



# Enabling the Nervous System to Repair Itself

Corporate Presentation

April 2025

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# NervGen Highlights

Multiple preclinical studies using NVG-291-R reported improvement in **axonal repair, plasticity, and motor, sensory and cognitive function**

**Q2 2025 – Phase 1b/2a proof-of-concept readout** in people living with chronic SCI

**Q3/Q4 2025 – Plans for meeting with FDA** to discuss regulatory path forward

# History of NervGen Technology



Jerry Silver, PhD



Phase 1b/2a Trial



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

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

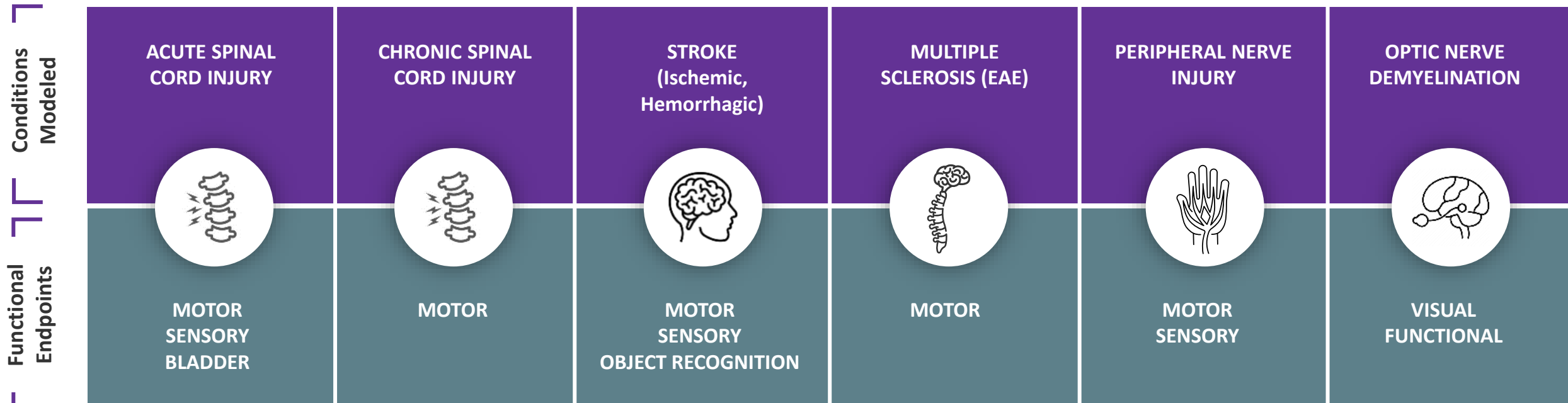
Dr. Silver's team designed a peptide (NVG-291-R) derived from  $PTP\sigma$  shown to relieve CSPG-mediated inhibition of nervous system repair; **NVG-291** is the humanized version of NVG-291-R

