



Enabling the Nervous System to Repair Itself

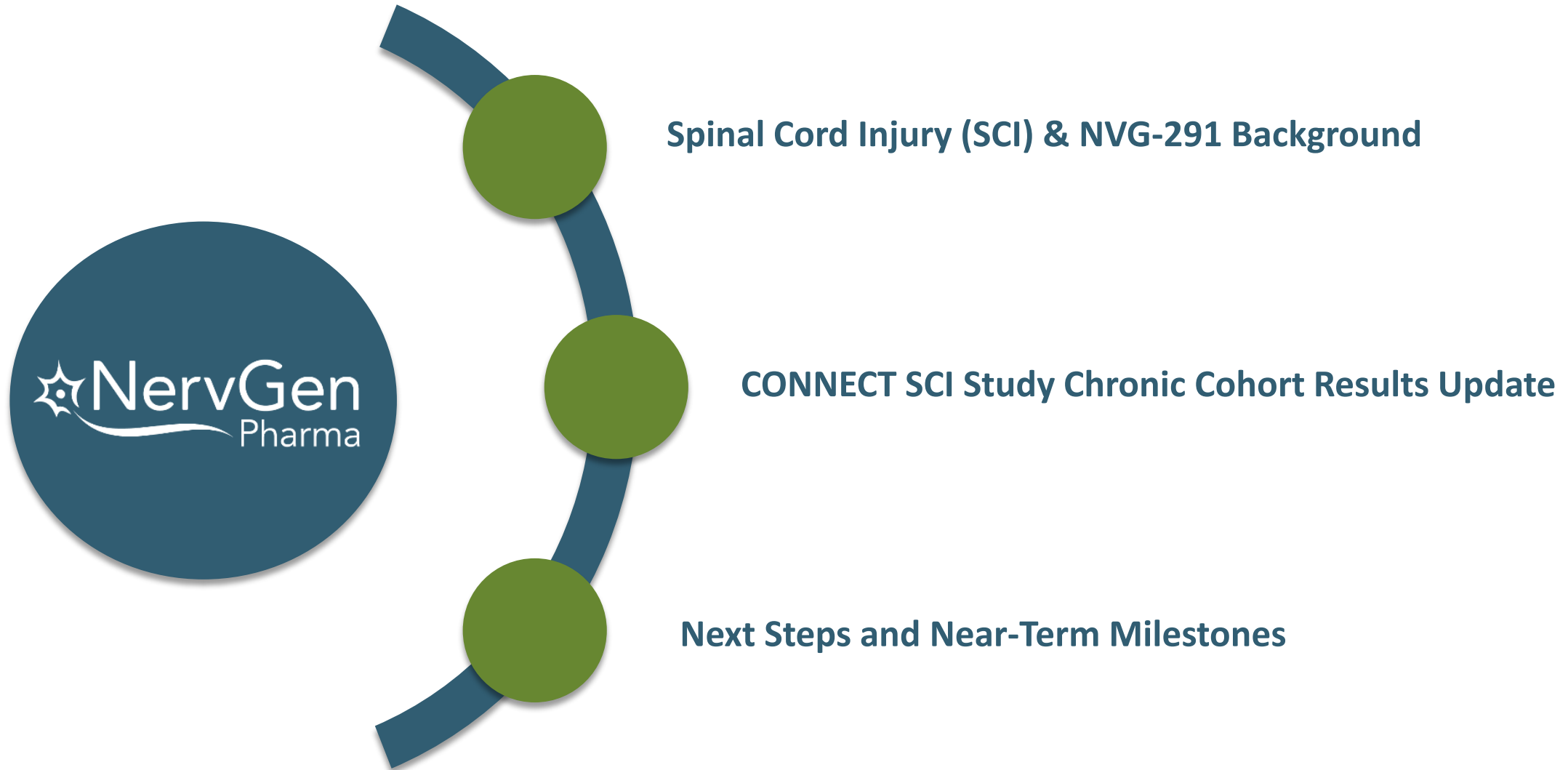
CONNECT SCI Trial Chronic Cohort Update

June 3, 2025

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Agenda for Today's Discussion



