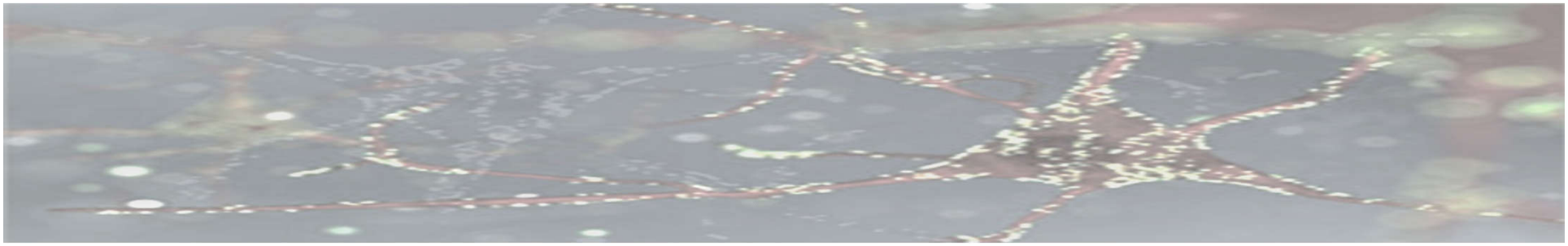


# NEURALSTEM INC.

April 2017

# Safe Harbor Statement

Safe Harbor statements under the Private Securities Litigation Reform Act of 1995: This presentation contains forward-looking statements as defined in Section 27A of the Securities Act of 1933 as amended, and section 21E of the Securities Exchange Act of 1934, as amended. Such forward-looking statements are based upon Neuralstem, Inc.'s management's current expectations, estimates, beliefs, assumptions, and projections about Neuralstem's business and industry. Words such as "anticipates," "expects," "intends," "plans," "predicts," "believes," "seeks," "estimates," "may," "will," "should," "would," "potential," "continue," and variations of these words (or negatives of these words) or similar expressions, are intended to identify forward-looking statements. In addition, any statements that refer to expectations, projections, or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking statements. These forward-looking statements are not guarantees of future performance and are subject to certain risks, uncertainties, and assumptions that are difficult to predict. Therefore, our actual results could differ materially and adversely from those expressed in any forward-looking statements as a result of various risk factors. These risks and uncertainties include the risks associated with the effect of changing economic conditions, trends in the products markets, variations in Neuralstem's cash flow, market acceptance risks, technical development risks and other risk factors detailed in Neuralstem's Securities and Exchange Commission filings. For links to SEC documents please visit the company's Web site: neuralstem.com.

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, 2016 filed with the Securities and Exchange Commission on March 23, 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 provides runway into 2Q 2018

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

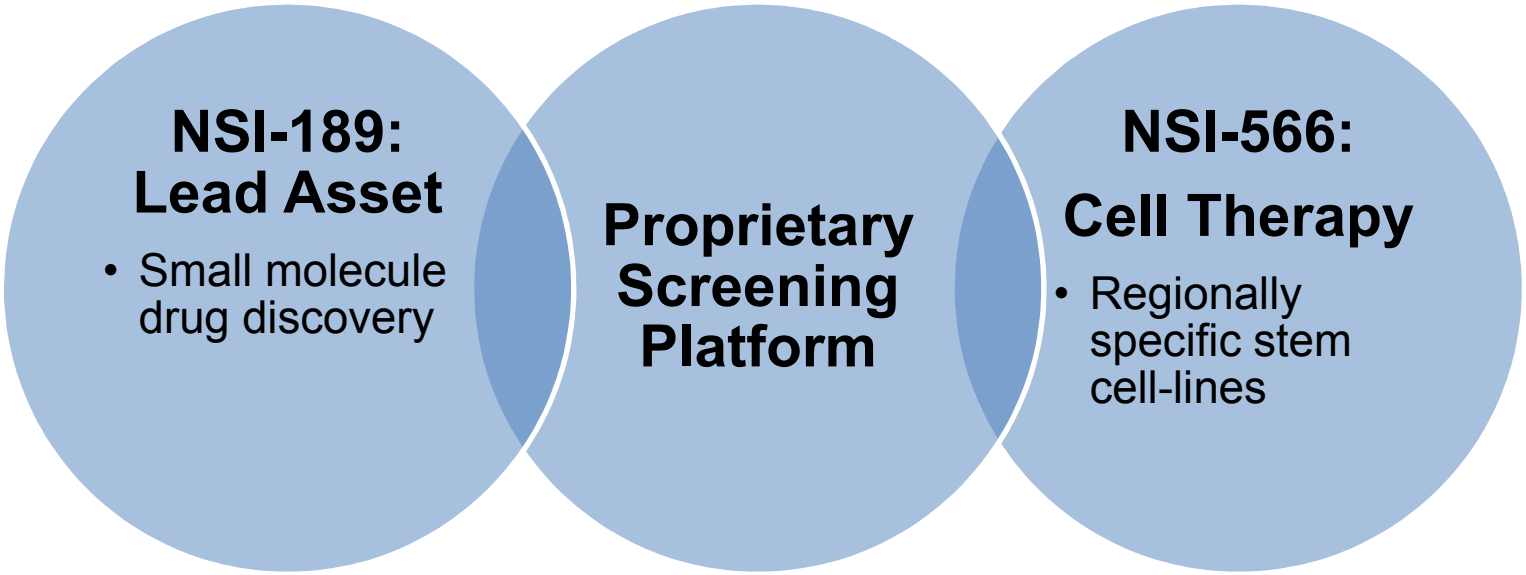
| | |
|---|---|
| Dr. Maurizio Fava | Harvard, MGH, Executive Vice Chair, Dept. of Psychiatry<br>Principal Investigator: NSI-189 Phase 2 MDD clinical trial |
| Dr. Michael Thase | Univ. of Pennsylvania, Chief. Division of Mood and Anxiety Disorders Treatment and Research Program |
| Dr. Mark Frye | Mayo 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

