



# Enabling the Nervous System to Repair Itself

Corporate Presentation

September 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

**NVG-291 – Phase 1b/2a proof-of-concept trial** in people living with SCI underway

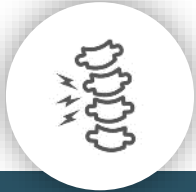
NVG-300 – preclinical evaluation advancing in **ischemic stroke, ALS and SCI**

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

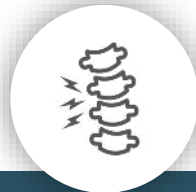
## Enhanced Plasticity, Repair (Axonal, Myelination), and Recovery of Function

Conditions Modeled

**ACUTE SPINAL CORD INJURY**



**CHRONIC SPINAL CORD INJURY**



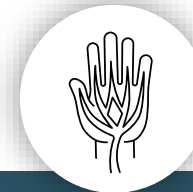
**STROKE**  
(Ischemic, Hemorrhagic)



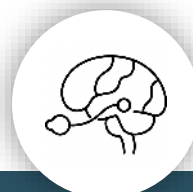
**MULTIPLE SCLEROSIS (EAE)**



**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

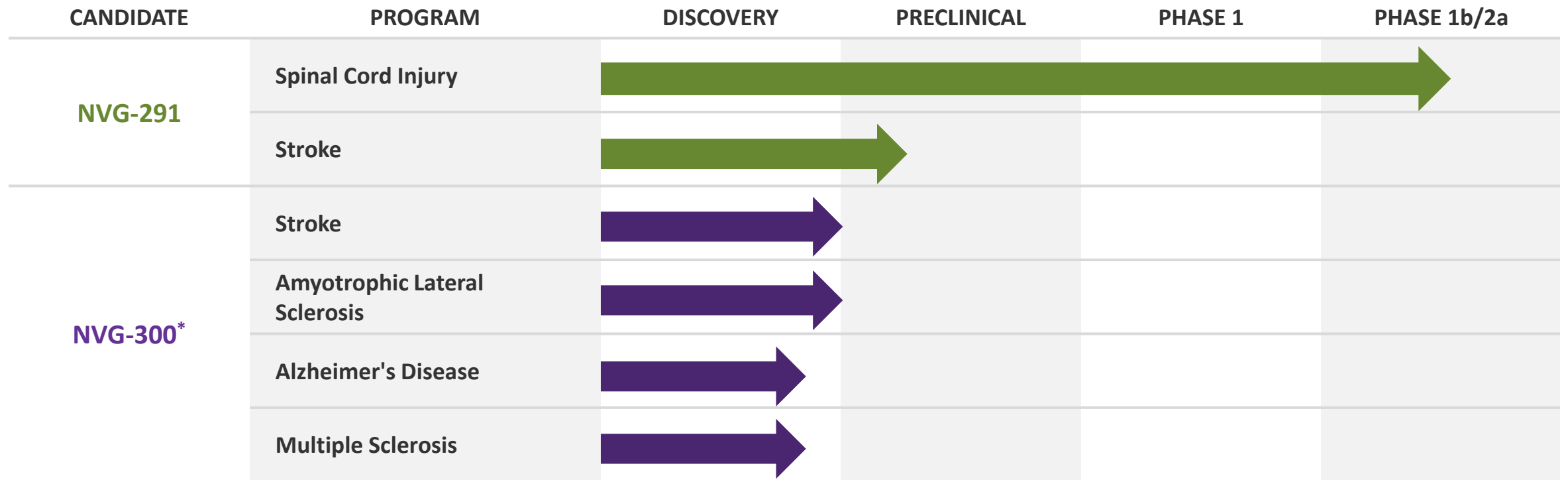
1. Luo, F. et al., Nature Communications, 9, 1–16. (2018).

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).