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

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

# NVG-291-R Improves CNS/PNS Repair in Preclinical Efficacy Models

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



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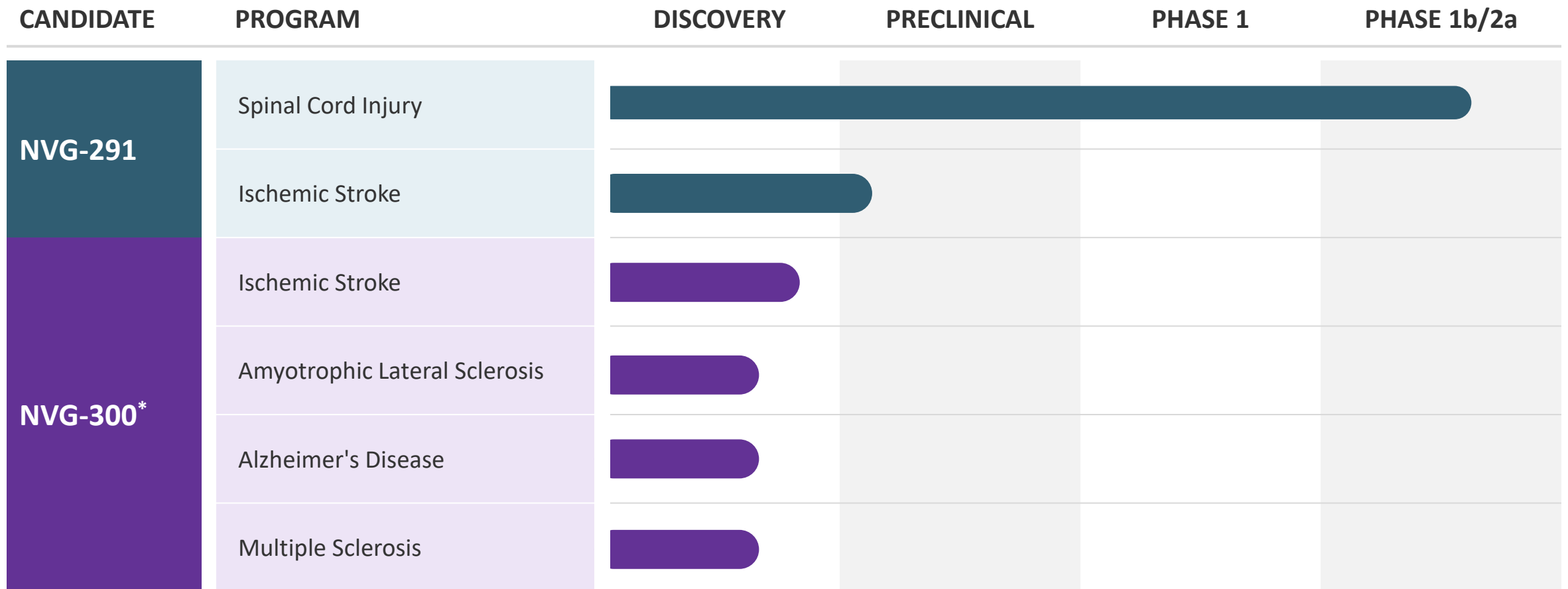
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Niknam, P. et al., Molecular and Cellular Neuroscience, 99, 103391. (2019).






# Product Pipeline

Multiple development opportunities




# Markets and Opportunity in Nervous System Injury & Disease

Significant medical costs and morbidity

	 Spinal Cord Injury	 Ischemic Stroke	 ALS	 Multiple Sclerosis	 Alzheimer's Disease
<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 & Characteristics