CONNECT SCI Study Chronic Cohort Key Results

Observed evidence of motor recovery in a chronic cervical motor incomplete population receiving NVG-291

Co-Primary Endpoint Achieved

- **Statistically significant 3-fold increase** in normalized first dorsal interosseus (FDI) motor evoked potential (MEP) amplitude (P=0.0155)
- Change in MEP amplitude for tibialis anterior (TA) not statistically significant

Secondary Endpoints

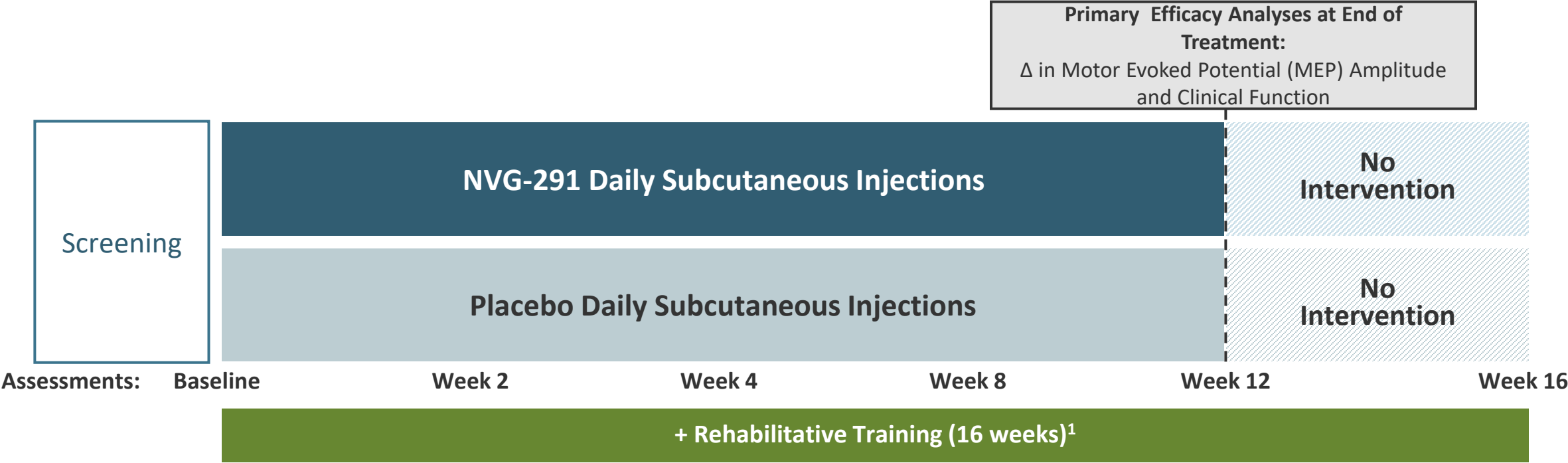
- **Positive trend change** from baseline in quantitative prehension (QtP) in Graded Redefined Assessment of Strength, Sensation and Prehension (GRASSP) – increase of 3.7 for NVG-291 v. 0.4 for placebo
- No clear separation from placebo on other clinical measures based on initial analyses of topline data
- Additional analyses forthcoming

Key Safety and Tolerability Data

- Generally well-tolerated
- High compliance, no treatment discontinuations
- Most common adverse events were mild/moderate injection site reactions

Full CONNECT SCI Chronic Cohort Dataset Analysis Underway

NVG-291: Phase 1b/2a CONNECT SCI Trial Design



Two Cohorts

- Chronic: 1-10 years post-injury (**complete**)
 - 20 subjects; 1:1 randomization
- Subacute: 20-90 days post-injury (**ongoing**)
 - 20 subjects; 2:1 randomization

Key Eligibility Criteria

- Age 18-75
- Traumatic cervical SCI (C7 or higher)
- Motor incomplete with min/max motor function
- Intact MEP in two qualifying muscle groups (hand, leg)

NVG-291: Phase 1b/2a Trial Endpoint Summary

Co-Primary Electrophysiological Endpoints

Change in MEP Amplitude of FDI (Hand) Muscle

Change in MEP Amplitude of TA (Leg) Muscle

Secondary Clinical Endpoints

Graded Redefined Assessment of Strength, Sensation and Prehension (GRASSP)

