

NEURALSTEM INC.

July 2017



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Although we believe that we have a reasonable basis for each forward-looking statement contained in this presentation, we caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this presentation as a result of, among other factors, the factors referenced in the "Risk Factors" section of our Annual Report on Form 10-K for the year ended December 31, 2017 filed with the Securities and Exchange Commission on March 14, 2017, Form 10-Q for the period ended September 30, 2017, and in other reports filed with the SEC. In addition, even if our results of operations, financial condition and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in this presentation, they may not be predictive of results or developments in future periods. Any forward-looking statements that we make in this presentation speak only as of the date of such statement, and we undertake no obligation to update such statements to reflect events or circumstances after the date of this presentation, except as required by law.

Key Highlights



Lead Program in Phase II Development

- Novel neurogenic small molecule approach
- NSI-189: Positive, randomized placebo-controlled Phase 1b in MDD
- Phase II Major Depressive Disorder (MDD)
 - Efficacy data expected in 3Q 2017
 - Montgomery-Asberg Depression Rating Scale (MADRS) primary endpoint
 - Cognition exploratory endpoint
 - Long-term durability data anticipated in 1H 2018
 - Strong IP position through 2035

Cell Therapy Strategy

- NSI- 566 biological activity across three indications
- Partnering efforts underway for continuing development

Cash balance as of 1Q17 provides runway into 3Q 2018

Scientific Advisory Board Comprised of World Class Psychiatric, Clinical and Regulatory Experts



Dr. Maurizio Fava	Harvard, MGH, Executive Vice Chair, Dept. of Psychiatry Principal Investigator: NSI-189 Phase 2 MDD clinical trial
Dr. Michael Thase	Univ. of Pennsylvania, Chief, Division of Mood and Anxiety Disorders Treatment and Research Program
Dr. Mark Frye	Mayo Clinic, Chair, Psychiatry and Psychology
Dr. John Greden	Univ. of Michigan, Founder and Executive Director, Healthy System Depression Center
Dr. Richard Keefe	Duke Institute for Brain Sciences, Director Schizophrenia Research Group
Dr. Thomas Laughren	Harvard, MGH, Director, Regulatory Affairs, Former Director of Psychiatric Division, CDER, FDA

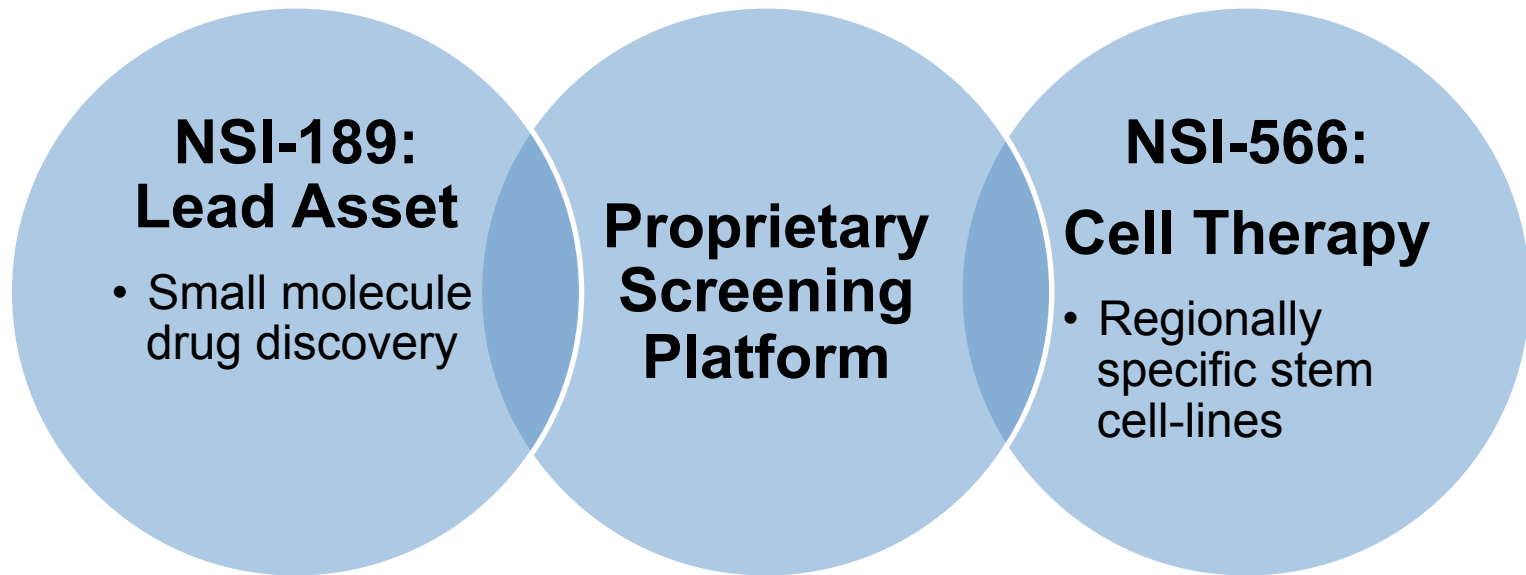
Management



<p>Richard Daly Chief Executive Officer & acting CFO</p>	<p>AstraZeneca  Bristol-Myers Squibb  </p>
<p>Karl Johe, Ph.D. Chief Scientific Officer</p>	<p> NEURALSTEM INC  National Institutes of Health  University of California San Francisco</p> <p>Co-founder</p>
<p>Thomas Hazel, Ph.D. Senior Vice President, Research</p>	<p> NEURALSTEM INC </p>

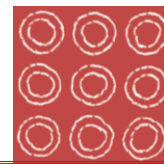


Neuralstem's proprietary technology uses regionally specific neural stem cells for the development of CNS therapies.



