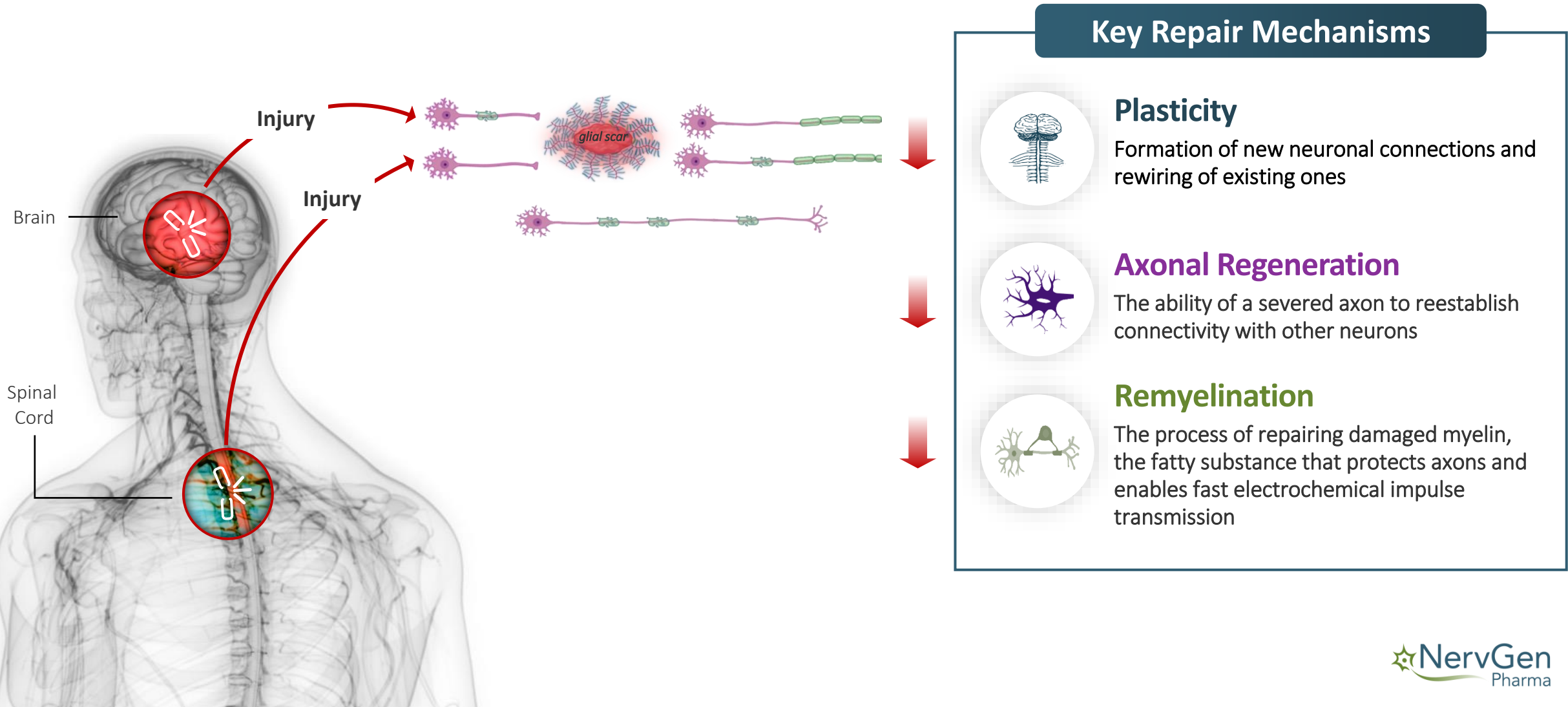
Product Pipeline

Multiple development opportunities



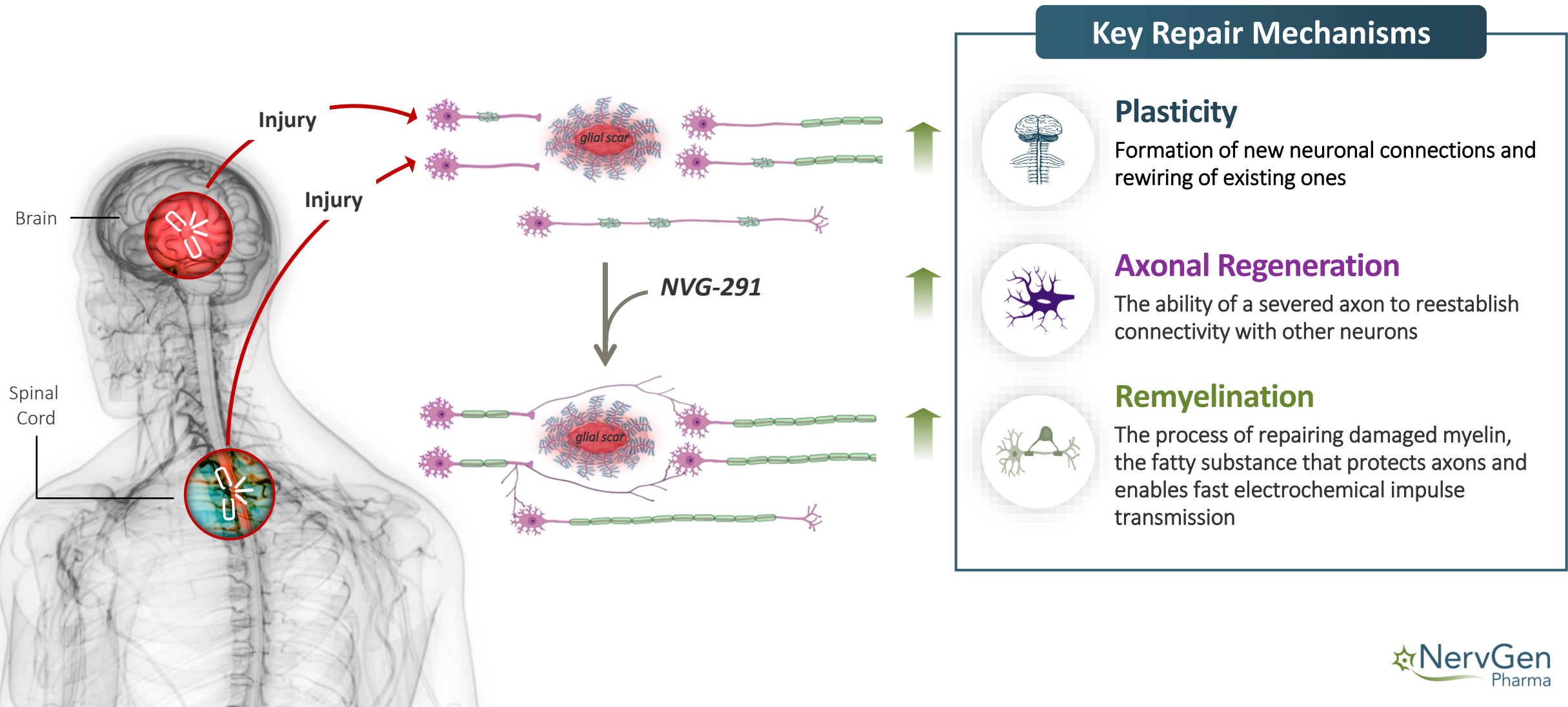
Nervous System Damage Has Limited Treatment Alternatives

Glial scars and accumulation of CSPGs suppress CNS repair



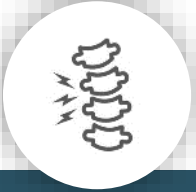
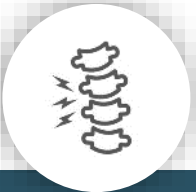