9-Hole Peg Test (9-HPT)

Pinch Force

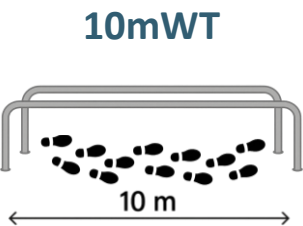
Ten Meter Walk Test (10mWT)

Lower Extremity Motor Score (LEMS)

Upper Extremity Motor Score (UEMS)

Statistical Analysis

- To control the type 1 error (alpha), both co-primary endpoints tested using an alpha of 0.025
- **Study considered positive if at least one of the co-primary endpoints is statistically significant ($p < 0.025$)**
- No hierarchy to secondary endpoints
- Looking for trends in one or more endpoints only



9-HPT



Pinch Force



GRASSP



LEMS / UEMS

- ☐ L2 Hip flexors / C5 Elbow flexors
- ☐ L3 Knee extensors / C6 Wrist extensors
- ☐ L4 Ankle dorsiflexors / C7 Elbow extensors
- ☐ L5 Long toe extensors / C8 Finger flexors
- ☐ S1 Ankle plantar flexors / T1 Finger abductors

NVG-291 Chronic Cohort – Baseline Demographic / Clinical Characteristics

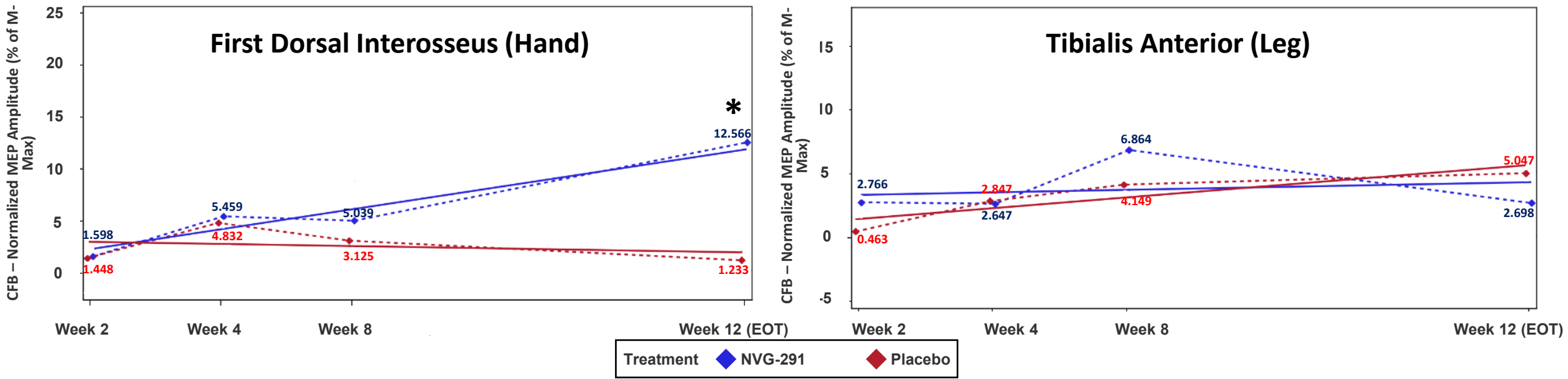
			NVG-291 (N=10)	Placebo (N=10)
Age (years)		Mean (SD)	43.0 (19.7)	50.3 (15.0)
Sex		N (% male)	8 (80%)	9 (90%)
Ethnicity	Not Hispanic or Latino	N (%)	9 (90.0%)	10 (100%)
Race	Black or African American	N (%)	1 (10.0%)	0
	White	N (%)	8 (80.0%)	10 (100%)
Time since SCI (years)		Mean (SD)	3.13 (2.36)	3.79 (2.99)
Cause of Injury	Fall	N (%)	1 (10.0%)	2 (20.0%)
	Sport	N (%)	6 (60.0%)	3 (30.0%)
	Transport	N (%)	3 (30.0%)	4 (40.0%)
	Other	N (%)	0	1 (10.0%)
Neurological level of injury		N (%) C2	2 (20.0%)	0
		N (%) C3	2 (20.0%)	3 (30.0%)
		N (%) C4	3 (30.0%)	4 (40.0%)
		N (%) C5	3 (30.0%)	0
		N (%) C6	0	2 (20.0%)
		N (%) C7	0	1 (10.0%)
AIS		N (%) C	5 (50.0%)	2 (20.0%)
		N (%) D	5 (50.0%)	8 (80.0%)
WISCI II score		Mean (SD)	7.8 (5.45)	10.1 (2.08)
GRASSP v2 total score		Mean (SD)	105.6 (36.7)	119.4 (23.3)
GRASSP v2 quantitative prehension		Mean (SD)	17.3 (8.9)	22.3 (6.8)
9-HPT (sec)		Mean (SD)	¹ 147.6 (98.8)	² 144.3 (97.5)
Pinch dynamometry force (Newtons)		Mean (SD)	30.7 (29.9)	34.5 (23.3)
UEMS		Mean (SD)	32.3 (11.0)	37.3 (6.8)
LEMS		Mean (SD)	31.4 (14.2)	34.8 (6.4)
10mWT (m/sec)		Mean (SD)	^{3,4} 0.37 (0.55)	³ 0.27 (0.14)
FDI-MEP amplitude, % of M-Max		Mean (SD)	6.2 (8.2)	6.5 (5.7)
TA-MEP amplitude, % of M-Max		Mean (SD)	6.4 (4.9)	7.0 (4.1)

