



Enabling the Nervous System to Repair Itself

Corporate Presentation

August 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

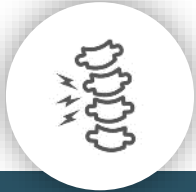
NVG-300 – preclinical evaluation advancing in **ischemic stroke, ALS and SCI**

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

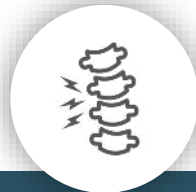
Enhanced Plasticity, Repair (Axonal, Myelination), and Recovery of Function

Conditions Modeled

ACUTE SPINAL CORD INJURY



CHRONIC SPINAL CORD INJURY



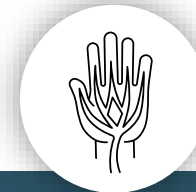
STROKE
(Ischemic, Hemorrhagic)



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

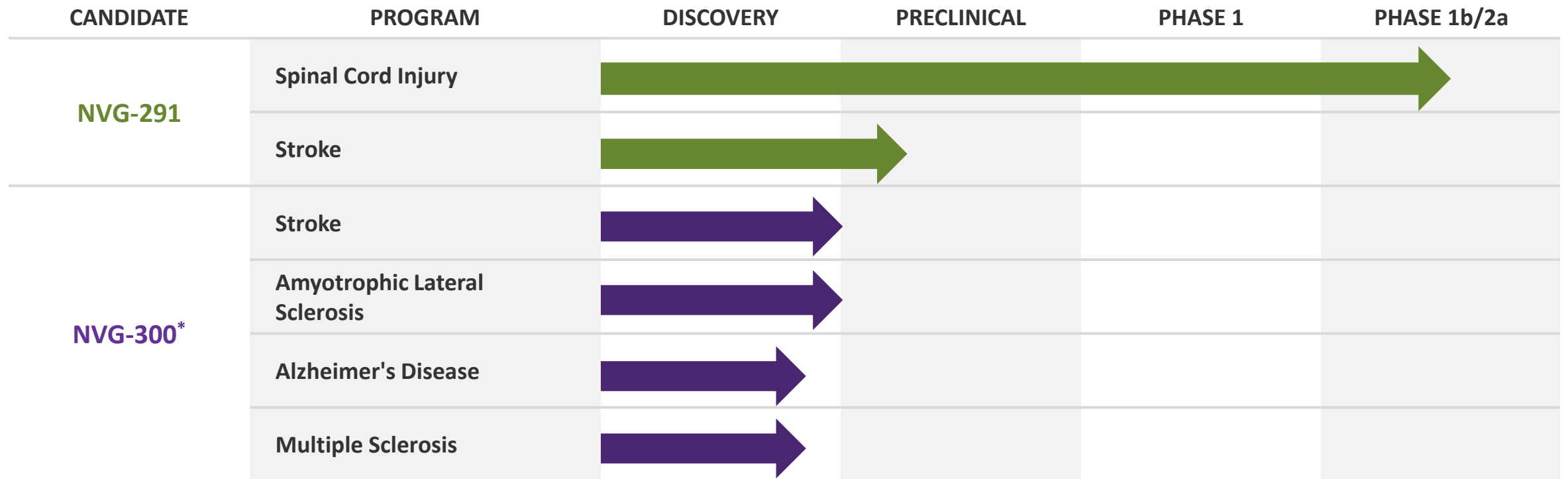
1. Luo, F. et al., Nature Communications, 9, 1–16. (2018).

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).

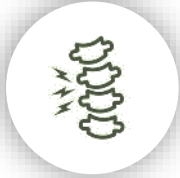
Product Pipeline

Multiple development opportunities



Nervous System Damage Markets and Opportunity

Significant medical costs and morbidity



	SCI	Ischemic Stroke	ALS	MS	AD
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

* 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 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