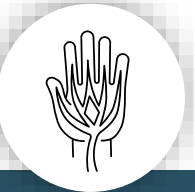

Novel Therapy Under Development to Repair Nervous System Damage

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
	<div>1. Lang, B.T. et al., Nature, 518, 404–408. (2015).</div> <div>2. Rink, S. et al., Experimental Neurology, 309, 148–159. (2018).</div> <div>3. Ham, T.R. et al., Ann Biomed Eng, 47, 744–753. (2019).</div> <div>4. Ham, T.R. et al., Materials Science and Engineering: C, 110, 110656. (2020).</div>	<div>1. Milton et al, Journal of Neurotrauma, (2023) doi:10.1089/neu.2023.0117</div>	<div>1. Luo et al., Cell Reports Volume 40, Issue 4, 111137, 2022</div> <div>2. Yao et al., Journal of Neuroinflammation 19:207, 2022</div>	<div>1. Luo, F. et al., Nature Communications, 9, 1–16. (2018).</div>	<div>1. Li, H. et al., Scientific Reports, 5, 1–14. (2015).</div> <div>2. Yao, M. et al., Neuropharmacology, 144, 208–218. (2019).</div>	<div>1. Niknam, P. et al., Molecular and Cellular Neuroscience, 99, 103391. (2019).</div>

Nervous System Damage Markets and Opportunity

Significant medical costs and morbidity

					
	SCI	Ischemic Stroke	ALS	MS	AD
Incidence*	18,000	~690,000	~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 and a bun, wearing a white t-shirt and grey pants, is sitting in a wheelchair. He is looking out a large window with vertical bars. The room has a light-colored floor and a white wall. A diagonal metal beam is visible in the background.