| | |
|---|---|
| **Richard Daly**<br>President & Chief Executive Officer | AstraZeneca, Bristol-Myers Squibb, Takeda, TAP |
| **Karl Johe, Ph.D.**<br>Chief Scientific Officer | NEURALSTEM INC (Co-founder), NIH National Institutes of Health, UCSF University of California San Francisco |
| **Jonathan Lloyd Jones**<br>Chief Financial Officer | genzyme, TransMolecular, Inc., TetraLogic PHARMACEUTICALS, COLUMBIA LABORATORIES, INC. |
| **Thomas Hazel, Ph.D.**<br>Senior Vice President, Research | NEURALSTEM INC (20 years as Stem Cell Discovery Program Director), National Institute of Neurological Disorders and Stroke |

# Utilizing Neural Stems Cells to Develop Novel CNS Therapies

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




*Small molecule development capability & regenerative medicine*

# Pipeline

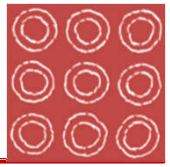
| Compound | Indication | Preclinical | Phase I | Phase II | Phase III | Status |
|---|---|---|---|---|---|---|
| **Small Molecule: Lead Asset** | | | | | | |
| NSI-189 | Major Depression Disorder (MDD) | | | | | Topline Results 3Q17 |
| | ***Supplementary Preclinical Program*** | | | | | |
| | Angelman Syndrome | | | | | Ongoing |
| | MCAO Stroke | | | | | |
| | Type 1 & 2 Diabetes-related neuropathy | | | | | |
| | Irradiation-induced cognition | | | | | |
| | 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 Molecular Entity for Major Depressive Disorder

# NSI-189

## A NCE with Novel Neurogenic Mechanism of Action



**Compelling Efficacy Demonstrated To-Date**

- Phase Ib in Major Depressive Disorder (MDD) randomized, double-blind data
  - New chemical entity
  - Large effect size
  - Cognitive benefit profile
  - Potentially disease modifying
  - Excellent safety profile

**Phase II 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**

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 and 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.