Small molecule development capability & regenerative medicine

Pipeline



Therapy	Indication	Preclinical	Phase I	Phase II	Phase III	Status
Small Molecule: Lead Asset						
NSI-189	Major Depression Disorder (MDD)					Topline Results 3Q17
	Long-term Follow-up Study (MDD)					6 Month Observation Ongoing
	<i>Supplementary Preclinical Program for Signal Generation</i>					
	Angelman Syndrome					Ongoing
	Ischemic Stroke					
	Type 1 & 2 Diabetes-related Neuropathy					
	Irradiation-induced Cognitive Deficit					
	LTP Enhancement					
Cell Therapy (to be advanced with external funding)						
NSI-566	Amyotrophic Lateral Sclerosis (ALS)					BD Initiatives
	Chronic Spinal Cord Injury					
	Ischemic Stroke					



NSI-189:
A New Chemical Entity for Major Depressive Disorder



Compelling Efficacy Demonstrated To-Date

Phase Ib in Major Depressive Disorder (MDD) randomized, placebo-controlled, double-blind data

- New chemical entity
- Large effect size
- Potential cognitive benefit
- Durability of effect that is potentially disease modifying
- Compelling safety profile

Phase II Efficacy Trial ongoing in MDD: randomized, double-blind, placebo-controlled study

MDD market opportunity

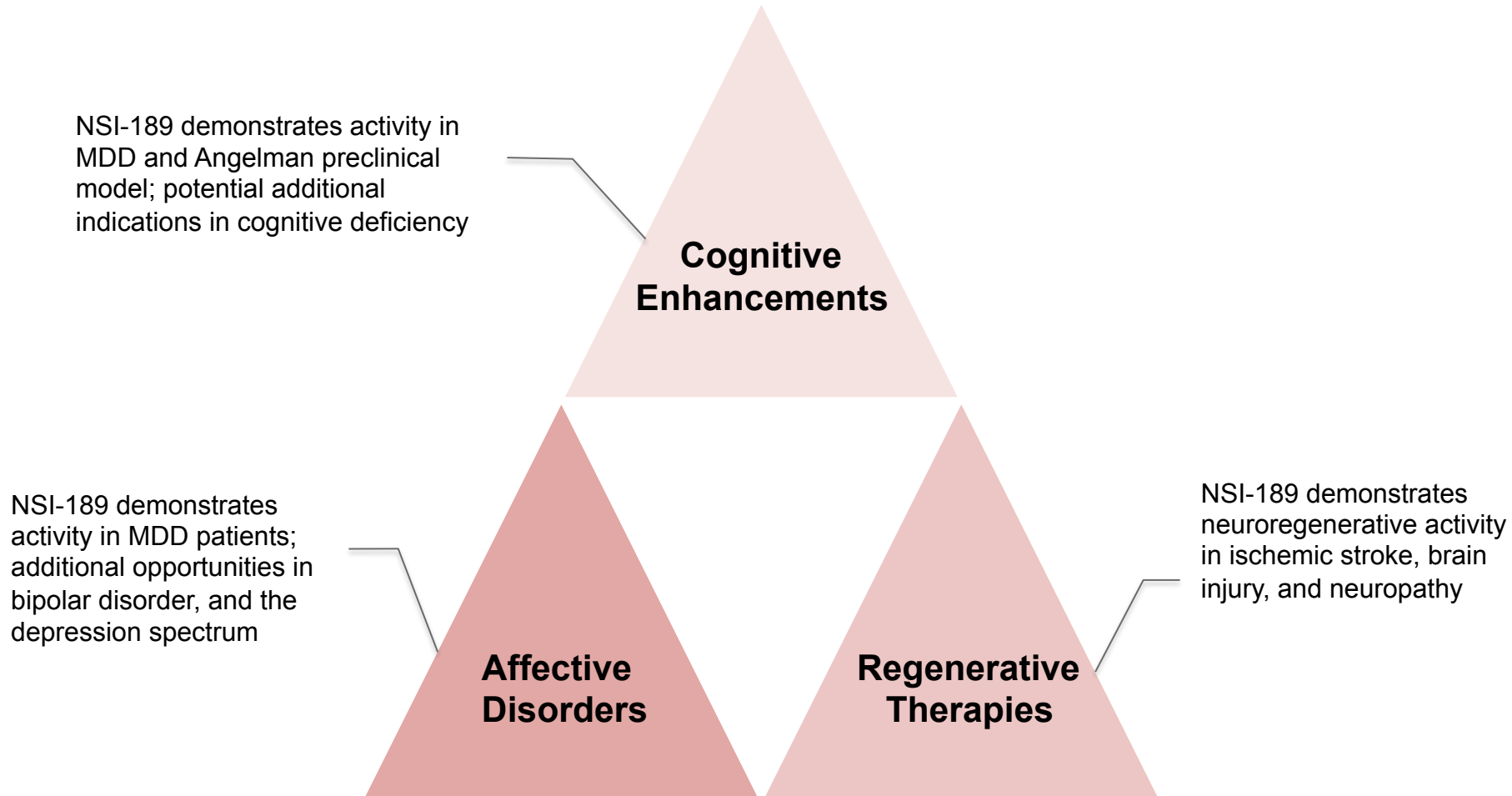
- Unmet need given high patient turnover rate with SOC in MDD due to low efficacy and significant side effects*

