NEURALSTEM INC.

June 2016 Corporate Presentation
MOA Insight

NEURALSTEM, INC.
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.

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, 2015 filed with the Securities and Exchange Commission on March 14, 2016. 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.

You should read carefully our Special Note Regarding Forward-Looking Statements and the factors described in the "Risk Factors" section of our Annual Report on Form 10-K for the year ended December 31, 2015 filed with the Securities and Exchange Commission on March 14, 2016, to better understand the risks and uncertainties inherent in our business.

Key Highlights

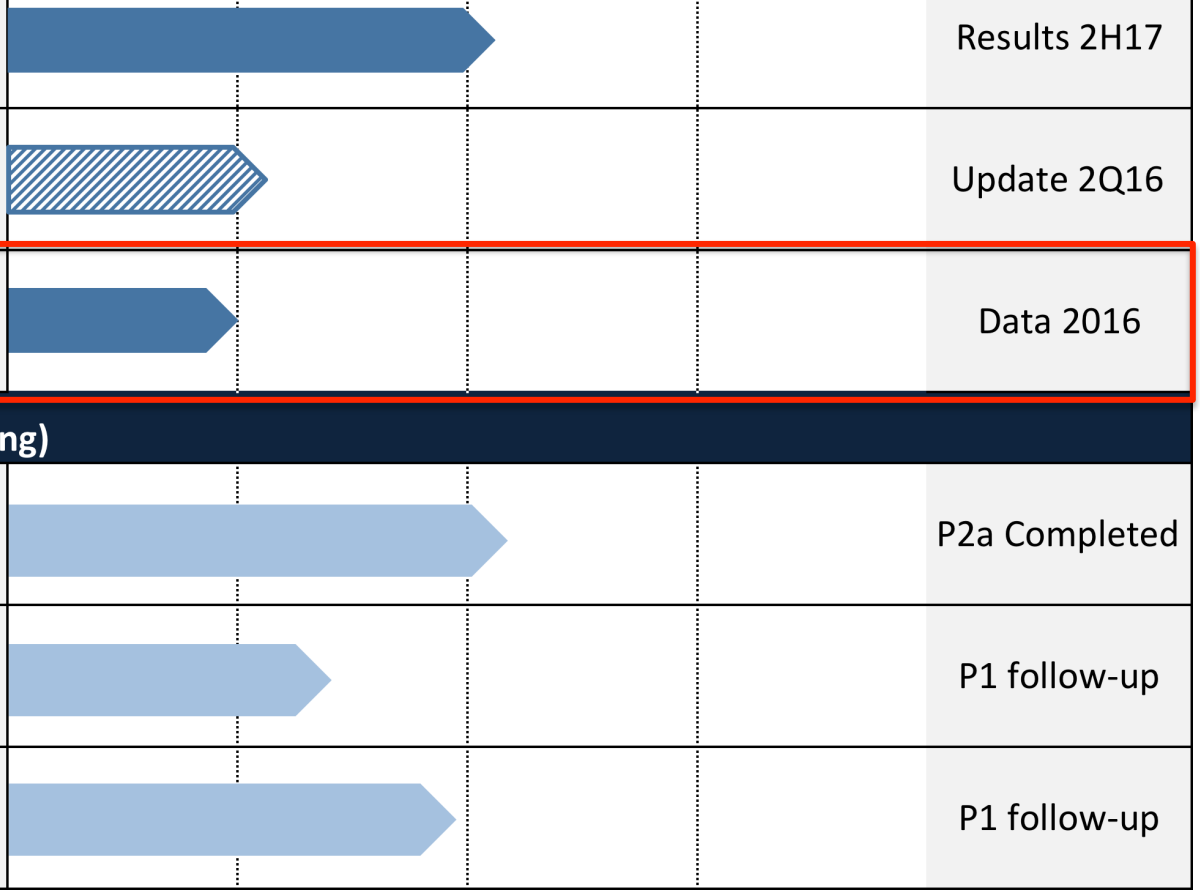
- Refocused Business Strategy:
  - New, experienced management team
  - Focus on lead program: NSI-189
  - Internal reorganization
  - Partner NSI-566 programs

- NSI-189: Novel Neurogenic Small Molecule targeting MDD
  - Compelling early clinical data
  - IP from 2024-2034
  - Phase II MDD Efficacy Data expected in 2H 2017
  - Proof-of-principle data for other indications throughout 2H 2016
  - Renowned scientific advisory team & academic collaborators

- NSI-566
  - Partner for continuing development
  - Cell therapy program updates throughout 2H 2016

Pipeline

Compound / Indication	Preclinical	Phase I	Phase II	Phase III	Status
Small Molecule: Lead Asset					
NSI-189 US Major Depression Disorder					Results 2H17
NSI-189 Pipeline Expansion					Update 2Q16
NSI-189 Preclinical Studies					Data 2016
Cell Therapy (outsourced funding)					
NSI-566 US Amyotrophic Lateral Sclerosis					P2a Completed
NSI-566 US Chronic Spinal Cord Injury					P1 follow-up
NSI-566 China Ischemic Stroke					P1 follow-up



NSI-189 Overview

- New Chemical Entity (NCE)
  - Novel neurogenic MOA
  - Highly stable and well characterized

- MDD Market Opportunity
  - Unsatisfied patient population*
  - High patient turnover rate in MDD*
  - Strong IP position through 2024 – 2034
- Efficacy:
  - Compelling Phase Ib MDD randomized, double-blind data
  - Large effect size
  - Cognitive benefit profile
  - Potential disease modifying, durability profile
  - Excellent safety profile

- Upcoming Data
  - Additional human data
  - Preclinical data in 4 indications

- 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.