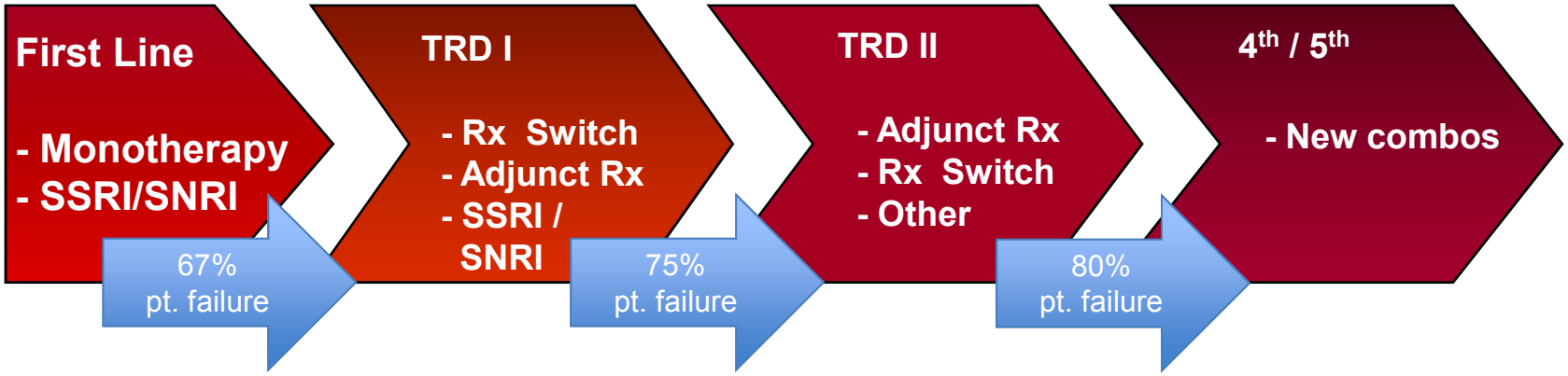
# Major Depressive Disorder
## Large, Unmet Medical Need: 16M US Patients

Large patient Rx turnover due to low efficacy

Low barrier to entry due to continued unmet need

Adjunct/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.

# NSI-189 MDD Phase Ib trial design

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

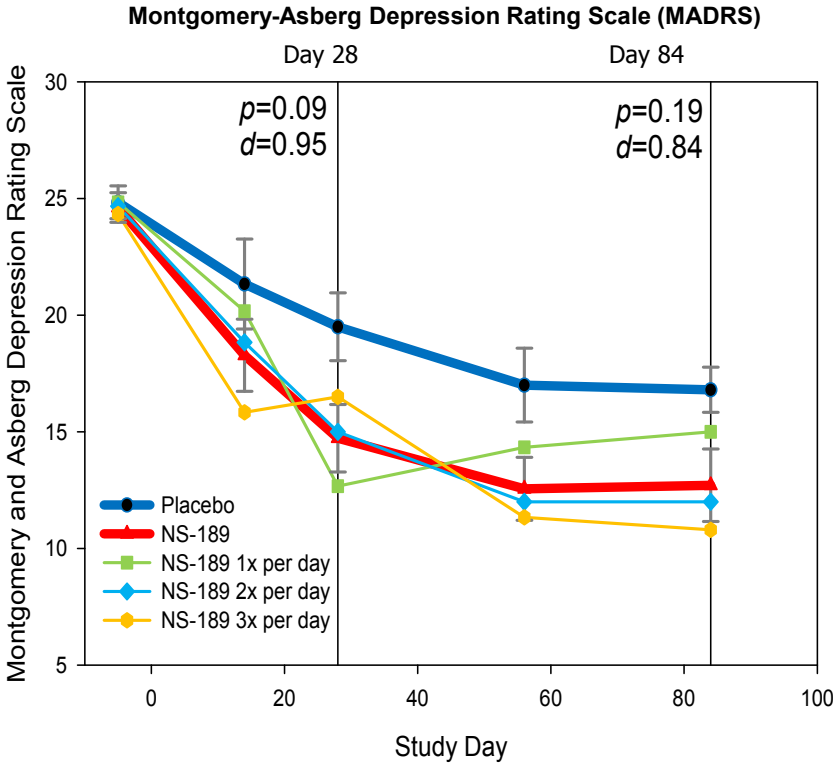
| | | |
|---|---|---|
| **Cohort 1** | N=8 (6 drug, 2 placebo) | 40 mg QD |
| **Cohort 2** | N=8 (6 drug, 2 placebo) | 40 mg BID |
| **Cohort 3** | N=8 (6 drug, 2 placebo) | 40 mg TID |