Preclinical Data

- MOA insight: Long-term potentiation (LTP) biomarker data associated with cognitive enhancement
- Orphan opportunity with Angelman Syndrome
 - Genetic disorder affecting the nervous system, causes developmental disabilities

Strong IP position through 2035

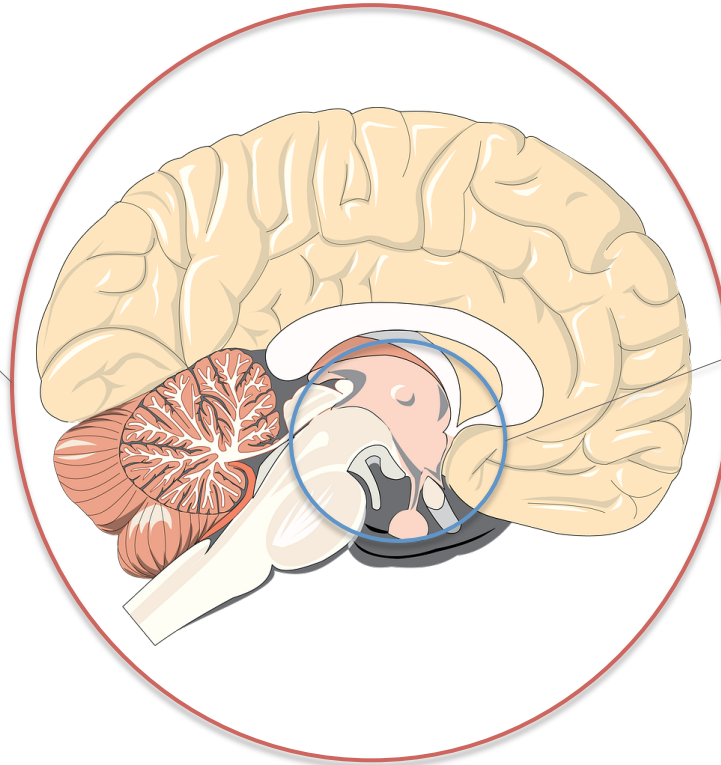
Functionality-Driven Development Strategy for NSI-189



Provides broad development paths in CNS



Serotonin hypothesis of MDD led to anti-depressants engineered to rectify serotonin imbalance.



Recent research in MDD pathology links disease to a cycle of hippocampal atrophy due to inhibition of neurogenesis.

NSI-189 is a neurogenic compound that potentially stimulates endogenous hippocampal neural stem cells and increases hippocampal volume

Major Depressive Disorder

Large, Unmet Medical Need: 16M US Patients

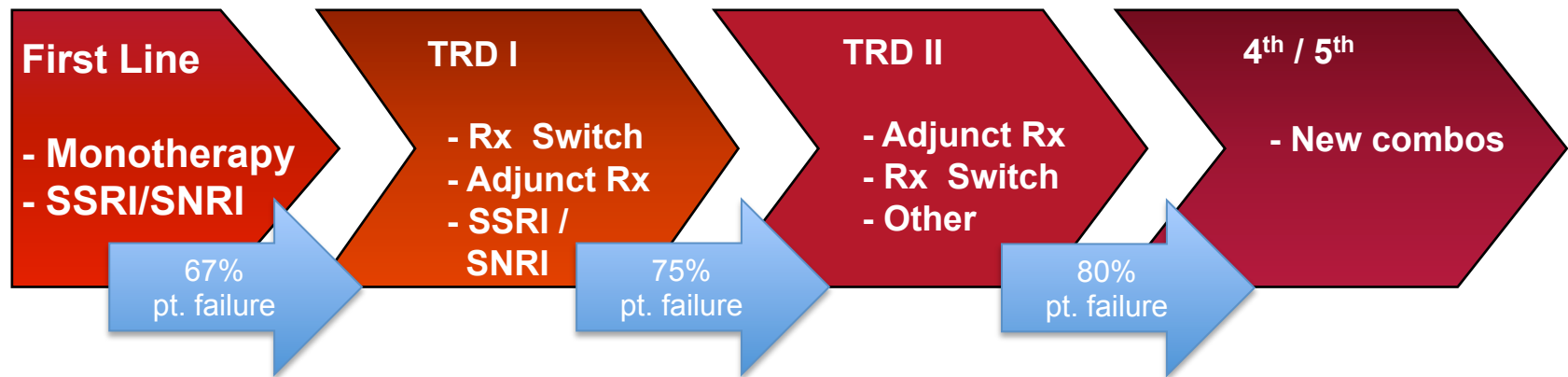


Large patient Rx turnover due to low efficacy

Low barrier to entry due to continued unmet need

Adjunctive/monotherapy provides large market opportunity

Treatment Resistant Depression Patient Journey



Patients	First Line	TRD I	TRD II	4th line +
% patients in given line of therapy	33%	17%	10%	40%
% patients that fail given line of therapy	67%	75%	80%	N/A

Source: 1. Gaynes BN, et al; A direct comparison of presenting characteristics of depressed outpatients from primary vs. specialty care settings: preliminary findings from the STAR*D clinical trial. *Gen Hosp Psychiatry*. 2005 Mar-Apr;27(2):87-96.