(1) N=5 in NVG-291 group unable to complete **9-HPT** at baseline
a) 2 unable to complete on either side (300 sec imputed)
b) 3 subjects unable to complete on one side

(2) N=4 in placebo group unable to complete **9-HPT** on one side at baseline
(3) Median 10mWT: 0.124 m/sec (NVG-291), 0.232 m/sec (placebo)
(4) N=2 (20%) in NVG-291 group unable to complete **10mWT** at baseline

Co-Primary Efficacy Endpoints:

Change from Baseline to Week 12 in Normalized MEP Amplitude (% of M-max)



Baseline (actual)	6.207 (8.22)	6.527 (5.74)	
Week 12 (actual)	18.773 (22.77)	7.760 (6.73)	
Mean Change (LME)	11.418	1.988	9.430
95% CI	(5.831, 17.005)	(-3.620, 7.596)	(1.512, 17.348)
p-value LME			*0.0155

Baseline (actual)	6.385 (4.86)	7.029 (4.12)	
Week 12 (actual)	9.083 (6.58)	12.076 (6.41)	
Mean Change (LME)	4.288	5.433	-1.144
95% CI	(-0.133, 8.710)	(0.994, 9.872)	(-7.415, 5.126)
p-value LME			0.3126

*Change in FDI MEP amplitude statistically significant vs. placebo

CFB = Change from Baseline; EOT = End of Treatment; MEP = Motor Evoked Potential; M-max = Maximum motor response; LSM = Least-square means; LME = Linear Mixed Effects Model
LME model contains CFB as dependent variable and fixed effects for intercept, baseline result, Treatment, Week (study day/7), and Treatment x Week interaction with random intercept
The actual mean CFB values are displayed as dotted lines and diamonds with 95% confidence interval.
The regression line of CFB values are displayed as solid lines.

GRASSP QtP – **Positive** Trends Towards Statistically Significant Improvement in Quantitative Prehension Sub-Score