NVG-291-R

Promotes Recovery in Acute SCI

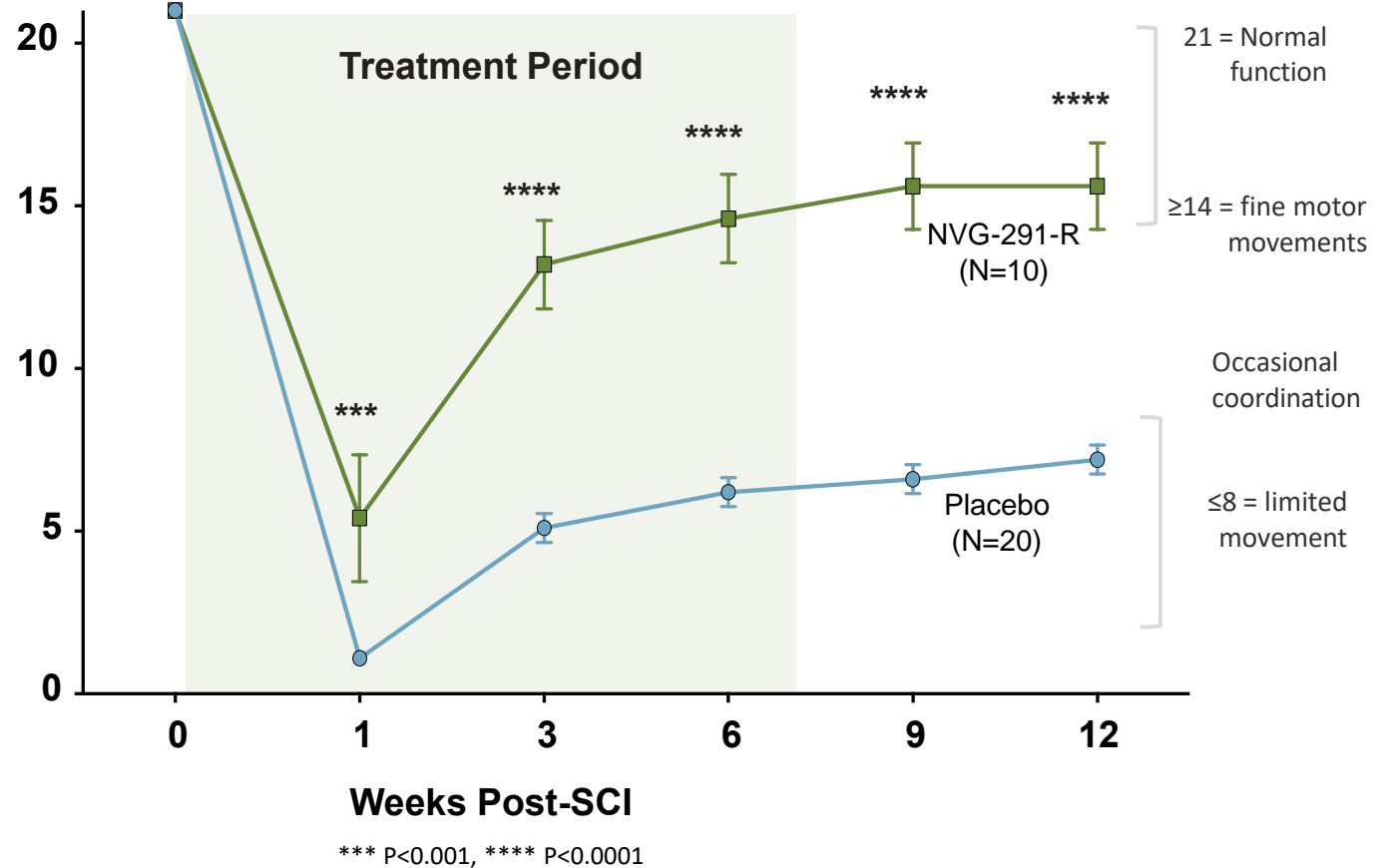
Overview

- 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