2. Rush AJ, Fava M, et al; STAR*D Investigators Group. Sequenced treatment alternatives to relieve depression (STAR*D): rationale and design. *Control Clin Trials*. 2004 Feb;25(1):119-42. ³ <https://www.nimh.nih.gov/health/statistics/prevalence/major-depression-among-adults.shtml>. Accessed February 13, 2017.

3. <https://www.nimh.nih.gov/health/statistics/prevalence/major-depression-among-adults.shtml>. Accessed February 13, 2017.

NSI-189 MDD Phase Ib trial design



NSI-189 Phase Ib double-blind, randomized, placebo-controlled, dose-escalating study assessing safety and tolerability

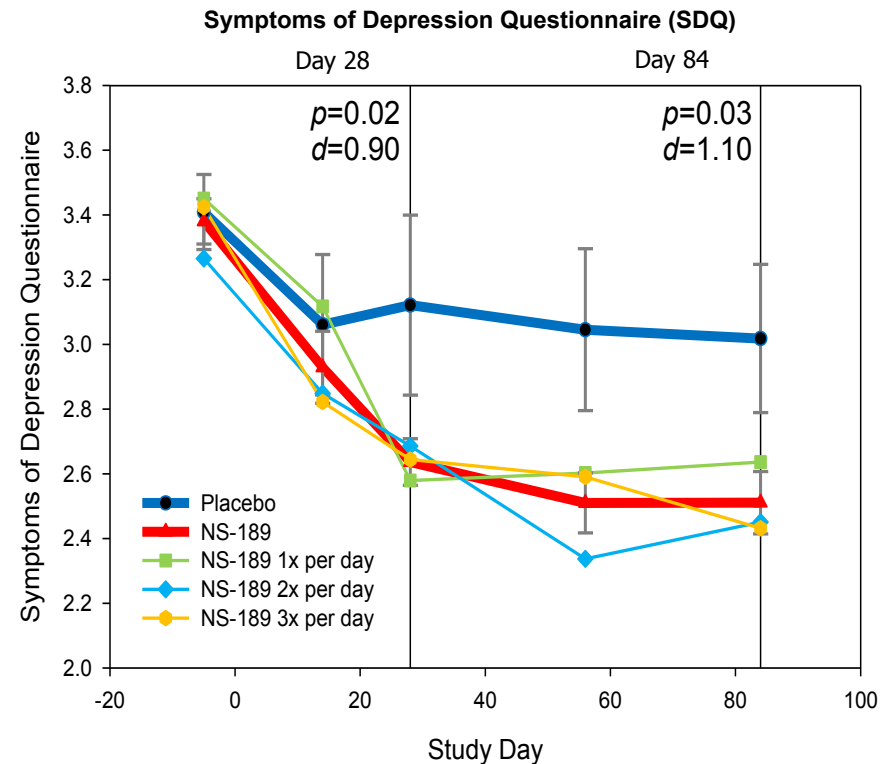
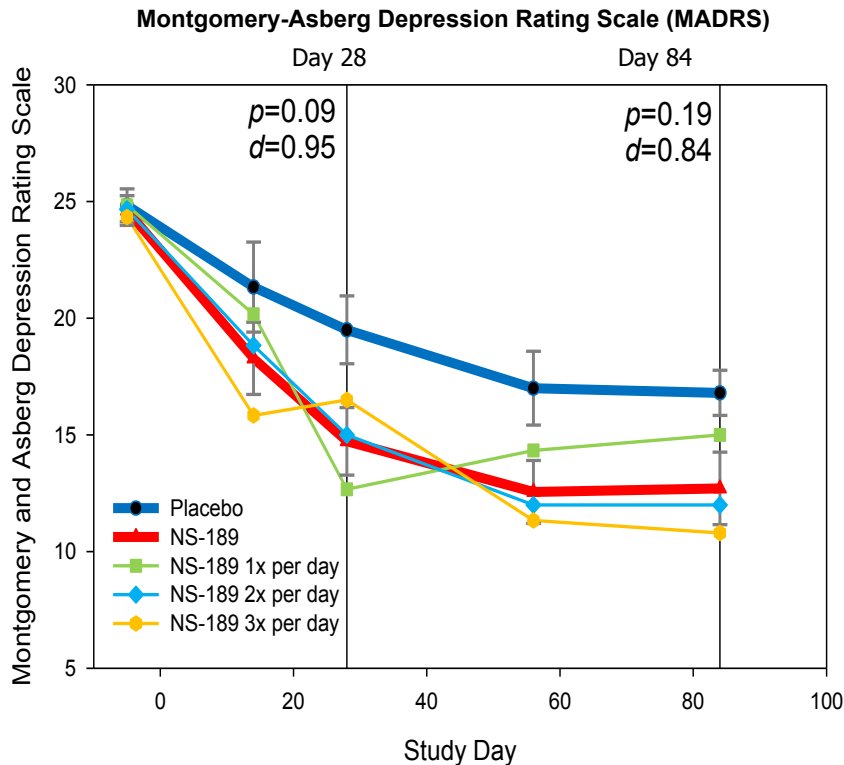
Cohort 1	N=8 (6 drug, 2 placebo)	40 mg QD
Cohort 2	N=8 (6 drug, 2 placebo)	40 mg BID
Cohort 3	N=8 (6 drug, 2 placebo)	40 mg TID