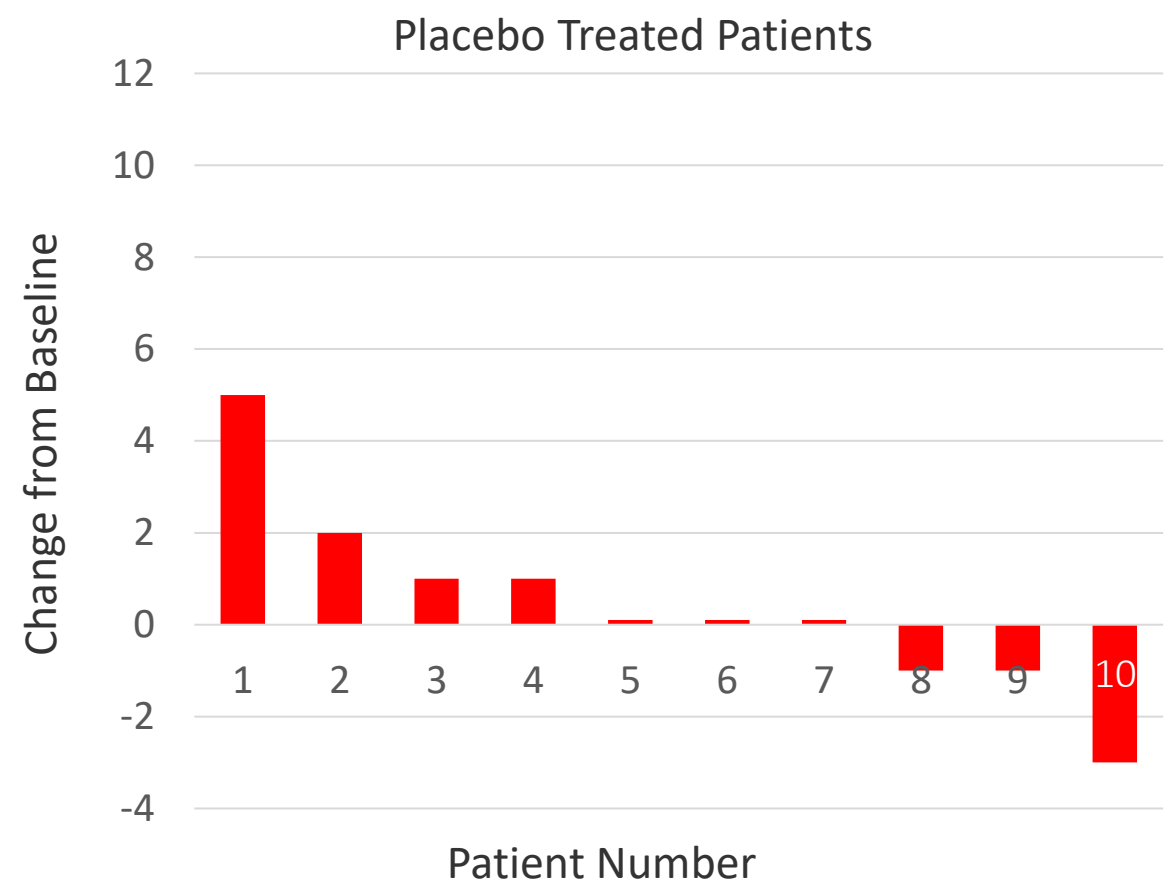
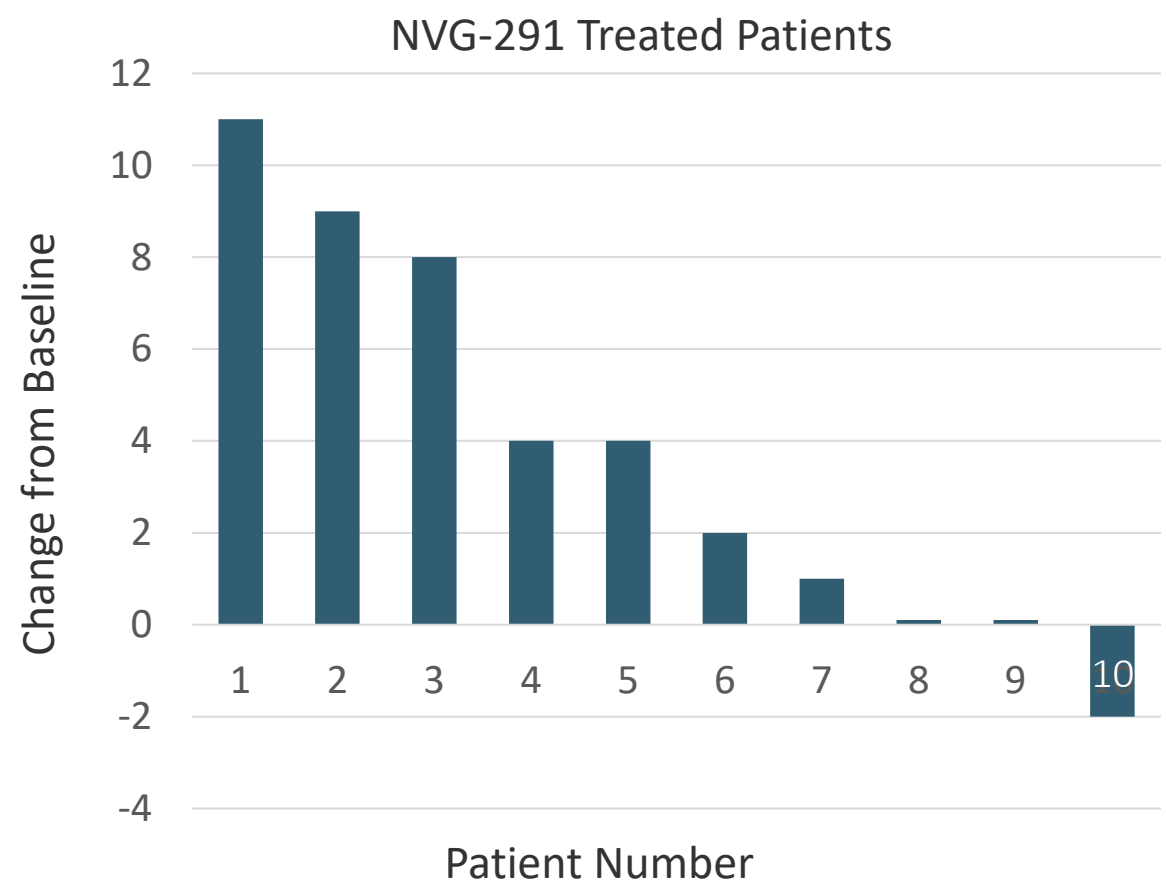
<u>Change in Score</u>	NVG-291 N=10	Placebo N=10	Placebo Adjusted	p-value (LME)	Min-Max
GRASSP Total Score Change	8.9	4.1	+4.7	0.2678	0-188
<i>quantitative prehension</i>	3.1	1.0	+2.2	0.1416	0-40
<i>qualitative prehension</i>	2.3	0.8	+1.6	0.3403	0-24
<i>strength</i>	2.3	2.6	-0.3	0.8793	0-100
<i>sensation</i>	0.8	0.1	+0.7	0.4283	0-24