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

## TREATMENT

**Surgery**  
(decompression)

**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>

Individuals with SCI face 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

# NVG-291-R Promotes Recovery in Acute SCI

## Overview

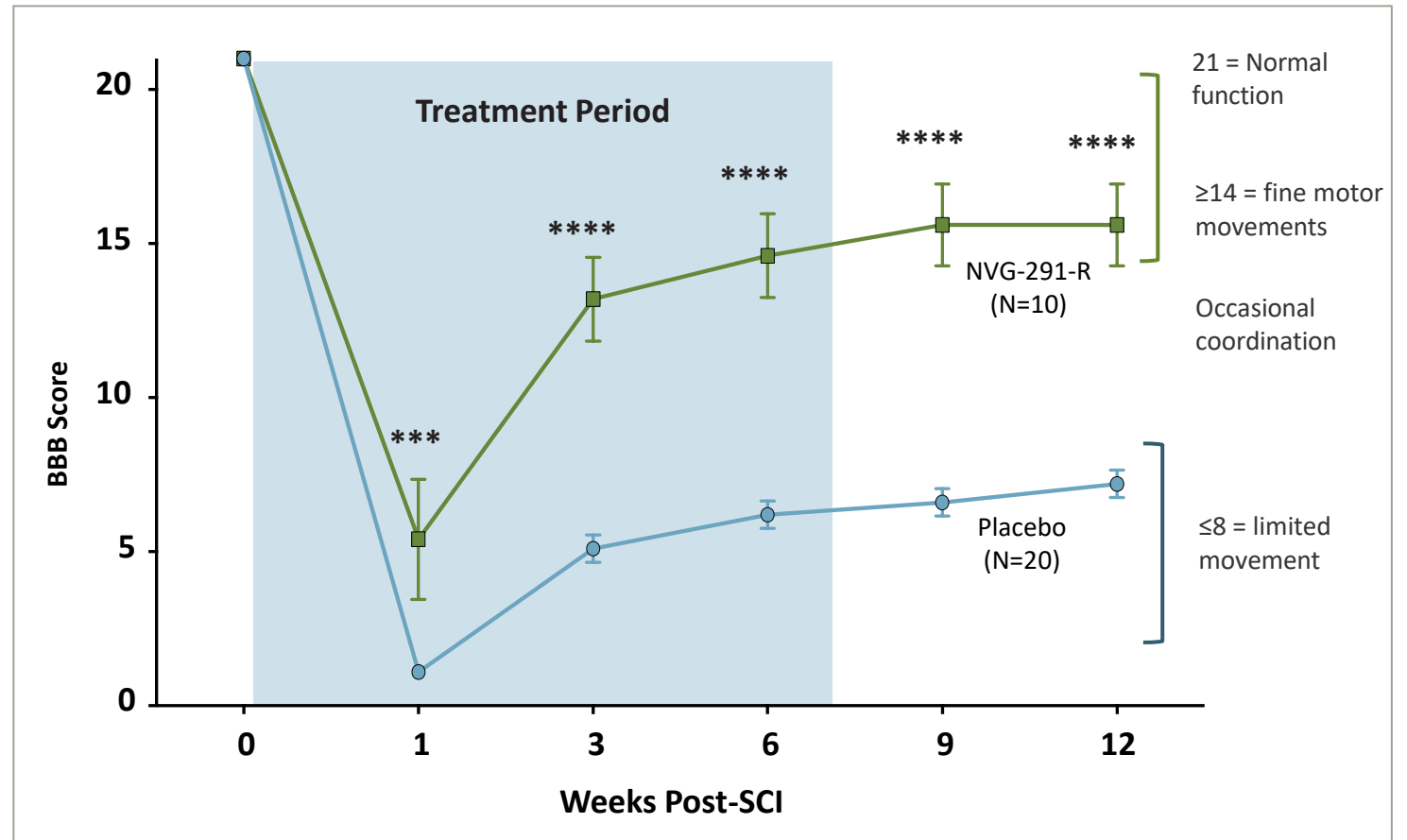
T8 compression injury

- Treatment start: 1 day post-injury
- Dose: 500 µg/day x 7 weeks

## Results

- Significant recovery of locomotor and bladder function
- Functional improvements persist after treatment
- Enhanced neuroplasticity (i.e. axonal sprouting) near and far from injury