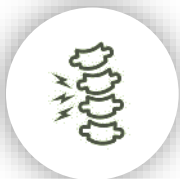
# Product Pipeline

## Multiple development opportunities



# 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

### 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>

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



# NVG-291-R

## Promotes Recovery in Acute SCI

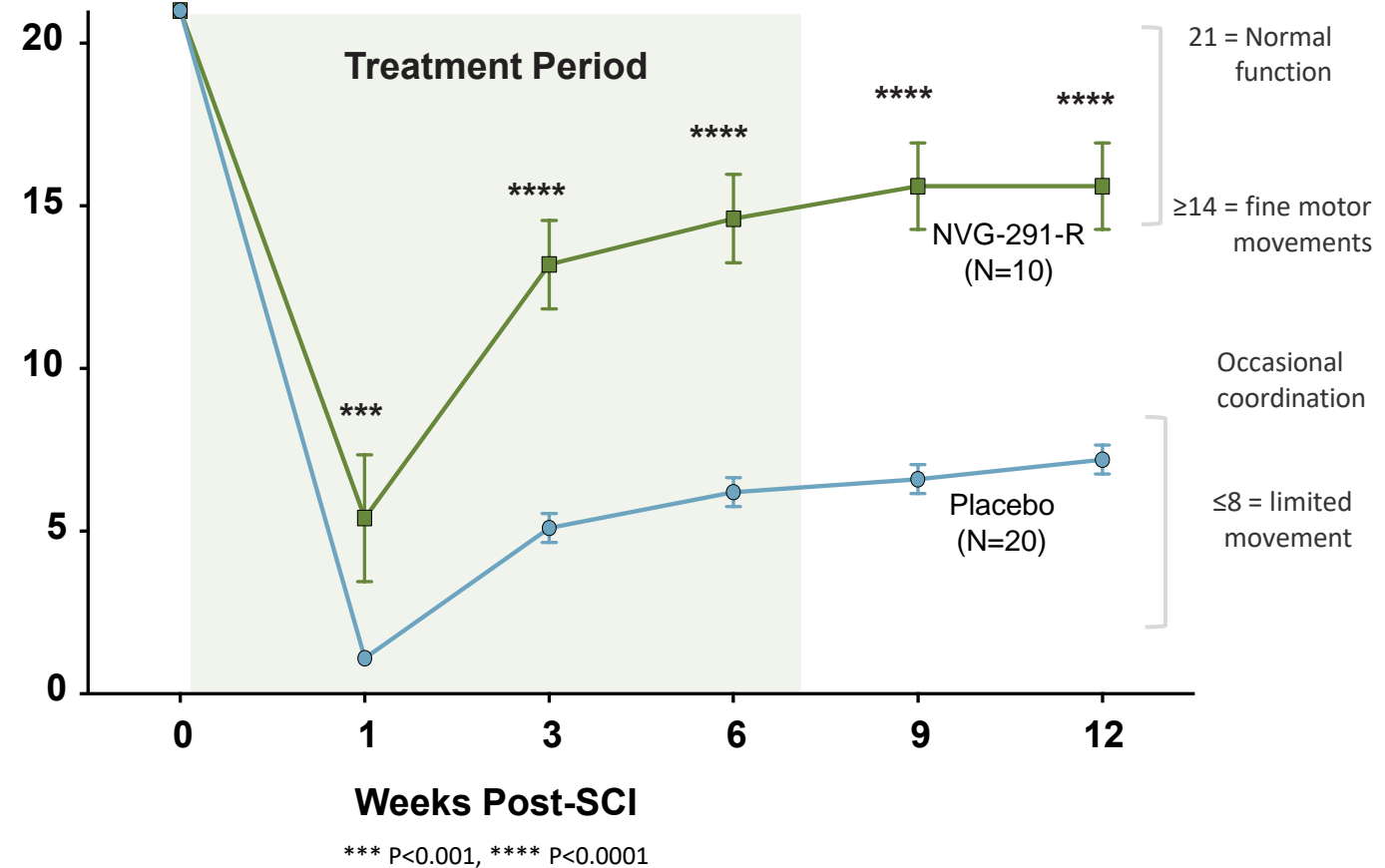