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

~18,000

Spinal cord injuries every year in the US¹

~300,000

People living in the US who have suffered a spinal cord injury in 2019¹

**up to
500,000**

Worldwide, the estimated **annual incidence** of spinal cord injury²

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**³

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

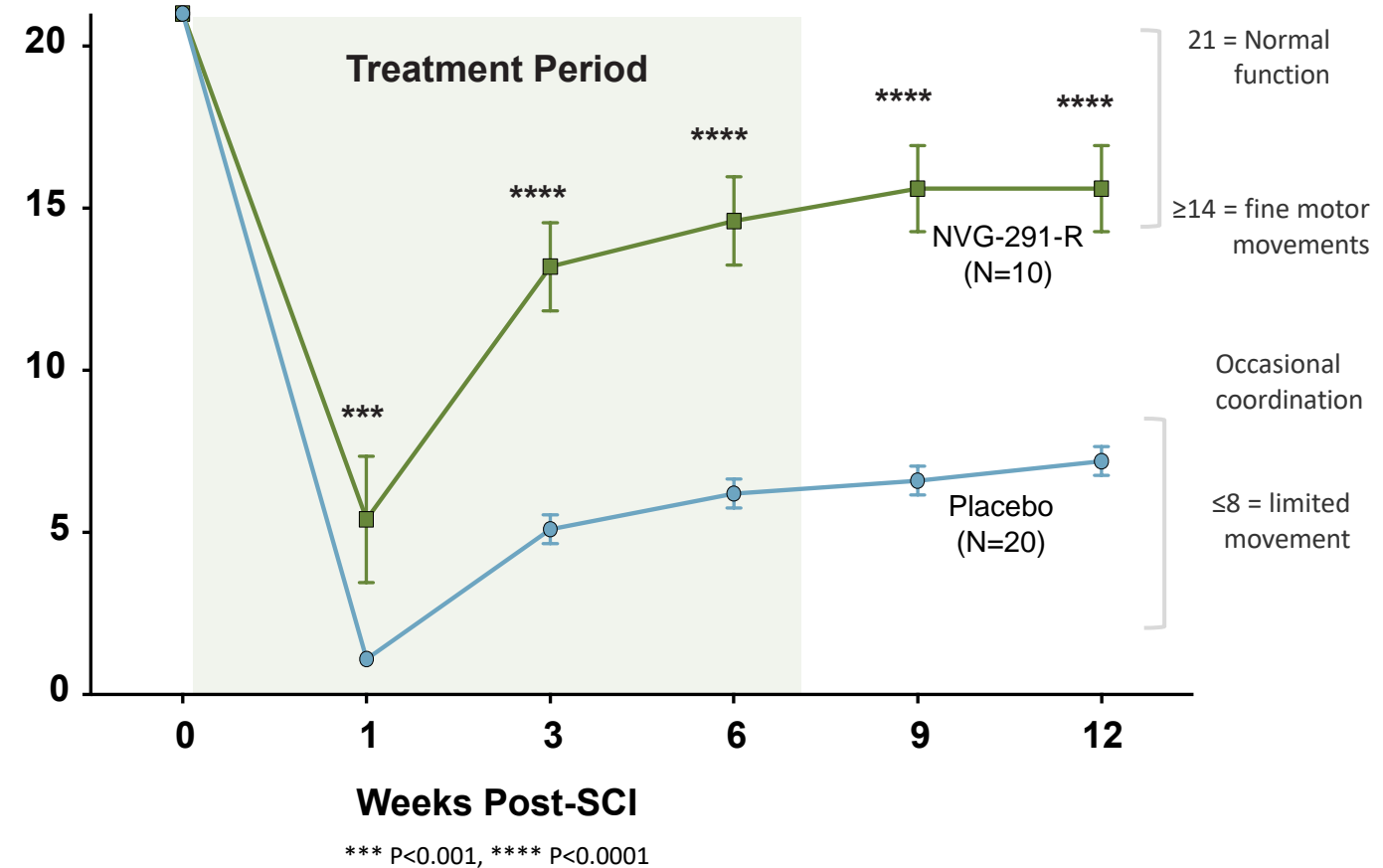
Overview

- 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