Improvements on GRASSP Quantitative Prehension Performance

<u>Actual Values</u>	NVG-291 N=10	Placebo N=10	Placebo Adjusted
Baseline (SD)	17.3 (8.92)	22.3 (6.83)	
Week 12 (SD)	21.0 (7.42)	22.7 (6.20)	
Mean change from baseline (SD)	+3.7 (4.35)	+0.4 (2.12)	+3.3 (1.53)
Median	+3.0	0.0	
P-value t-test			0.0447

Secondary Endpoints: GRASSP QtP – Promising Change from Baseline to Week 12

Seven of ten patients that received NVG-291 showed improvement vs. four of ten patients that received placebo

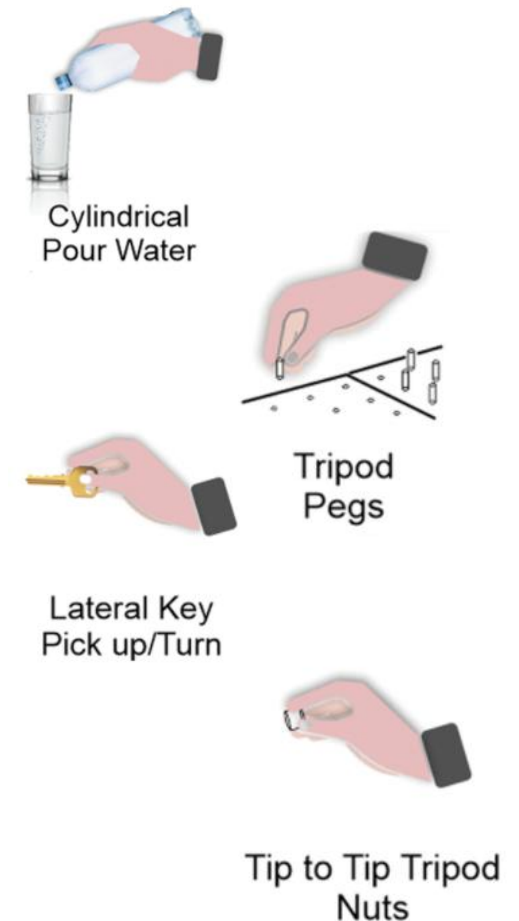


GRASSP: Graded Redefined Assessment of Strength, Sensation and Prehension

A validated clinical endpoint

Quantitative Prehension Sub-Score Parameters

1. Take the bottle and pour the water into the cup, approx. $\frac{3}{4}$ full; cylindrical grasp
2. Pull the 9 pegs, one by one, out of the foam and stick them back into the holes on the opposite side; tip to tip pinch
3. Take the key from the table, insert it in the lock and turn it 90°; lateral key pinch
4. Pick up the 4 nuts, one by one, from the table and screw them on the matching screws; tip to tip pinch and/or tripod pinch



Other Secondary Endpoints: 10mWT, 9-HPT, Pinch Force, UEMS, LEMS

Did not see clear separation / trends between drug-treated and placebo-treated

Possible reasons vary across endpoints

Endpoint	Result	Learnings / Implications
9-HPT	<ul style="list-style-type: none">Subjects who could not finish the test automatically assigned max value (300 seconds)Roughly half of subjects couldn't complete in one or both arms	<ul style="list-style-type: none">Excluding those who could not complete the test showed 13 second improvement on drug versus placebo (25 sec v. 13 sec, P=0.14; post hoc analysis)Possible future endpoint but need to pre-specify how to handle those with least function
10m-WT	<ul style="list-style-type: none">Two subjects receiving NVG-291 could not complete at baseline but could at end of study (slowest times of entire study)One subject receiving placebo showed 1200% improvement	<ul style="list-style-type: none">Improvements likely due to an exercise effectThis endpoint may not be good for Phase 3 trials
Pinch Force	<ul style="list-style-type: none">No difference between subjects receiving NVG-291 and subjects receiving placebo	<ul style="list-style-type: none">Could be from rehabilitationNot a good endpoint for future trials
UEMS / LEMS	<ul style="list-style-type: none">No observed effect	<ul style="list-style-type: none">Not very sensitive endpoint – included due to historical trials using these endpointsNot a good endpoint for future trials

Treatment-Emergent Adverse Events

Treatment-Emergent adverse events (TEAEs) generally mild to moderate; most common were injection site reactions

% of Subjects with each at least one TEAE	NVG-291 (N=10)	Placebo (N=10)
All	10 (100%)	8 (80.0%)
Injection site reaction (ISR)-related	9 (90.0%)	3 (30.0%)
Fatigue	1 (10.0%)	2 (20.0%)
Nausea	2 (20.0%)	1 (10.0%)
Urinary tract infection	3 (30.0%)	0
Nasopharyngitis	1 (10.0%)	1 (10.0%)
Urinary incontinence	2 (20.0%)	0
TEAE leading to treatment discontinuation	0	0
Serious TEAE (SAE)*	0	1 (10.0%)

All ISR TEAEs mild or moderate

*SAE: "Bowel obstruction due to internal hernia defect" – subject with worsening nausea, constipation and abdominal pain due to small bowel obstruction, requiring surgical closure of internal hernia – considered unrelated to study drug (likely related to prior gastric bypass)