Acute treatment: 28 days	Drug free observational follow up: days 35, 42, 49, 56, 70, 84
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- FDA safety protocol for in-clinic dosing (28 days)
- Patient criteria: At least two prior depressive episodes and currently taking or history of antidepressant medication(s)
- Moderate severity
 - Avg. MADRS 22.5, avg. age 35

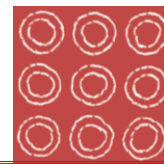
NSI-189 Phase 1b Results

Demonstrate Large Effect Size & Durability

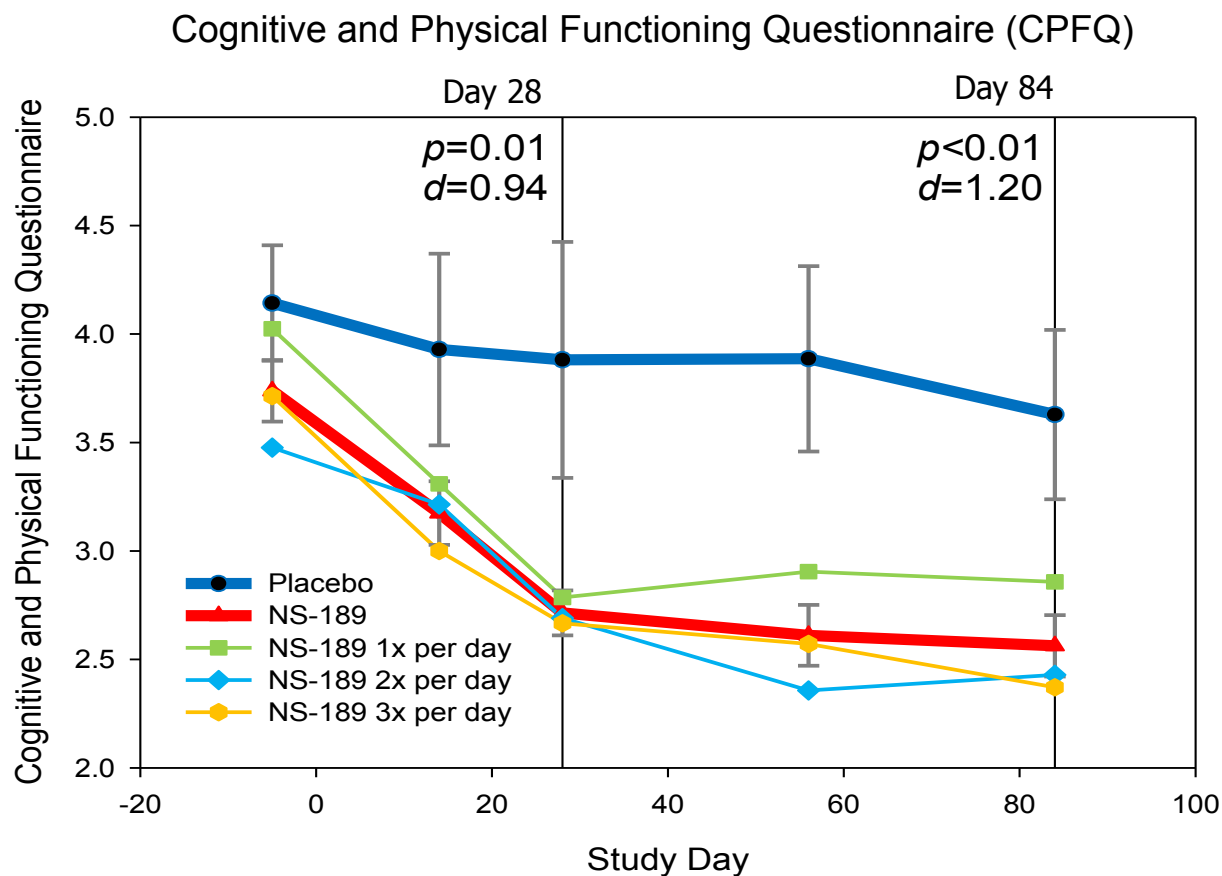


Large MADRS effect size: d=0.95 <i>D-value, or Cohen's effect size, is used to indicate the standardized difference between two means</i>	MADRS outcome	#	Definition
	56% Responder	10/18	(≥ 50% reduction)
	50% Remission	9/18	(≤ 10 score)
	72% Partial + Responder	13/18	(<14 score)

NSI-189 MDD Phase Ib clinical results

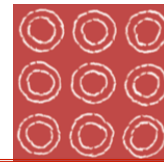


Demonstrates improved cognition effect in MDD patient reported outcomes



Large effect size ($d=0.94$)