### Overview

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

### 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 (BBB Score)



# NVG-291-R

## Promotes Recovery in Chronic SCI

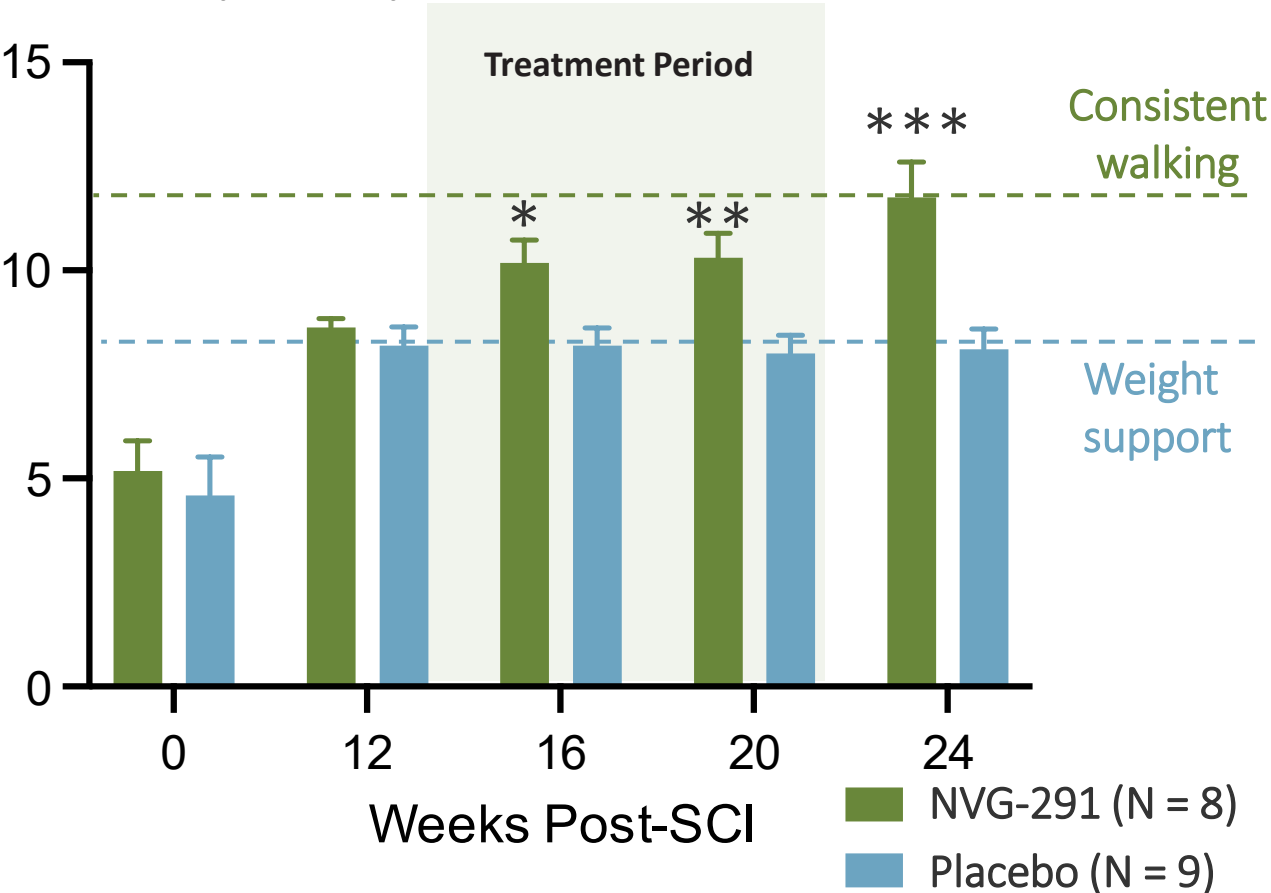
### Overview

- 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

Forelimb function (FLS score)