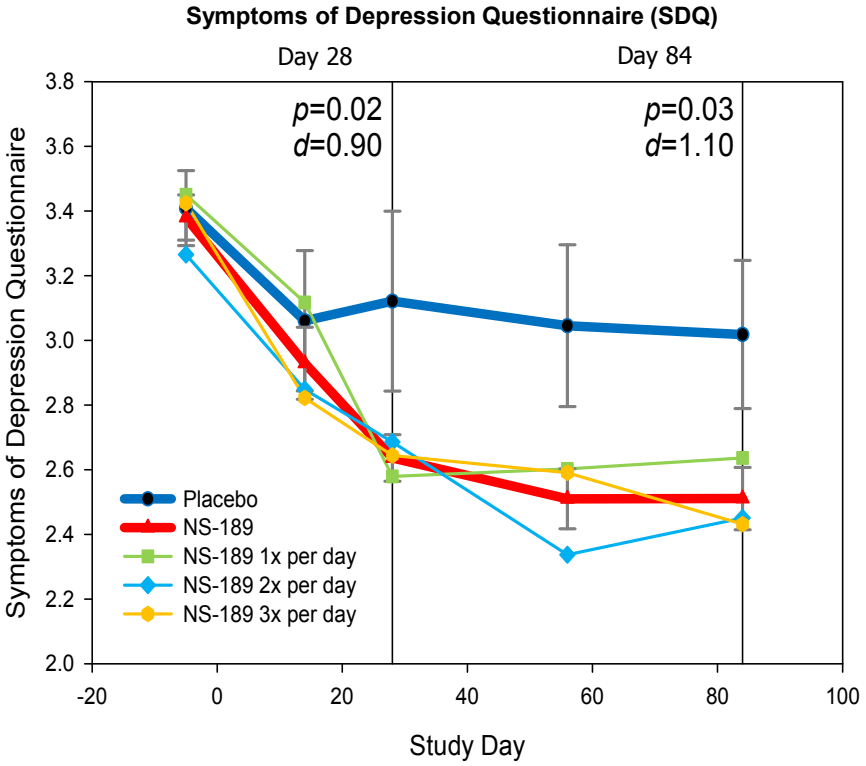
| | |
|---|---|
| **Acute treatment: 28 days** | **Drug free observational follow up: days 35, 42, 49, 56, 70, 84** |

- FDA NCE 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)
  - Five day washout period
- Moderate severity
  - Avg. MADRS 25.7, avg. age 35

# NSI-189 Phase 1b Results

## Demonstrate Trends in Efficacy & Durability Across Physician & Patient Depression Scales




**Large MADRS effect size: d=0.95**

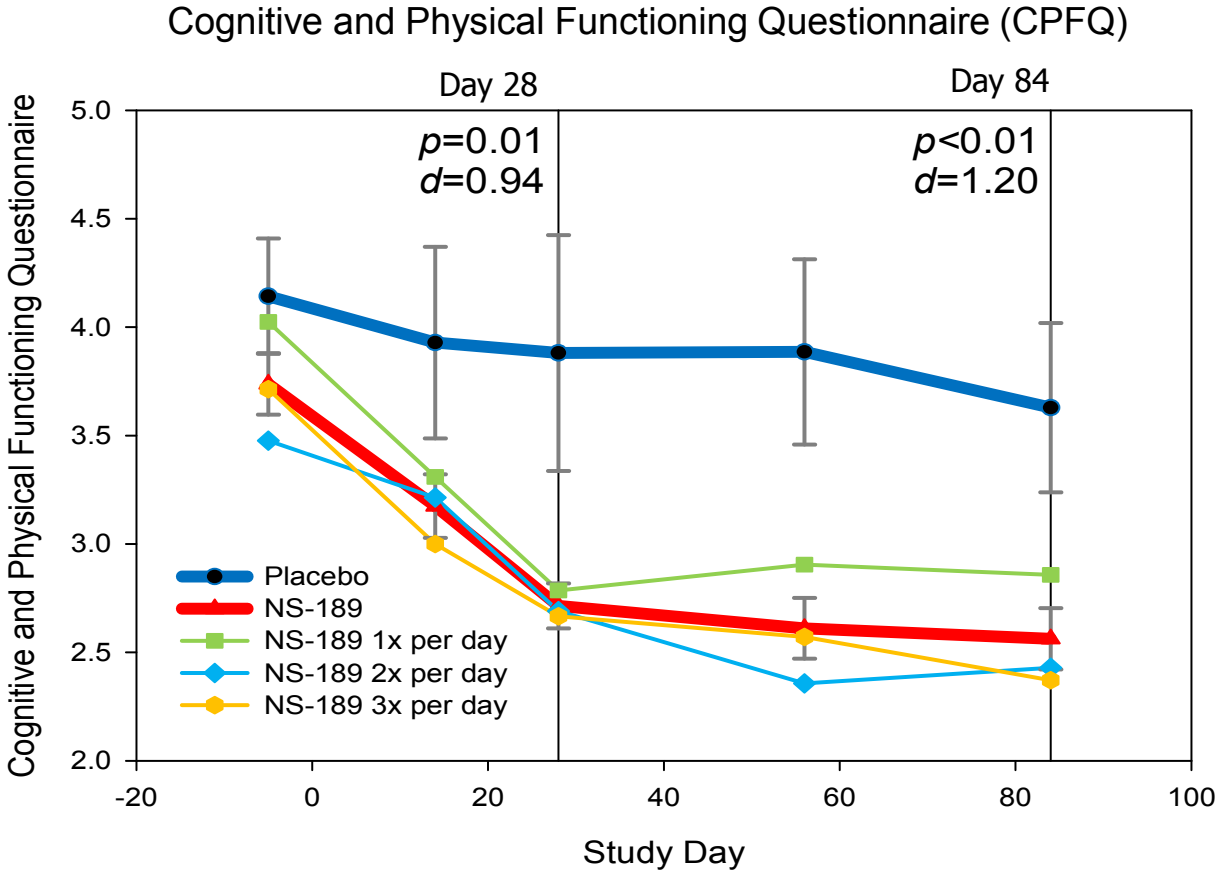
*D-value, or Cohen's effect size, is used to indicate the standardized difference between two means*