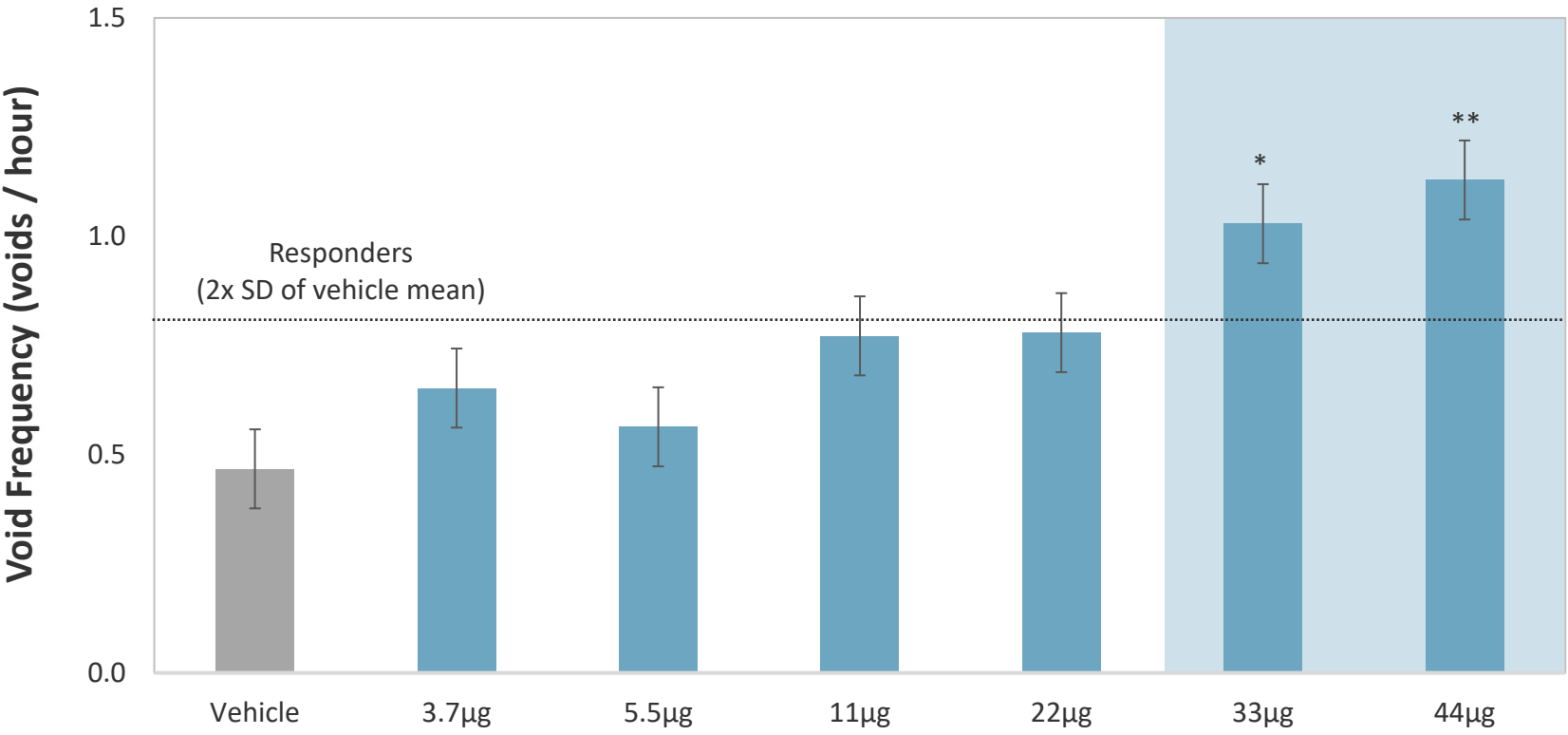
## Hindlimb Function



\*\*\* P<0.001, \*\*\*\* P<0.0001

# Improved Bladder Function After NVG-291-R in Preclinical Models

Bladder Dose Response<sup>1</sup>



**100%**

of animals in the two highest dose groups had improved bladder control function

<sup>1</sup>Animals tested at week 12 post-SCI; graphs show group averages

\*p <0.05, \*\* p <0.01, n=5 per dosing group

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

# NVG-291-R Improves Function in 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 Enables Significant Motor Recovery in Severe SCI Model

## Representative of Placebo Group



Hind legs are immobile in placebo-treated animals



[Click here to play video](#)

## Representative of NVG-291 Group



Significant motor recovery with NVG-291-R: consistent coordination, toe clearance, tail held high consistently