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

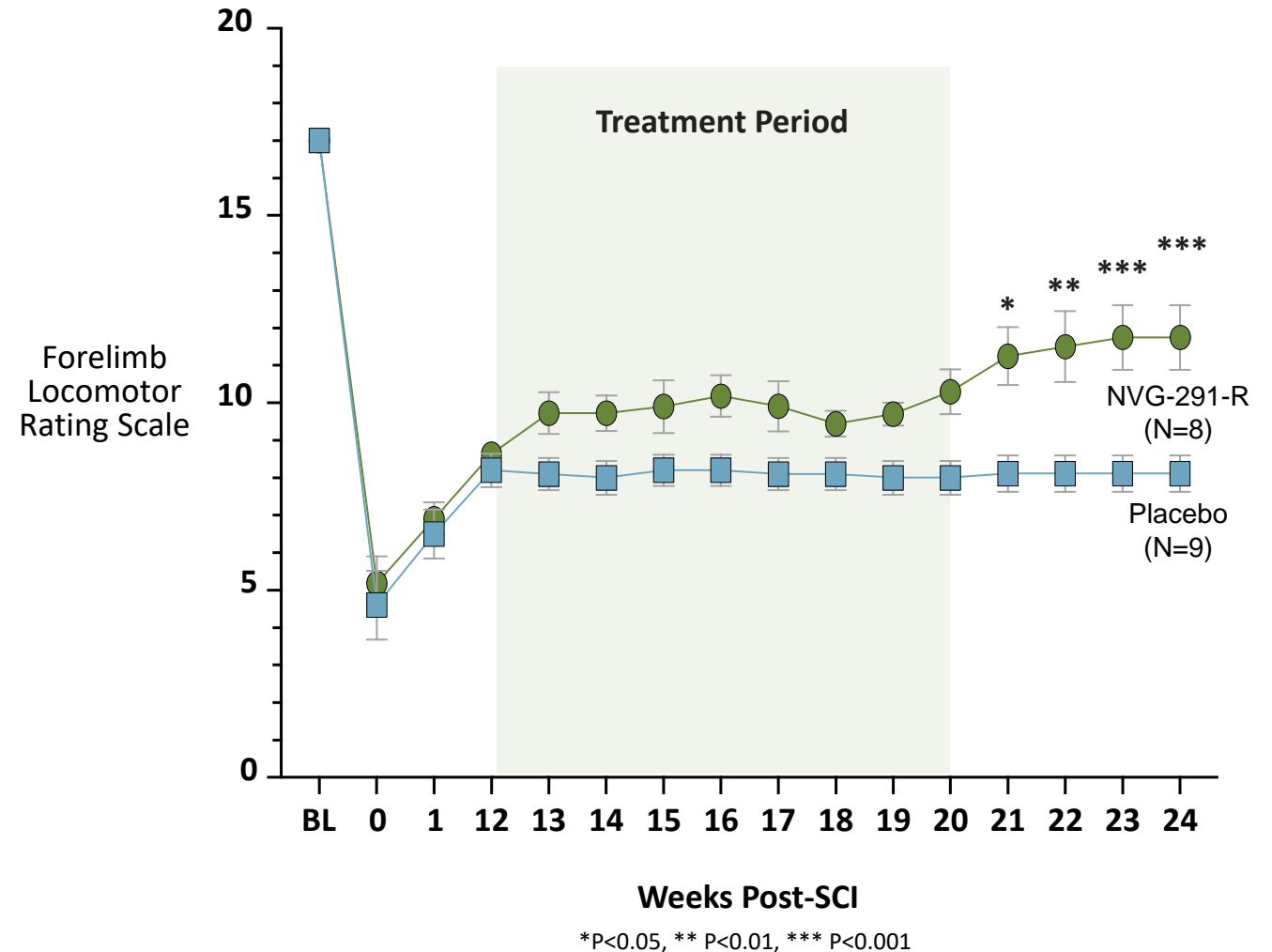
Chronic SCI Preclinical Study

Overview

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

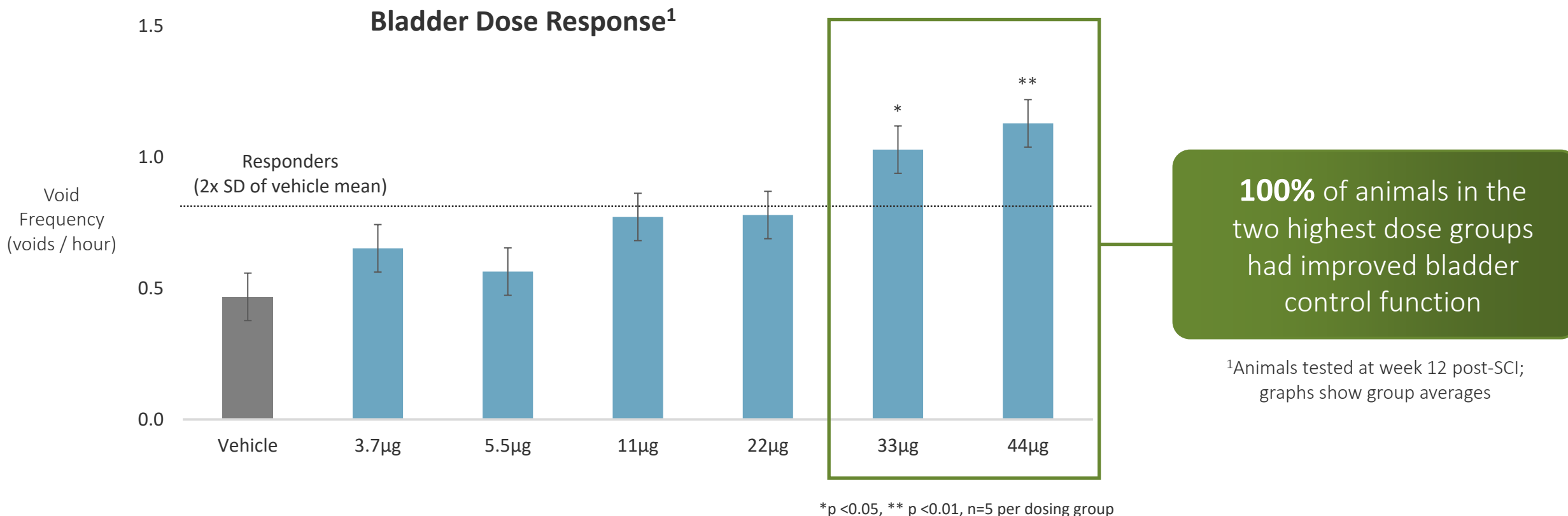
Results

- 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)



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

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Chairman & Co-Founder



Glenn Ives

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CMO, Longboard Pharmaceuticals