| MADRS outcome | # | Definition |
|---|---|---|
| 56% Responder | 10/18 | (≥ 50% reduction) |
| 50% Remission | 9/18 | (≤ 10 score) |
| 72% Partial + Responder | 13/18 | (<14 score) |

All: *A Phase 1B, Randomized, Double-Blind, Placebo-Controlled, Multiple-Dose Escalation Study Evaluating the Effects of NSI-189 Phosphate, a Neurogenic Compound, in Patients with Major Depressive Disorder (MDD)*, presented June 2014, by Maurizio Fava, M.D., Karl Johe, Ph.D., Lev G. Gertsik, MD, Larry Ereshefsky, PharmD, Bettina Hoeppner, Ph.D., Martina Flynn, David Mischoulon, M.D., Ph.D., Gustavo Kinrys, M.D., and Marlene Freeman, M.D.

# NSI-189 MDD Phase Ib clinical results

## Demonstrate trends in improved cognition in patient reported outcomes



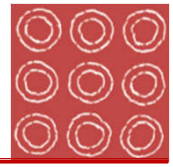

**Large effect size (d=0.94)**

All: *A Phase 1B, Randomized, Double-Blind, Placebo-Controlled, Multiple-Dose Escalation Study Evaluating the Effects of NSI-189 Phosphate, a Neurogenic Compound, in Patients with Major Depressive Disorder (MDD)*, presented June 2014, by Maurizio Fava, M.D., Karl Johe, Ph.D., Lev G. Gertsik, MD, Larry Ereshefsky, PharmD, Bettina Hoeppner, Ph.D., Martina Flynn, David Mischoulon, M.D., Ph.D., Gustavo Kinrys, M.D., and Marlene Freeman, M.D.

# NSI-189: Excellent Safety Profile with No Serious SAEs

| Side effect | Pooled placebo (n=6) N (%) | 40mg q.d. (n=6) N (%) | 40mg b.i.d. (n=6) N (%) | 40mg t.i.d. (n=6) N (%) | Pooled active (n=18) N (%) | Pooled placebo (n=6) N (%) |
|---|---|---|---|---|---|---|
| *Autonomic* | | | | | | |
| 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%) | – |
| | | | | | | |
| *CNS/psychiatric* | | | | | | |
| 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%) |
| | | | | | | |
| *Gastrointestinal* | | | | | | |
| 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%) | – |
| | | | | | | |
| *Skin and subcutaneous tissue disorders* | | | | | | |
| 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, HAMD17, CGI-S, CPFQ, SFI
- Exploratory: Cogscreen Battery, Cogstate Brief Battery