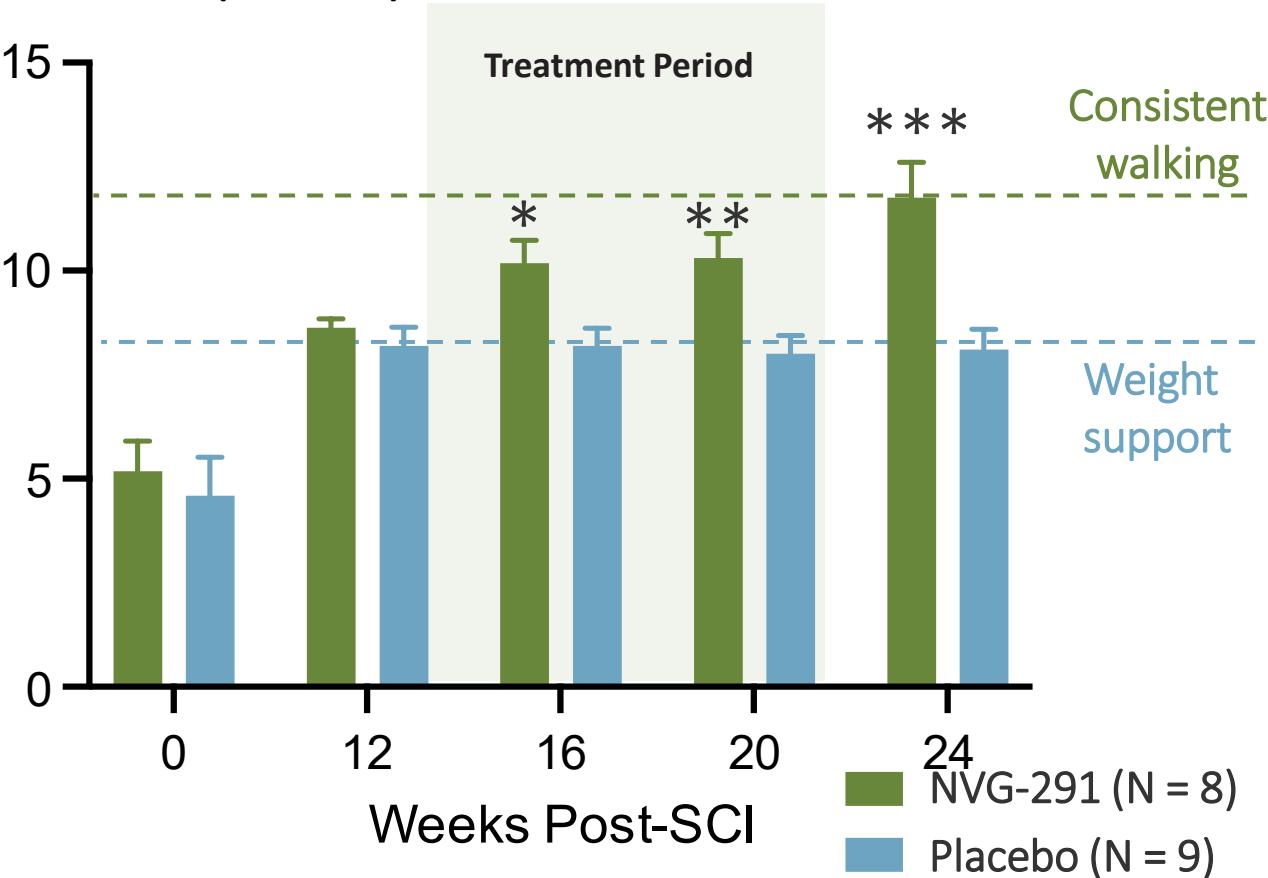
Overview

- 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)