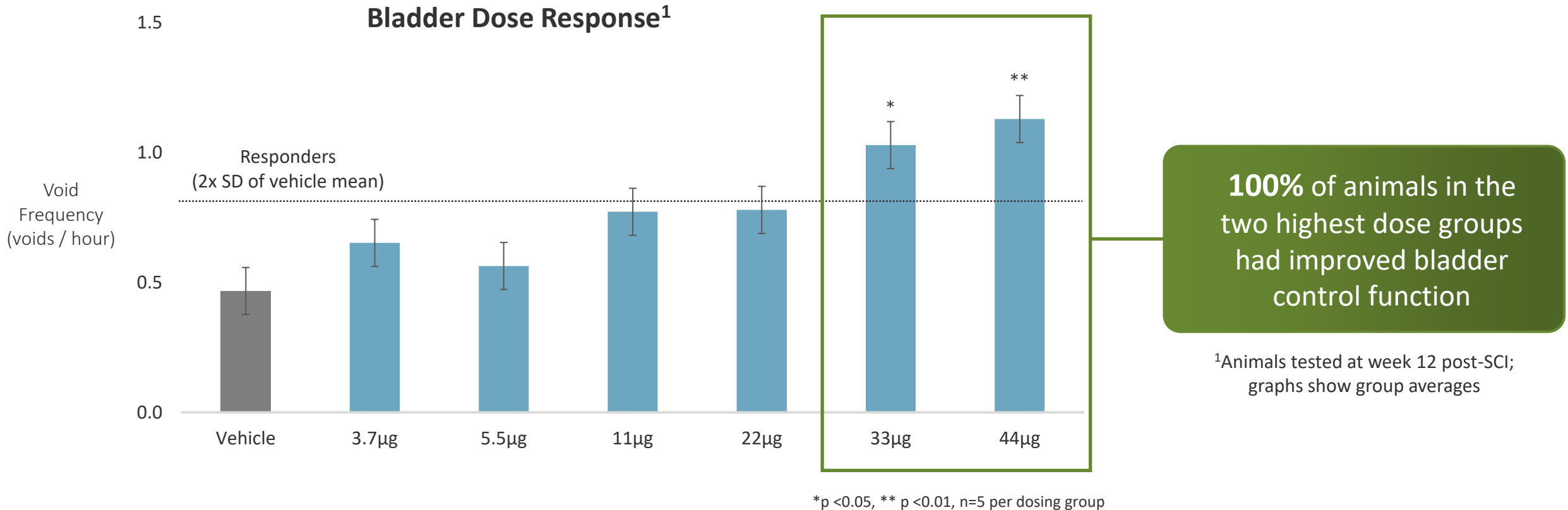
\*P<0.05, \*\* P<0.01, \*\*\* P<0.001

Adapted from Milton et al, Journal of Neurotrauma, (2023) doi:10.1089/neu.2023.0117



# 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

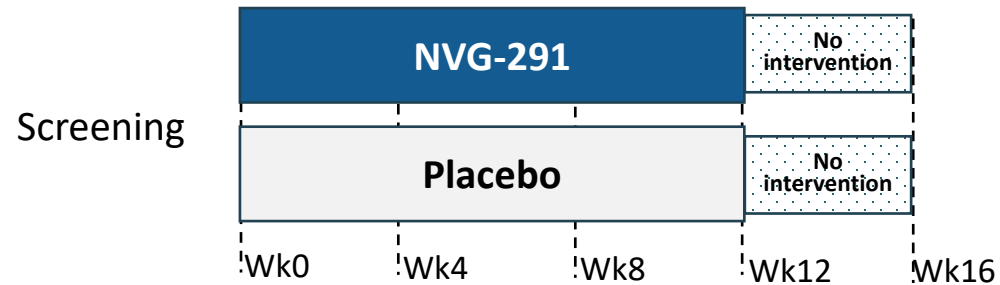
### Multiple Dose

- 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 Trial: Study NVG-291-201



Over 16 weeks:

- Daily sub-cue 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 (coils, electrodes etc.), technique, analysis
- **Two cohorts** planned (~N=20 each)
  - Randomized 1:1 to NVG-291 (fixed dose) or placebo
  - Weeks 1-12: blinded treatment

*clinicaltrials.gov* NCT05965700

Shirley Ryan  
**Abilitylab**



# Study Population

## Cohorts of motor incomplete cervical SCI:

1. **Chronic:** 1-10 years post-injury
2. **Subacute:** 20-90<sup>1</sup> days post-injury

Key Inclusion Criteria	Key Exclusion Criteria
<ul style="list-style-type: none"> <li>• Age 18-75</li> </ul>	<ul style="list-style-type: none"> <li>• Non-traumatic SCI</li> </ul>
<ul style="list-style-type: none"> <li>• Traumatic SCI</li> </ul>	<ul style="list-style-type: none"> <li>• SCI from gunshot or penetrating/stab injury</li> </ul>
<ul style="list-style-type: none"> <li>• Neurological level of injury C7 or higher</li> </ul>	<ul style="list-style-type: none"> <li>• Two or more (non-contiguous) spinal cord lesions</li> </ul>
<ul style="list-style-type: none"> <li>• <b>Motor incomplete</b> with minimal/maximal level of motor function in upper and lower extremities</li> </ul>	<ul style="list-style-type: none"> <li>• Ventilator dependence</li> </ul>
<ul style="list-style-type: none"> <li>• <b><i>Intact motor evoked potential (MEP)<sup>2</sup> in two qualifying muscle groups:</i></b> <ul style="list-style-type: none"> <li>• <b>At least 1 tibialis anterior (TA)</b></li> <li>• <b>At least 1 first dorsal interosseus (FDI)</b></li> </ul> </li> </ul>	