# Chronic SCI Preclinical Study

## Overview

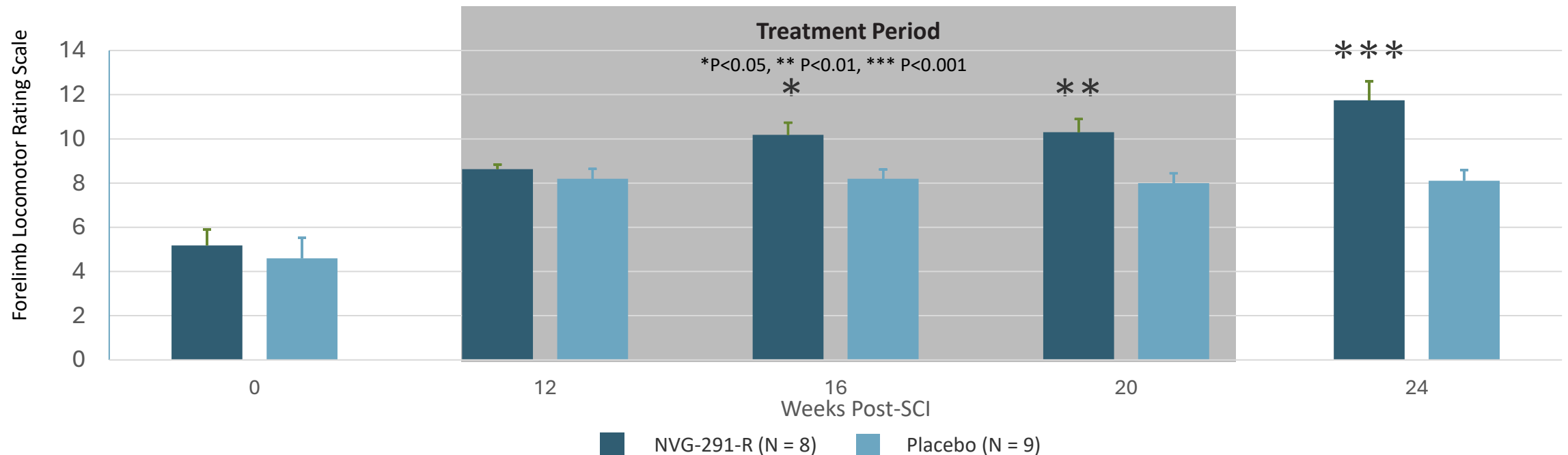
C2 lateral hemisection model of SCI

- Treatment start: 12 weeks post-injury
- Dose: 500 µg/day x 8.5 weeks

## Results

NVG-291-R promoted recovery in chronic SCI

- Significant recovery of forelimb locomotor function
- Functional improvements persist after treatment





# NVG-291 Phase 1 Clinical Trial in Healthy Volunteers

## Study Design

### Single Dose

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

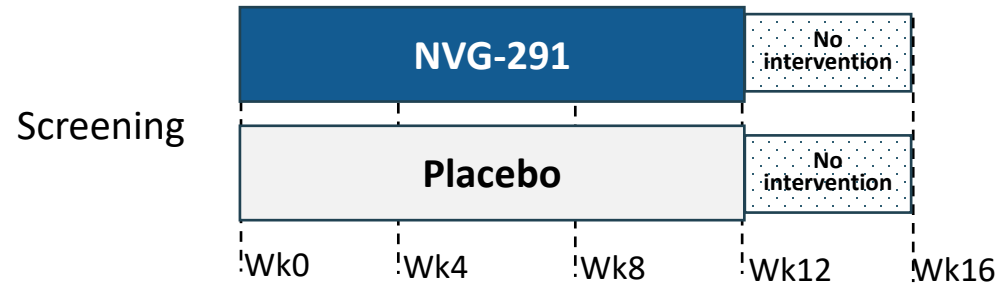
### Multiple Dose

- 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 Grade 1/2 injection site reactions (ISR)
- No clinically significant effects related to NVG-291 treatment across all study parameters

# Phase 1b/2a Trial of NVG-291-201 in SCI



Over 16 weeks

- Daily SQ injections (12 weeks)
- Electrophysiological assessments
- Clinical assessments
- Exercise/training: ~5 days per week

## Single-center study – Shirley Ryan AbilityLab (Chicago, IL, USA)

- Uniform assessments and training regimen – reduces variability of results
- Electrophysiological measurements easily standardized – same assessors, equipment, technique

## Two cohorts

- Approximately 20 patients per cohort
- Randomized 1:1 to NVG-291 (fixed dose) or placebo
- Weeks 1-12: blinded treatment

# Phase 1b/2a Study Inclusion & Exclusion Criteria

## Key Inclusion Criteria

Age 18-75

Traumatic SCI

Neurological level of injury C7 or higher

Motor incomplete with minimal/maximal level of motor function in upper and lower extremities

*Intact motor evoked potential (MEP)*<sup>1</sup> in two *qualifying* muscle groups:

(1) At least 1 tibialis anterior (TA)

(2) At least 1 first dorsal interosseus (FDI)