## Innovative Study Design

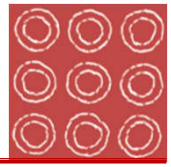
- Randomized, double blind, 3 cohorts (n=220): 40mg BID, 40mg QD, & placebo
- 12-week study, additional 6 month follow-up study
- Fewer, quality MDD trial sites (n=12)
- Prescreen process to manage placebo risk
- SAFER Interview: confirmatory, independent, remote MADRS diagnosis by MGH
- Potential registration study if successful in either active arm
  - Power: >80%, 2-sided p≤ 0.05; 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 17) Clinical Global Impressions Scale (CGI-S) Cognitive and Physical Functioning Questionnaire (CPFQ) Sexual Functional Index (SFI)

# NSI-189:
# Preclinical Data Support Characteristics of Neurogenesis, Cognitive Enhancement & Durability

# Preclinical Overview

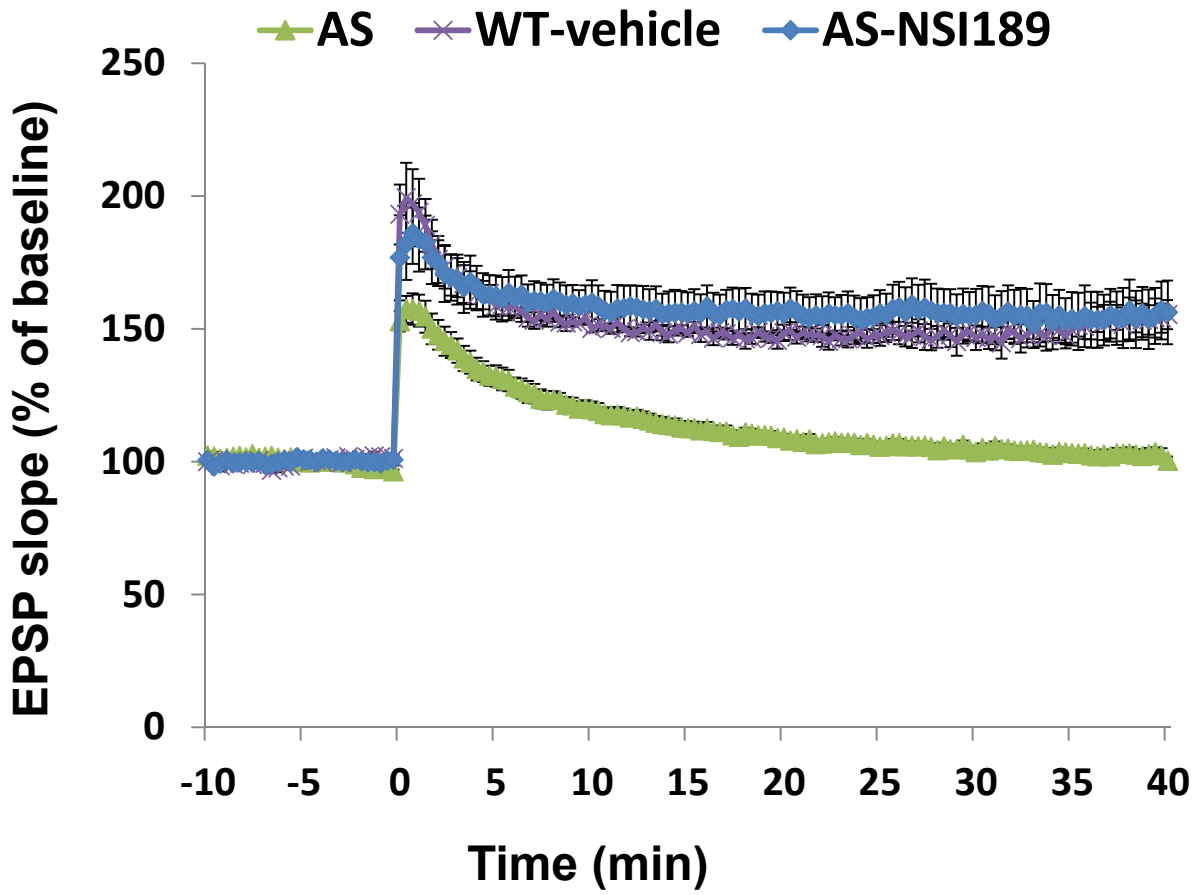


*Preclinical data suggests a new paradigm for reversing damage caused by disease/injury*

- Treatment of a rat model for ischemic stroke shows a durable effect in promoting behavioral recovery that corresponds with increased neurogenesis
- Type 1 & 2 diabetic neuropathy reversal and prevention
- Prevention of cognitive deficit in irradiated mice
- MOA:  Enhances long-term potentiation (LTP) in normal mice
- Restores LTP in Angelman Syndrome mouse