NSI-189: Compelling safety profile with no serious AEs



Side effect	Pooled placebo	40 mg q.d.	40 mg b.i.d.	40 mg t.i.d.	Pooled active	Pooled placebo
	(n=6) N (%)	(n=6) N (%)	(n=6) N (%)	(n=6) N (%)	(n=18) N (%)	(n=6) N (%)
<i>Autonomic</i>						
Dry mouth	0 (0%)	0 (0%)	2 (33.3%)	0 (0%)	2 (11.1%)	–
Palpitation	0 (0%)	1 (16.7%)	0 (0%)	0 (0%)	1 (5.6%)	–
<i>CNS/psychiatric</i>						
Headache	3 (50.0%)	3 (50.0%)	3 (50.0%)	3 (50.0%)	9 (50%)	3 (50%)
Dizziness	1 (16.7%)	0 (0%)	1 (16.7%)	4 (66.7%)	5 (27.8%)	1 (16.7%)
Somnolence	1 (16.7%)	3 (50.0%)	1 (16.7%)	1 (16.7%)	5 (27.8%)	1 (16.7%)
Fatigue	0 (0%)	1 (16.7%)	0 (0%)	0 (0%)	1 (5.6%)	–
Restlessness	0 (0%)	0 (0%)	0 (0%)	1 (16.7%)	1 (5.6%)	–
Poor quality of sleep	0 (0%)	1 (16.7%)	0 (0%)	0 (0%)	1 (5.6%)	–
Nightmare/vivid dream	0 (0%)	1 (16.7%)	1 (16.7%)	1 (16.7%)	3 (16.7%)	–
Paresthesia	0 (0%)	1 (16.7%)	0 (0%)	1 (16.7%)	2 (11.1%)	–
Insomnia	0 (0%)	1 (16.7%)	1 (16.7%)	1 (16.7%)	3 (16.7%)	–
Irritability	0 (0%)	1 (16.7%)	0 (0%)	0 (0%)	1 (5.6%)	–
Difficulty concentrating	1 (16.7%)	0 (0%)	0 (0%)	0 (0%)	–	1 (16.7%)
Hyperthymia	1 (16.7%)	0 (0%)	0 (0%)	0 (0%)	–	1 (16.7%)
<i>Gastrointestinal</i>						
Dyspepsia	1 (16.7%)	0 (0%)	0 (0%)	0 (0%)	–	1 (16.7%)
Abdominal pain	1 (16.7%)	0 (0%)	0 (0%)	0 (0%)	–	1 (16.7%)
Nausea	0 (0%)	0 (0%)	0 (0%)	2 (33.3%)	2 (11.1%)	–
<i>Skin and subcutaneous tissue disorders</i>						
Skin pain	0 (0%)	1 (16.7%)	0 (0%)	0 (0%)	1 (5.6%)	–
Rash	0 (0%)	0 (0%)	0 (0%)	1 (16.7%)	1 (5.6%)	–

NSI-189: Ongoing Phase 2 MDD Trial, Topline Results

Expected 3Q 2017



Study Objectives

- Primary: Montgomery-Asberg Depression Rating Scale (MADRS)
- Secondary*: SDQ, HAM-D17, CGI-S, CPFQ, SFI
- Exploratory: Cogscreen Battery, Cogstate Brief Battery

Innovative Study Design

- Randomized, double blind, 3 cohorts (n=220): 40mg QD, 40mg BID & placebo
- 12-week study, additional 6 month follow-up study
- Fewer, quality MDD trial sites (n=12)
- SAFER Interview: confirmatory, independent, remote MADRS diagnosis by MGH
- Prescreen process to manage placebo risk
- Potential registration study if successful in either active arm
 - Power: >80%, 2-sided $p \leq 0.05$
 - Cohen effect size: $d=0.5$

Principal Investigator: Maurizio Fava, M.D. Slater Family Professor of Psychiatry at Harvard Medical School, Massachusetts General Hospital

*Symptoms of Depression Questionnaire (SDQ) Hamilton Depression Rating Scale 17-items (HAM-D17) Clinical Global Impressions Scale (CGI-S) Cognitive and Physical Functioning Questionnaire (CPFQ) Sexual Functional Index (SFI)



NSI-189:

Preclinical data provides insight into MOA and supports broad potential in CNS

Preclinical Overview



Preclinical data suggests a new paradigm for reversing damage caused by disease/injury

Restores LTP in Angelman Syndrome mouse

Treatment of a rat model for ischemic stroke shows a durable effect in promoting behavioral recovery that corresponds with increased neurogenesis/remodeling