## Key Exclusion Criteria

Non-traumatic SCI

SCI from gunshot or penetrating/stab injury

Two or more (non-contiguous) spinal cord lesions

Ventilator dependence

## Cohorts of motor incomplete cervical SCI

1. Chronic: 1-10 years post-injury
2. Subacute: 20-90 days post-injury

<sup>1</sup>Intact MEP = amplitude of at least 50  $\mu$ V is observed in at least 5 out of 10 trials

# Phase 1b/2a Trial Primary Objective and Co-Primary Endpoints

## Primary Objective

To evaluate the effect of NVG-291 compared to placebo on relative percentage change in corticospinal connectivity to *qualifying* muscle groups

## Co-Primary Endpoints

Relative percentage change from baseline to Week 12 in the normalized MEP amplitudes (corticospinal contribution) in the *qualifying* **FDI** and **TA** muscle groups

Ten Muscle Groups Assessed	
Upper extremity	Lower extremity
Biceps brachii	Quadriceps
Triceps brachii	Hamstrings
<b>First dorsal interosseous (FDI)<sup>Q</sup></b>	<b>Tibialis anterior (TA)<sup>Q</sup></b>
Flexor carpi radialis	Soleus
Extensor carpi radialis	Abductor hallucis

<sup>Q</sup> *Qualifying* muscle group

Assuming a treatment effect on and variability of MEPs similar to that observed with electrical stimulation studies<sup>1</sup>, with **8 subjects per arm** this study will have **≥80% power** to detect a difference ( $\alpha = 0.025$ , Student t-test 2-sided)