# Orphan Opportunity in Angelman Syndrome

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



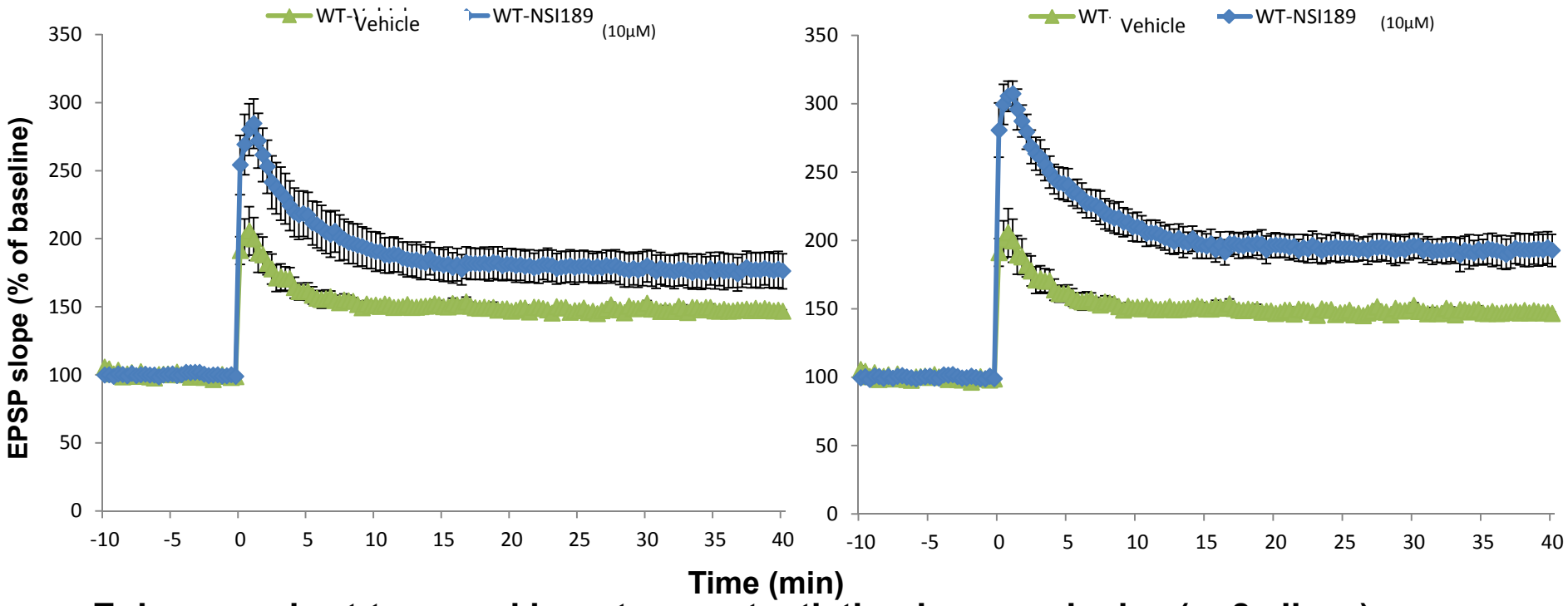

By courtesy of Yan Liu[1], Xiaoning Bi[1], Michel Baudry[1]
Western University of Health Sciences, Pomona, CA 91766

# 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**

By courtesy of Yan Liu[1], Xiaoning Bi[1], Michel Baudry[1]
Western University of Health Sciences, Pomona, CA 91766

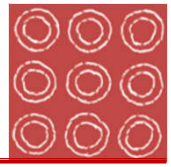
# Stem Cell Development Efforts & Strategy

# 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

# 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

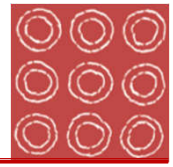
## Efficient expansion

- 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 of of the four subjects treated was confirmed via clinical and electrophysiological follow-up examinations

**MARKET CONSIDERATIONS**
- 270,000 Americans live with cSCI
- 11,000 new injuries per year
- No treatment options

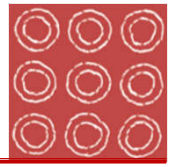
## Ischemic Stroke

**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 25% 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

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- NSI-189: Positive, randomized placebo-controlled Phase 1b in MDD
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