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Mike Kelly

President & CEO, NervGen

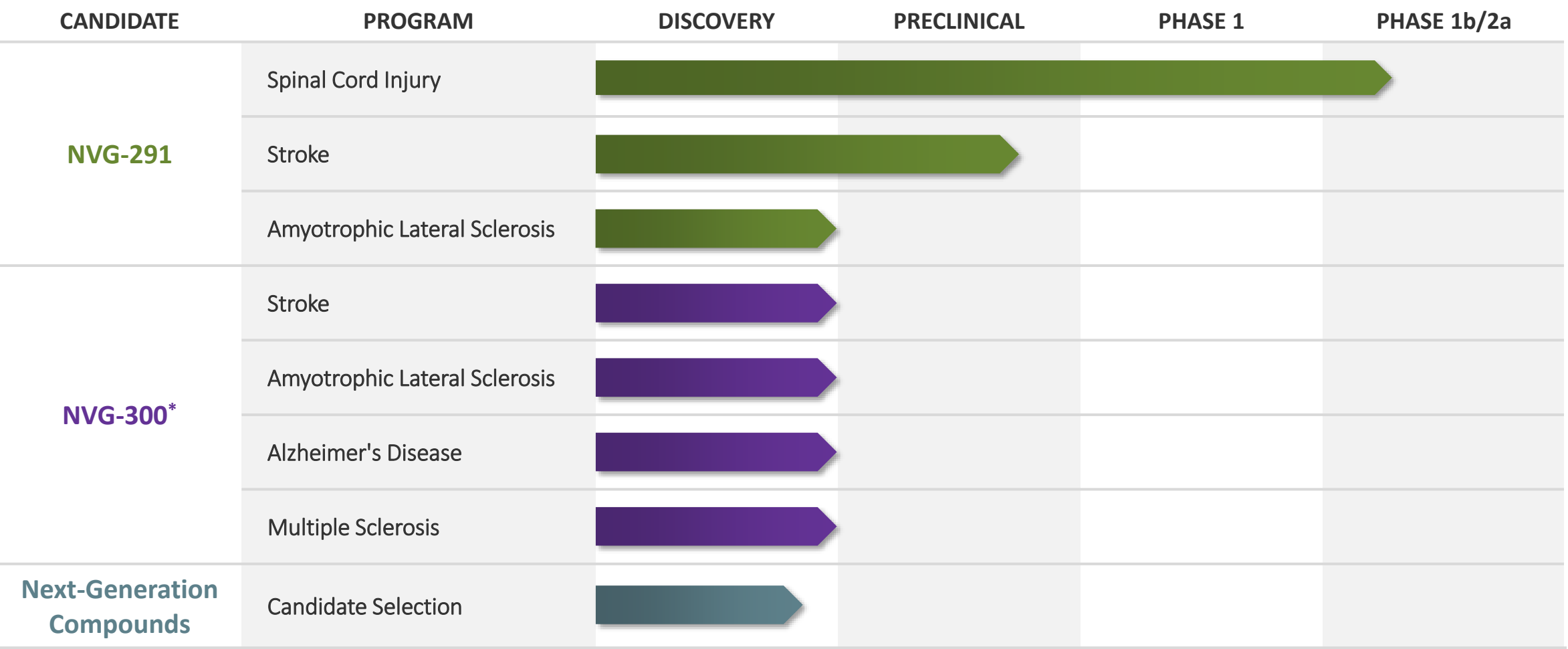


Craig Thompson

CEO, Cerevance

Product Pipeline

Multiple development opportunities



Share and Capital Structure

Exchange/Market: Ticker	TSX: NGEN.V	OTCQX: NGENF
Recent Share Price (September 8, 2023)	CA \$2.01	US \$1.45
Shares Outstanding	59.5 million	
Fully Diluted	78.0 million (~10.9 million options & retention securities, ~7.6 million warrants*)	
Insider Ownership	21.7%	
Cash & Cash Equivalents (June 30, 2023)	CA \$16.1 million	US \$12.1 million

*Warrant exercise price range US\$1.75 (5M) to CA\$3.20 (~2.6M)

Key Value Drivers

Phase 1b/2a clinical trial: study initiated (2023)

Preclinical data in multiple indications (2023/24)

Next generation compound progress (2023/24)

Phase 1b/2a Proof-of-concept readout in chronic SCI (mid-2024)



Enabling the Nervous System to Repair Itself

www.nervgen.com

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