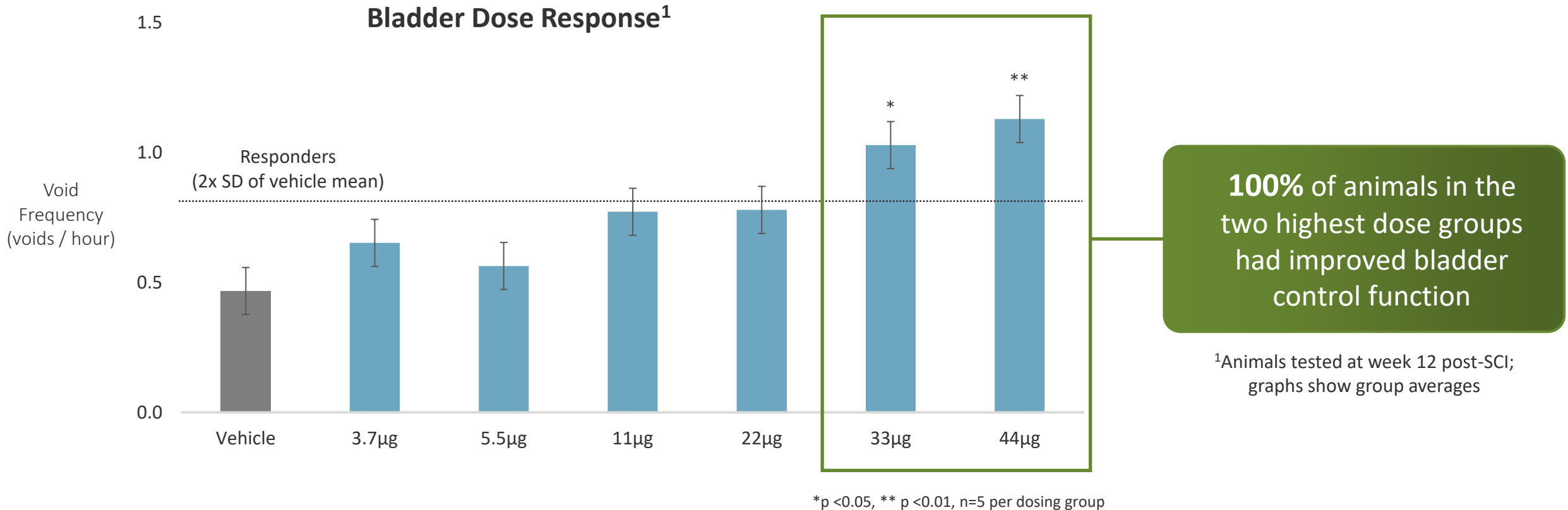
*P<0.05, ** P<0.01, *** P<0.001

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

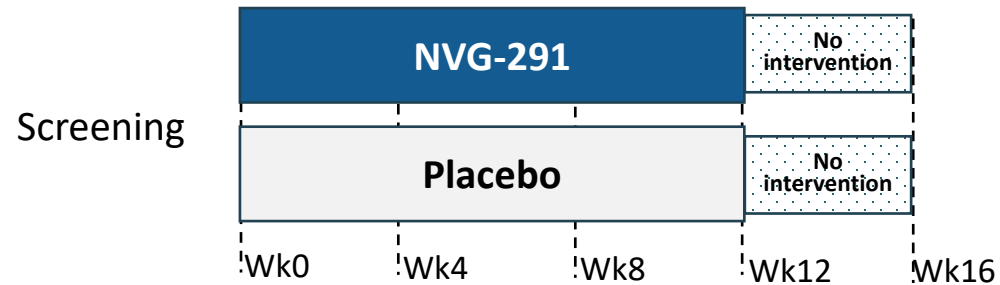
Multiple Dose

- 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:** 20-90¹ days post-injury

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

¹Pending protocol amendment

²Intact 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
First dorsal interosseous (FDI) ^Q	Tibialis anterior (TA) ^Q
Flexor carpi radialis	Soleus
Extensor carpi radialis	Abductor hallucis

^Q *Qualifying* muscle group

Assuming a treatment effect on and variability of MEPs similar to that observed with electrical stimulation studies¹, with **8 subjects per arm** this study will have **≥80% power** to detect a difference ($\alpha = 0.025$, Student t-test 2-sided)

¹Jo 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:

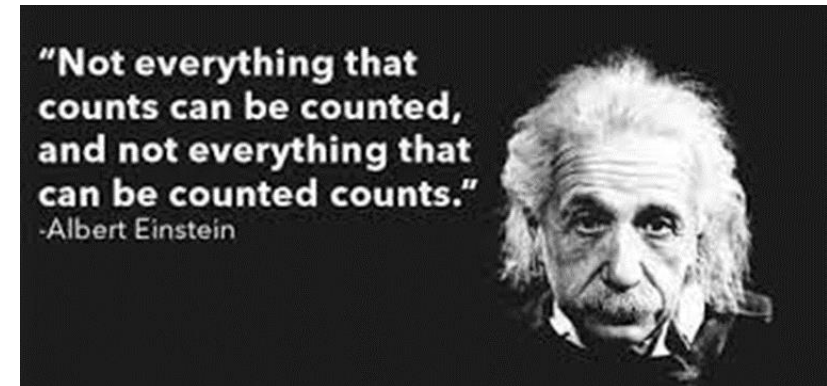
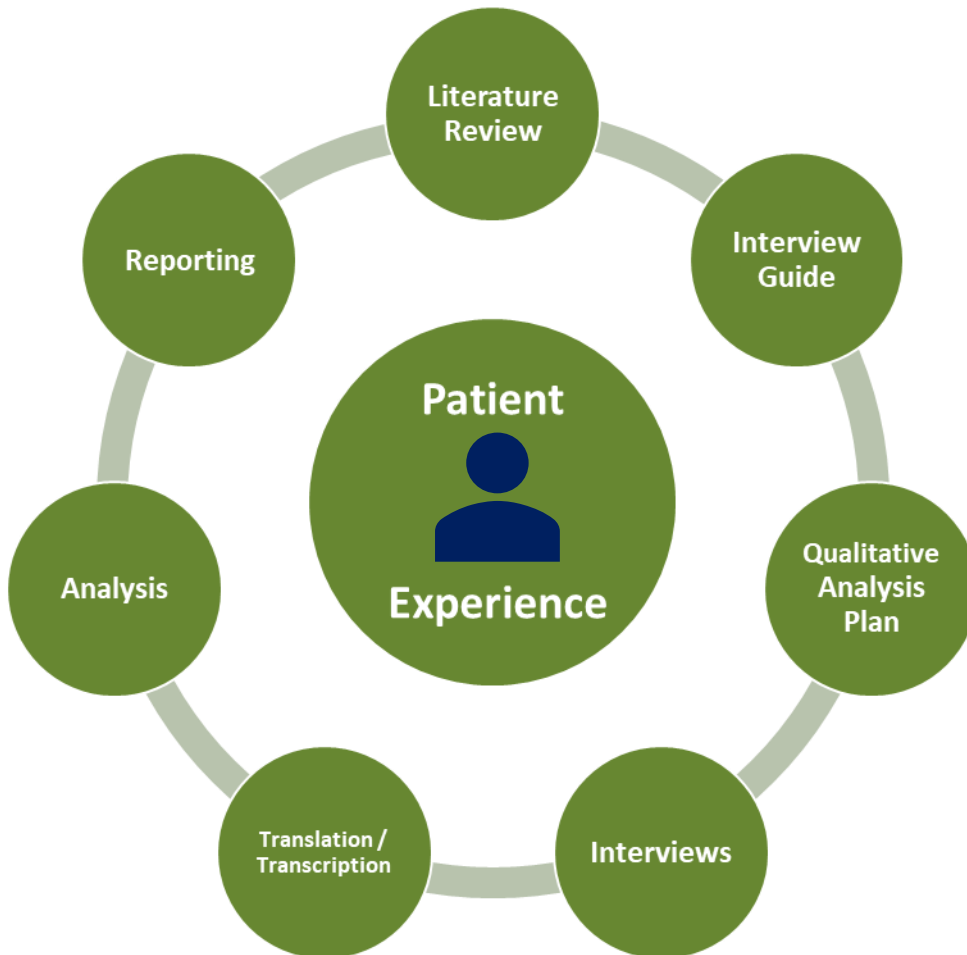
- Changes in other electrophysiological parameters
 - Change in MEP amplitudes (corticospinal) of non-qualifying muscle groups
 - Change in reticulospinal MEP amplitudes
 - Change in MEP latencies
 - Change in maximal voluntary contractions
- Safety/tolerability of NVG-291; pharmacokinetics of NVG-291

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



Blinded Baseline Demographic and Clinical Characteristics

*Chronic cohort		
Age (years)	Mean (SD)	45.2 (17.82)
Sex	N (% male)	11 (91.7%)
Time since SCI (years)	Mean (SD)	3.76 (2.717)
Neurological level of injury	N (%) C2	2 (16.7%)
	N (%) C3	4 (33.3%)
	N (%) C4	3 (25%)
	N (%) C5	1 (8.3%)
	N (%) C6	2 (16.7%)
	N (%) C7	0 (0%)
	AIS	N (%) C
N (%) D		9 (75%)
✓ UEMS	Mean (SD)	35.2 (9.21)
✓ LEMS	Mean (SD)	34.1 (9.08)
WISCI II score	Mean (SD)	9.3 (3.55)
✓ ¹ 10mWT (m/sec)	Mean (SD)	0.43 m/sec (0.478)
✓ ² 9-HPT (sec)	Mean (SD)	159.89 (105.245)
✓ Pinch dynamometry force (Newtons)	Mean (SD)	32.92 (32.312)
✓ GRASSP v2 total score	Mean (SD)	54.8 (14.95)
✓ FDI-MEP amplitude, % of M-Max	Mean (SD)	5.35 (3.999)
✓ TA-MEP amplitude, % of M-Max	Mean (SD)	6.63 (4.094)

*First 12 randomized subjects

¹N=2 (16.7%) unable to complete at baseline

²N=3 (25%) unable to complete at baseline

✓ Primary or secondary outcome measure

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

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

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.



Share and Capital Structure

Exchange/Market: Ticker	TSX: NGEN.V	OTCQB: NGENF
Recent Share Price (August 9, 2024)	CA \$2.96	US \$2.15
Shares Outstanding	70.2 million	
Fully Diluted	92.5 million (~12.2 million options & retention securities, ~10.1 million warrants*)	
Insider Ownership	23.3%	
Cash & Cash Equivalents (March 31, 2024)	CA \$30.3 million	US \$22.4 million

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



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www.nervgen.com

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