Reversal of cognitive deficit in irradiated mice

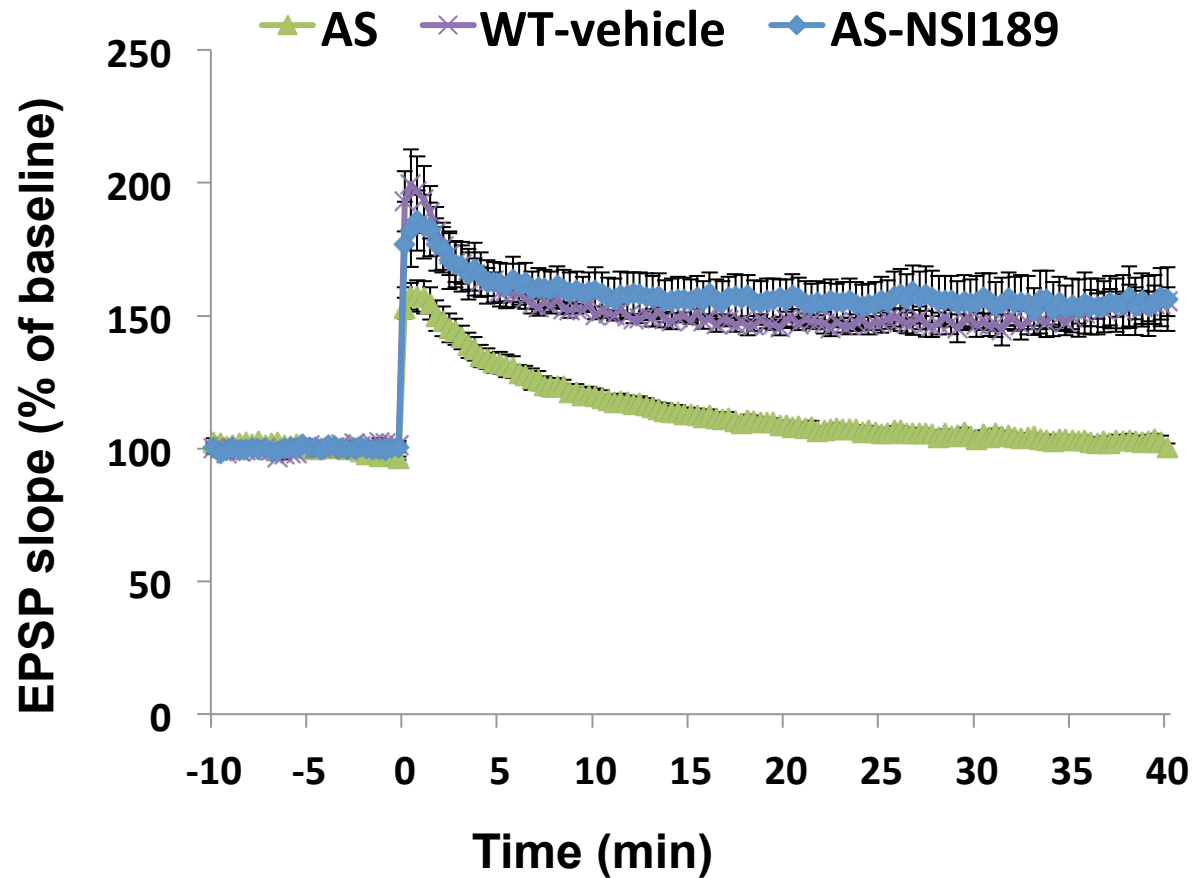
MOA: Enhances short-term and long-term potentiation in normal mice

Type 1 & 2 diabetic neuropathy reversal and prevention

Orphan Opportunity in Angelman Syndrome



NSI-189 restores LTP in Angelman Syndrome Mice Confirmatory model in a genetic disease