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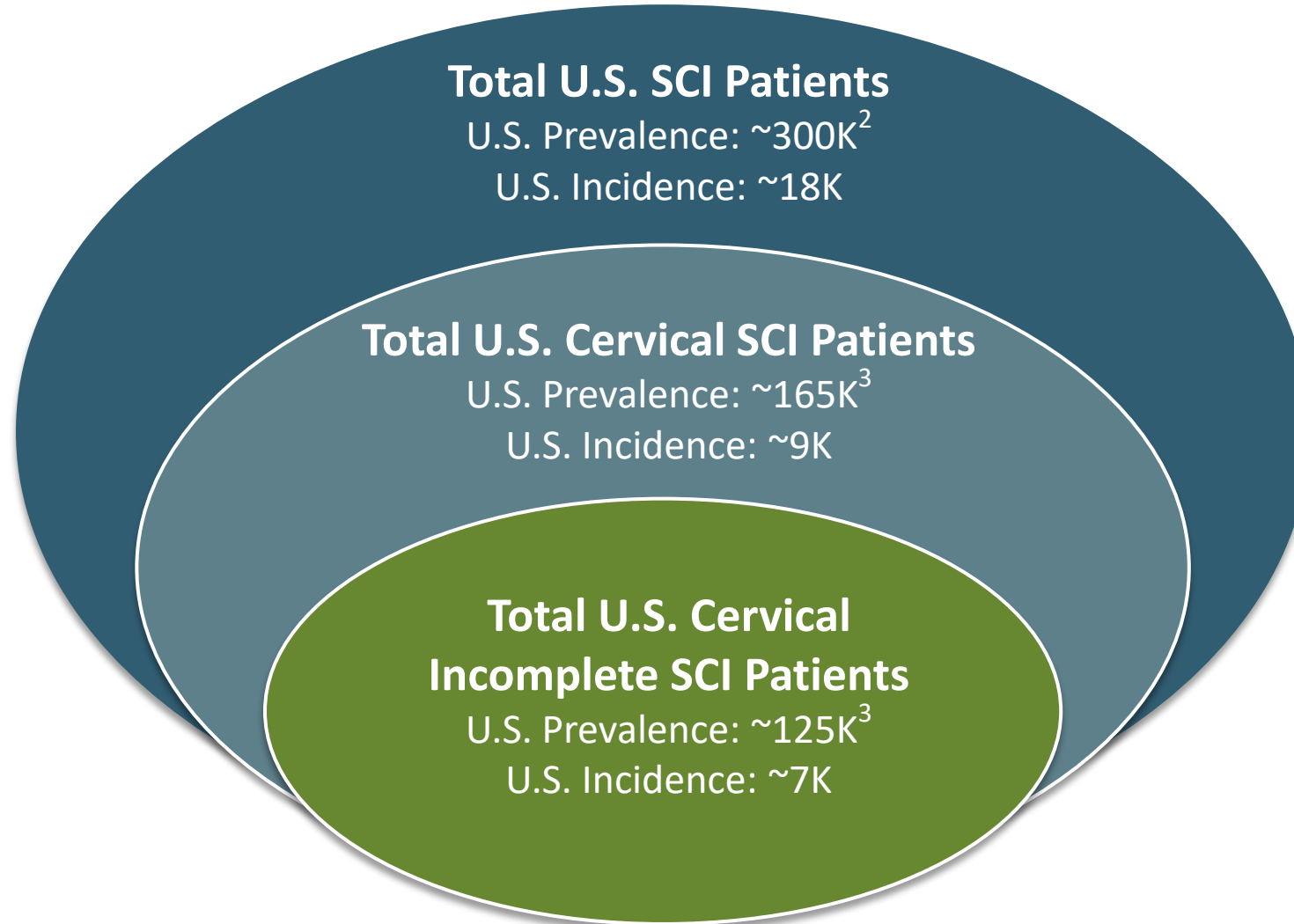
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Full CONNECT SCI Chronic Cohort Dataset Analysis Underway

Untapped Potential Market Opportunity with No Current Approved Therapies

SCI affects ~15M people worldwide, with ~250-500K new cases every year¹



(1) World Health Organization (2013), International perspectives on spinal cord injury

(2) National Spinal Cord Injury Statistical Center, 2025 Facts and Figures at a Glance

(3) Internal data based on: National Spinal Cord Injury Statistical Center, 2025 Facts and Figures at a Glance

Anticipated Next Steps and Near-Term Milestones