# Phase 1b/2a Trial Secondary Endpoints (Clinical)

01

Change from baseline to Week 12 in **10mWT** time

02

Change from baseline to Week 12 in **9-HPT** time

03

Change from baseline to Week 12 in **pinch** dynamometry force

04

Change from baseline to Week 12 in **GRASSP** version 2 scores

05

Change from baseline to Week 12 in lower extremity **motor scores**

06

Change from baseline to Week 12 in upper extremity **motor scores**

## Other secondary objectives:

Changes in other electrophysiological parameters

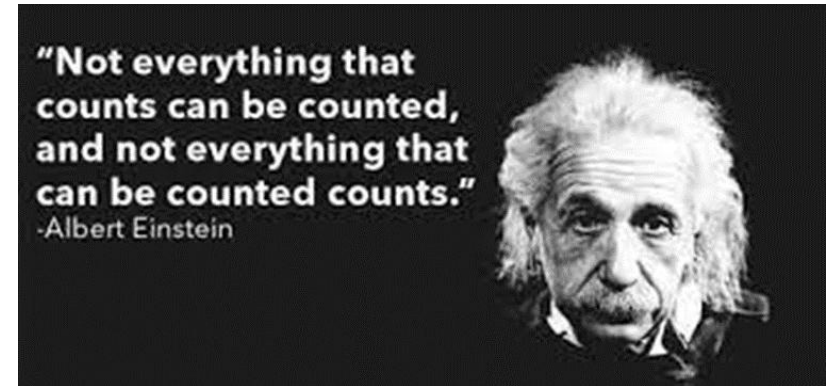
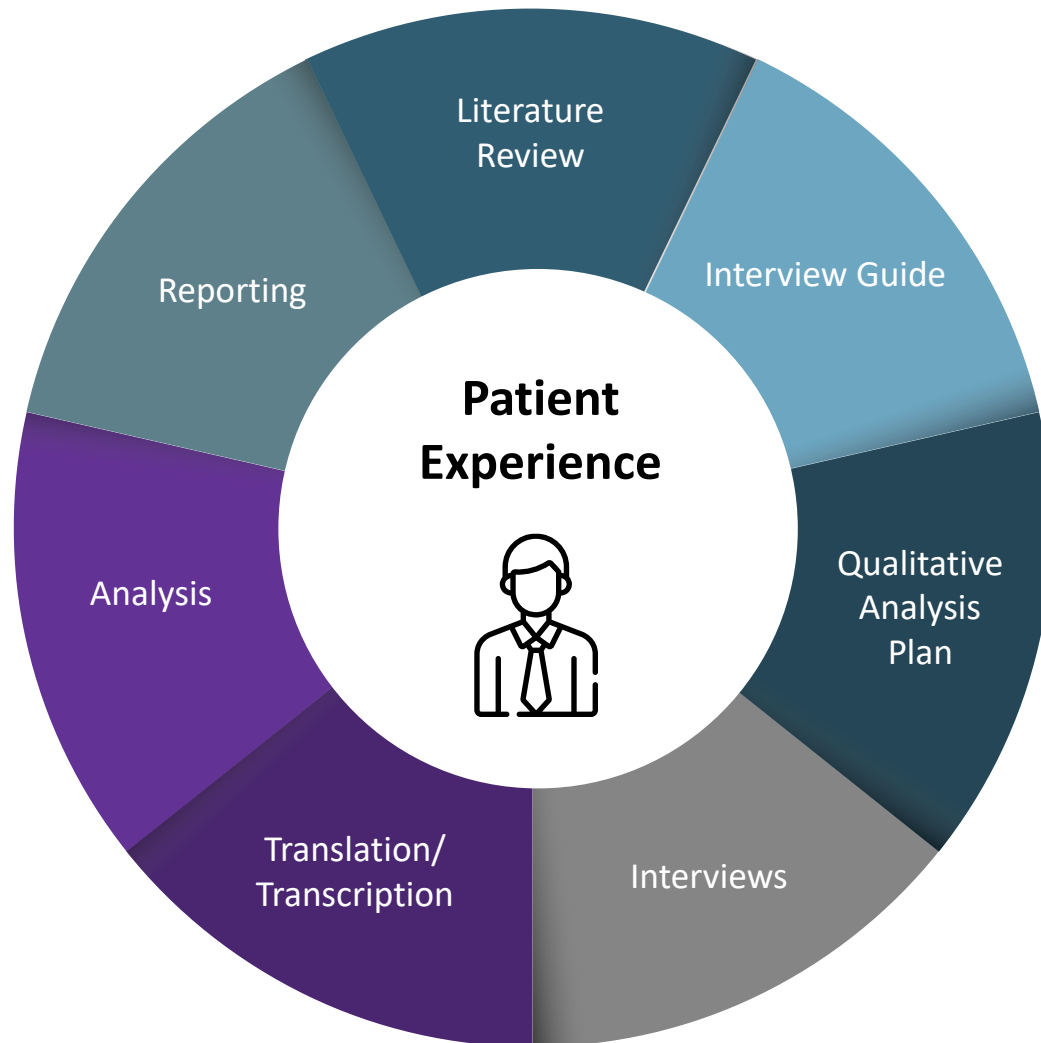
- Change in MEP amplitudes (corticospinal) of non-qualifying muscle groups
- Change in reticulospinal MEP amplitudes
- Change in MEP latencies
- Change in maximal voluntary contractions

Safety/tolerability of NVG-291; pharmacokinetics of NVG-291

## Exploratory objectives:

Changes in spasticity (modified Ashworth, pendulum test), SCAR, ISNCSCI sensory scores, autonomic function (ISAFSCI), mobility/ADLs (SCIM III), quality of life (SCI-QOL), advanced MRI imaging, blood biomarkers

# Additional Patient-Reported Data: Qualitative Review of Subject Experience



Incorporating qualitative semi-structured subject interviews

Exploring subjects' experiences of potential beneficial treatment

Aligns with FDA Patient-Focused Drug Development Guidance



# SCI Development Programs

Company	Product	Stage	Comments
AbbVie	Elezanumab: Intravenous RGMa protein inhibitors	Phase 2	<ul style="list-style-type: none"> <li>Phase 2 initiated Sep 2020, results expected H2 2025</li> <li>Electrophysiology-based secondary endpoint recently added to trial design (NCT04295538)</li> </ul>
Mitsubishi Tanabe	MT-3921: Intravenous RGMa protein inhibitors	Phase 2	<ul style="list-style-type: none"> <li>Phase 2 initiated – last update posted Apr 2024</li> <li>Results expected H1 2025 (NCT04683848)</li> </ul>
Lineage Cell Therapeutic	OPC-1: Intraparenchymal hESC-derived oligodendrocyte progenitor cells	Phase 1/2	<ul style="list-style-type: none"> <li>Amended IND to include new delivery device and initiate DOSED trial in 2024</li> <li>Open label, subacute and chronic, primary endpoint is safety with new device (NCT05975424)</li> </ul>
ReNetX Bio	AXER-204: Intrathecal Anti Nogo-A, MAG, and Omgp	Phase 1/2	<ul style="list-style-type: none"> <li>Missed primary endpoint in Ph 1/2 ITT population but showed signal in motor incomplete patients in post hoc analysis* (NCT03989440)</li> </ul>