<sup>1</sup>Pending protocol amendment

<sup>2</sup>Intact MEP = amplitude of at least 50 µV is observed in at least 5 out of 10 trials

# Primary Objective and Endpoint

- 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)</b> <sup>Q</sup>	<b>Tibialis anterior (TA)</b> <sup>Q</sup>
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)

<sup>1</sup>Jo and Perez, 2020 (Brain 143:1368–1382), Corticospinal-motor neuronal plasticity promotes exercise-mediated recovery in humans with spinal cord injury.

# Secondary Endpoints (Clinical)

1. Change from baseline to Week 12 in **10mWT** time
2. Change from baseline to Week 12 in **9-HPT** time
3. Change from baseline to Week 12 in **pinch** dynamometry force
4. Change from baseline to Week 12 in **GRASSP** version 2 scores
5. Change from baseline to Week 12 in *lower* extremity **motor scores**
6. 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

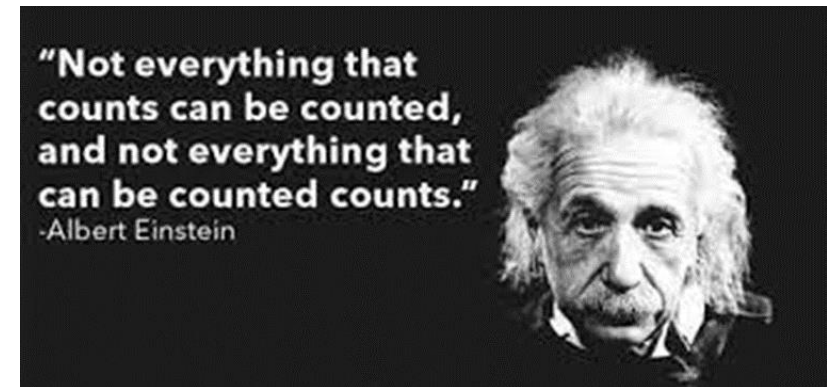
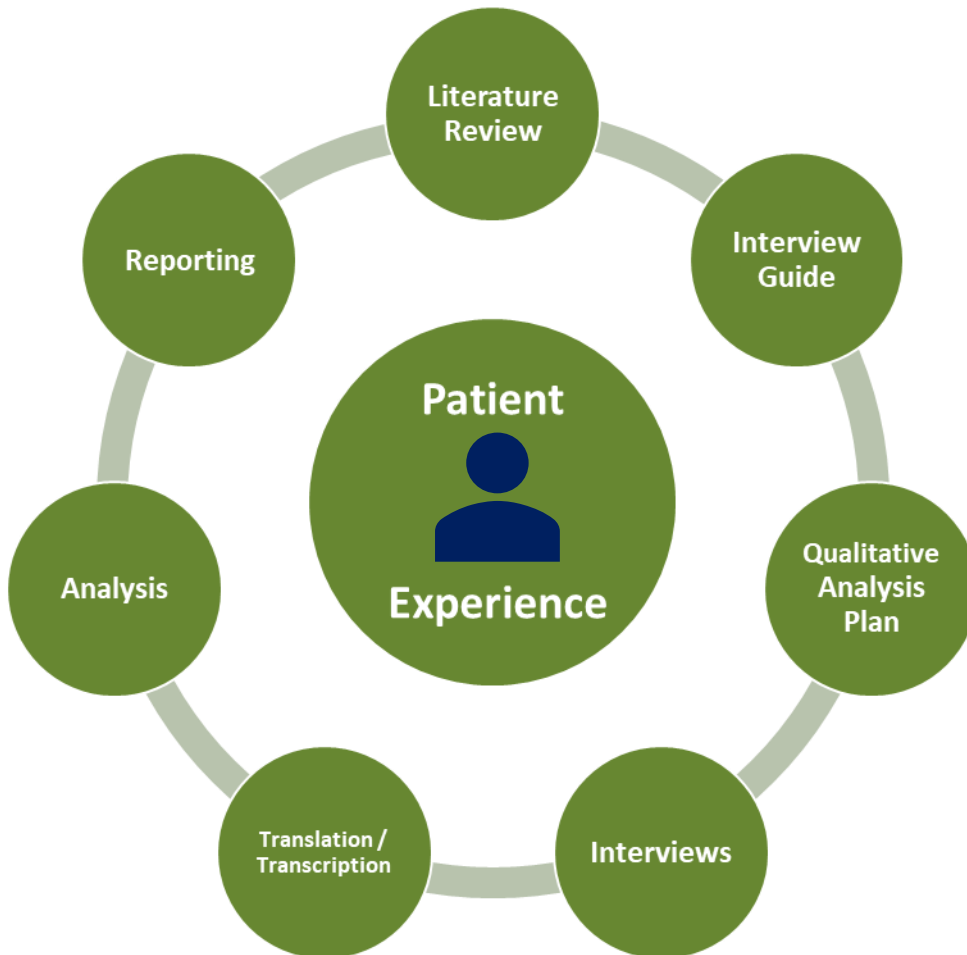
## Exploratory objectives:

- 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 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



# Advancing NVG-300

- A new proprietary molecule discovered at NervGen in 2022
- Demonstrated promising efficacy during initial preclinical evaluation in SCI
  - Severe injury model characterized by heightened spinal cord damage and impaired spontaneous recovery
- Demonstrated favorable pharmaceutical properties (solubility, metabolic stability)
- Eligible for the BLA development path
- Composition of matter IP protection expected to extend beyond 2040

## Next steps

- Formulation development
- Further preclinical evaluation in SCI
- Initiating evaluation in preclinical models of ischemic stroke and ALS

**Adds diversity to pipeline and provides strategic optionality for future partnering opportunities**

# NervGen Summary

- NVG-291 proof-of-concept trial underway in subjects with chronic SCI
  - Evaluating motor connectivity, function and subject-perceived benefit
  - Targeting to complete chronic cohort enrollment in Q3
  - Subacute cohort targeted to initiate enrollment in Q3
- NVG-300 advancing
  - Furthering preclinical evaluation in SCI
  - Initiating evaluation in preclinical models of ischemic stroke and ALS

# 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.



**Chuck Olson, DSc**  
**Sr. VP, Technical Operations**

Chuck has over 40 years of experience as a biotechnology industry professional with a broad scientific and operational 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**

Liz has over 25 years of biotech experience in product leadership and program management. Throughout her career, Liz has taken multiple compounds through all stages of development including preclinical and commercialization.



**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.



# Board of Directors



**Glenn Ives**

Chairman  
Former Partner, Deloitte LLP



**Mike Kelly**

President & CEO, NervGen



**Adam Rogers, MD**

Former CEO & Co-Founder, Hemera



**Harold Punnett, DMD**

Co-Founder



**Neil Klompas**

President & CEO, Augurex



**John Ruffolo**

Founder & Managing Partner, Maverix



**Brian Bayley**

Director, Earlston Investments



**Krista McKerracher**

Former Global Franchise Head, Novartis



**Craig Thompson**

CEO, Cerevance



**Randall Kaye, MD**

CMO, Longboard Pharmaceuticals

# Upcoming Milestones

**Targeting Q3 to complete Phase 1b/2a enrollment in chronic cohort**

**Initiating enrollment in subacute cohort**

**NVG-300 preclinical data in stroke, ALS, SCI**

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

# Share and Capital Structure

<b>Exchange/Market: Ticker</b>	TSX: NGEN.V	OTCQB: NGENF
<b>Recent Share Price</b> (September 3, 2024)	CA \$2.72	US \$2.00
<b>Shares Outstanding</b>	70.2 million	
<b>Fully Diluted</b>	92.6 million (~12.3 million options & retention securities, ~10.1 million warrants*)	
<b>Insider Ownership</b>	21.4%	
<b>Cash &amp; Cash Equivalents</b> (June 30, 2024)	CA \$26.6 million	US \$19.4 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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