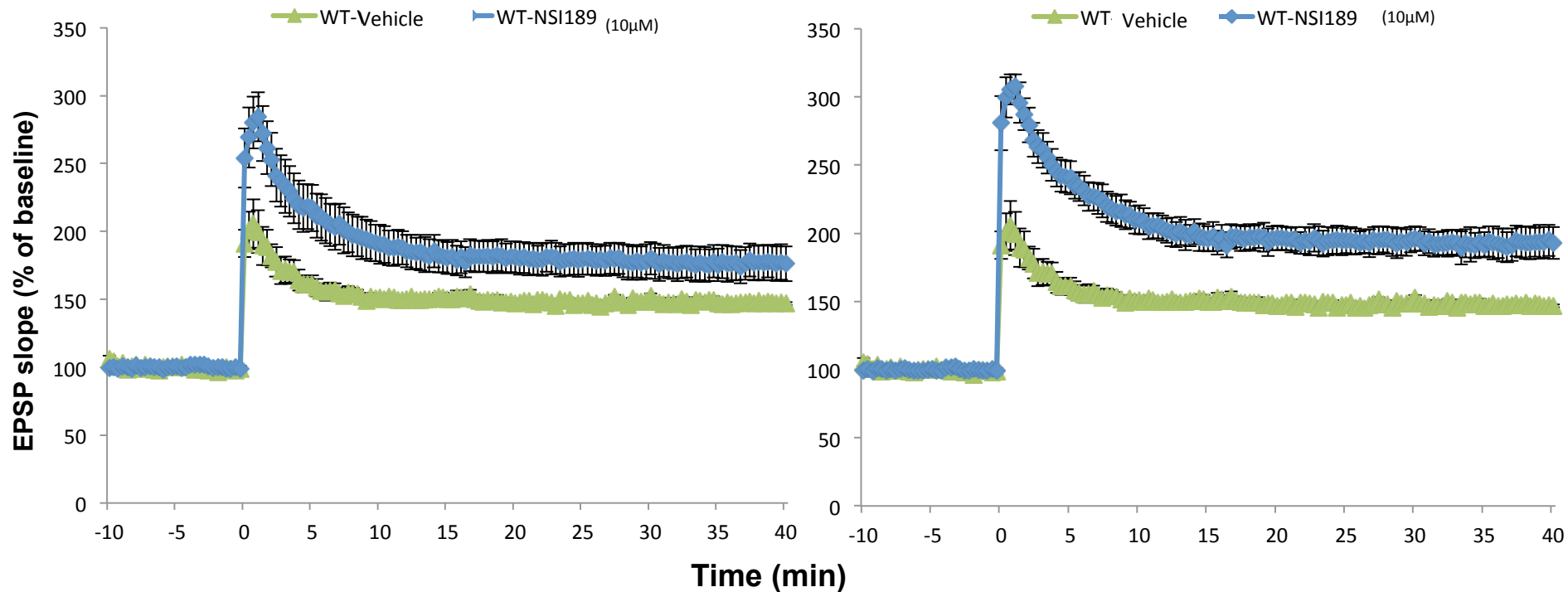
NSI-189 Enhances LTP Magnitude



For mechanistic studies: cognition = memory
LTP is a cellular biomarker of memory

TBS after 2.5 h incubation

TBS after 3.5 h incubation



- Enhances short-term and long-term potentiation in normal mice (n=8 slices)
- Increases with exposure time and concentration

Excitatory postsynaptic potential (EPSP)
Theta burst stimulation (TBS)

By courtesy of Yan Liu¹, Xiaoning Bi¹, Michel Baudry¹
Western University of Health Sciences, Pomona, CA 91766



Stem Cell Development Efforts & Strategy

Cell Therapy: Biological Activity Across Three Indications



	Indication	Preclinical	Phase I	Phase II	Phase III	Status	
Cell Therapy (to be advanced with external funding)							
NSI-566	Amyotrophic Lateral Sclerosis (ALS)						Phase 2a completed
	Chronic Spinal Cord Injury						Phase 1 follow-up
	Ischemic Stroke						Phase 1 follow-up

- ALS Phase 1 & 2 follow-up evaluation
- Phase I stroke completed dosing all 9 patients and currently evaluating safety
- cSCI is currently evaluating 4 Phase 1 thoracic patients; Phase 1 trial recruiting additional (Group B) 4 cervical patients
- Over 300 proprietary neural stem cells

Lead Product: NSI-566



Chemically defined culture system

- No serum, no feeder cells, no particulates, no unknown raw material
- Fully tested for potential pathogens; validated SOPs

Efficient expansion

- Multi-tiered cell banks for maximum efficiency
- Scalable expansion
- Relatively small infrastructure

Stable phenotype

- Normal karyotype of 44 + XY chromosomes
- Reproducible bank release characteristics (identity, purity, potency)
- Predictable in vivo differentiation

NSI-566: Preliminary Data in 3 Indications



ALS

PROGRAM OVERVIEW

- Transplantation into spinal cord of ALS
- Phase 1 & Phase 2a dose-escalation, safety studies completed
- 30 subjects with 2-6 years of safety data

KEY TAKEAWAYS

- Procedure and treatment is well-tolerated
- Long-term cell graft survival (2.5 years) in autopsy

MARKET CONSIDERATIONS

- Orphan condition
- Rapid accelerating disease
- Limited treatments

Chronic Spinal Cord Injury

PROGRAM OVERVIEW

- USCD funded
- Phase I cSCI Group A 4 Thoracic AISA-A complete spinal cord injury (dosing completed)
- Phase I cSCI Group B 4 Cervical AISA-A complete spinal cord injury (recruiting)

KEY TAKEAWAYS

- Stem cell treatment was safe and well-tolerated
- No serious adverse events
- Self-reported ability to contact some muscles below the level of injury in 4 of the 4 subjects treated was confirmed via clinical and electrophysiological follow-up examinations

MARKET CONSIDERATIONS

- Approximately 270,000 Americans live with cSCI
- 17,000 new injuries per year
- No treatment options

Ischemic Stroke

PROGRAM OVERVIEW

- Phase 1 open-label, dose-escalation, feasibility & safety study for the treatment of paralysis from chronic motor stroke
- Patient profile: 9 subjects 3-24 months post stroke with stable hemi-paralysis

KEY TAKEAWAYS

- Treatment well-tolerated
- Innovative brain injection cannula

MARKET CONSIDERATIONS

- 15mm people suffer stroke worldwide
- Estimated 87% of ischemic stroke

Continued Execution of New Corporate & Clinical Development Strategy



2016

- ✓ *Jan:* Refocused clinical development strategy on NSI-189
- ✓ *Feb:* Rich Daly joins as the new CEO
- ✓ *May:* Initiation of Phase 2 MDD study for NSI-189
- ✓ \$9mn institutional capital raise
- ✓ Corporate reorganization to align with updated strategy
- ✓ *Jun:* Rich Daly appointed Chairman, Board of Directors
- ✓ Business development/partnering efforts in cell therapy begin
- ✓ *Sept:* 50% enrollment in Phase 2 MDD trial achieved ahead of schedule
- ✓ *Dec:* Closing of Tianjin Pharmaceutical Group \$20mn strategic investment

2017

- ✓ *Jan:* 13-1 reverse split, regaining Nasdaq compliance
- ✓ *Feb:* Last patient enrolled NSI-189 Phase 2 MDD study
- ☐ **3Q: Phase 2 MDD MADRS results expected 4 months ahead of schedule**

2018

- ☐ *1H:* Phase 2 MDD 6-month durability results expected

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