\*Maynard et al., 2023. *The Lancet Neurology* Vol 22 Issue 8: 672-684

# NVG-300, A Proprietary Molecule Diversifying Pipeline and Opportunity for Partnering

01

A new proprietary molecule discovered at NervGen in 2022

02

Demonstrated favorable pharmaceutical properties (solubility, metabolic stability)

- Severe injury model characterized by heightened spinal cord damage and impaired spontaneous recovery

03

Eligible for the BLA development path

04

Composition of matter IP protection expected to extend beyond 2040

## Next steps

Formulation development

Evaluating in a preclinical model of ischemic stroke and confirmatory SCI study

# Experienced Leadership Team



**MIKE KELLY, MBA, CHIEF EXECUTIVE OFFICER**

Over 30 years of pharmaceutical experience. Formerly President of US Ops for Adapt Pharma, Inc., which developed and commercialized NARCAN Nasal Spray in the US and Canada and was sold to Emergent BioSolutions for US\$735 million.



**BILL ADAMS, CPA, CA, CHIEF FINANCIAL OFFICER**

Over 25 years of strategic financial management experience including mergers and acquisitions, operations and capital markets in Canada and the US.



**DAN MIKOL, MD, PHD, CHIEF MEDICAL OFFICER**

Over 25 years of experience in neurology clinical research. Former Head of clinical development at Amgen in neuroscience and nephrology and was instrumental in the approval of Aimovig, and development lead for Tysabri at Biogen.



**CHUCK OLSON, DSC, SR. VP, TECHNICAL OPERATIONS**

Over 40 years of experience in process development, manufacturing and CMC associated quality and regulatory activities for many clinical and commercial products.



**LIZ EBERHARDT, BSC, SR. VP, PROJECT MANAGEMENT**

Over 25 years of biotech experience in product leadership and program management and has taken multiple compounds through all stages of development including preclinical and commercialization.



**KEVIN ROONEY, MBA, SR. VP, CORPORATE DEVELOPMENT & STRATEGY**

Over 30 years of experience in building businesses in oncology, central nervous system, diabetes, anesthesia, rare disease, cardiovascular, gastrointestinal, and infectious disease therapeutic areas.



**MATVEY LUKASHEV, PHD, VP, RESEARCH & PRECLINICAL DEVELOPMENT**

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



# Board of Directors



**Glenn Ives**

Chairman  
Former Partner, Deloitte LLP



**Harold Punnett, DMD**

Co-Founder



**Mike Kelly**

President & CEO, NervGen



**Adam Rogers, MD**

Former CEO & Co-Founder, Hemera



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Director, Earlston Investments



**Neil Klompas**

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**John Ruffolo**

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**Randall Kaye, MD**

CMO, Longboard Pharmaceuticals



**Krista McKerracher**

Former Global Franchise Head, Novartis



**Craig Thompson**

CEO, Cerevance

# Upcoming Milestones

**Q2 2025**

**Phase 1b/2a proof-of-concept readout** in people living with chronic SCI

**Q3/Q4 2025**

**Plan to meet with FDA** to discuss next steps in NVG-291 development

# Share and Capital Structure

Exchange/Market: Ticker	TSX: NGEN.V OTCQB: NGENF
Recent Share Price (Apr 3, 2025)	CA\$3.09 / US\$2.17
Shares Outstanding	71.0 million
Fully Diluted	94.8 million (~13.7 million options & retention securities, ~10.1 million warrants*)
Insider Ownership	20.9%
Cash & Cash Equivalents (Dec 31, 2024)	CA\$17.3 million / US\$12.0 million

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





# Enabling the Nervous System to Repair Itself

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

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