NSI-189 MDD Phase Ib trial design

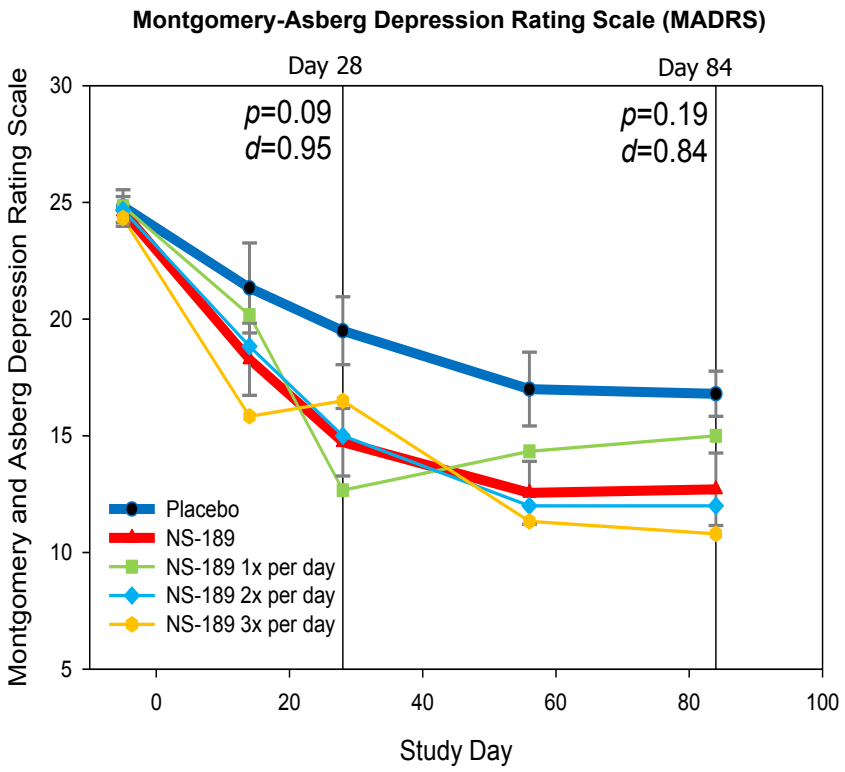
NSI-189 Phase Ib double-blind, randomized, placebo-controlled, dose-escalating study assessing safety and tolerability

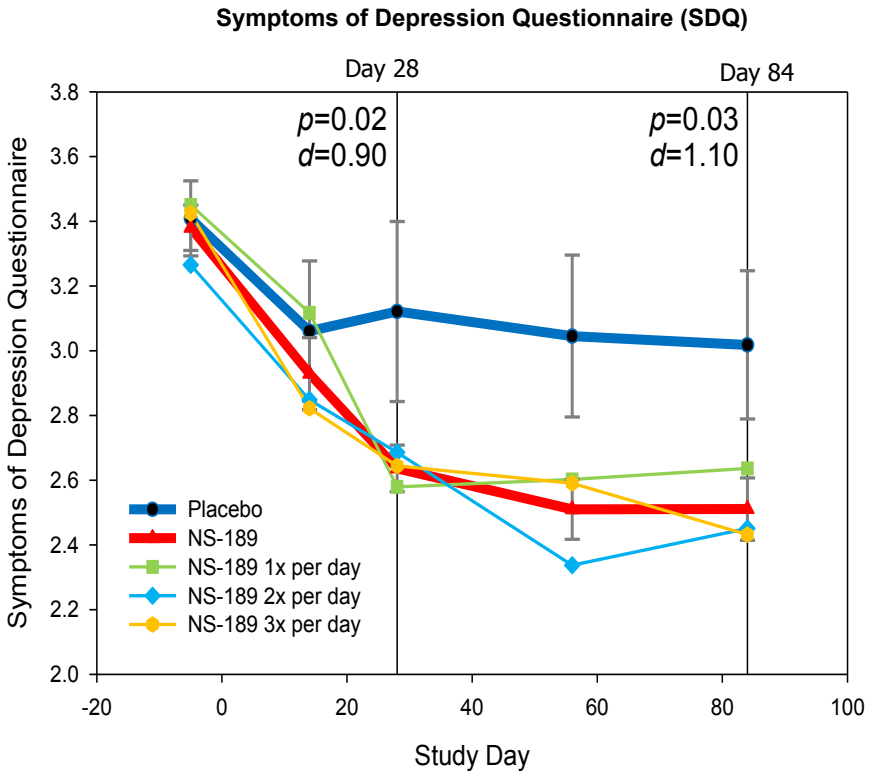
Cohort 1	N=8 (6 drug, 2 placebo)	40 mg QD
Cohort 2	N=8 (6 drug, 2 placebo)	40 mg BID
Cohort 3	N=8 (6 drug, 2 placebo)	40 mg TID

Acute treatment: 28 days	**Follow up: Days 35, 42, 49, 56, 70, 84 (End-of-study)**

- Early indication of efficacy in MDD and Cognition
- Large effect size

Clinical Results from NSI-189 MDD Phase Ib

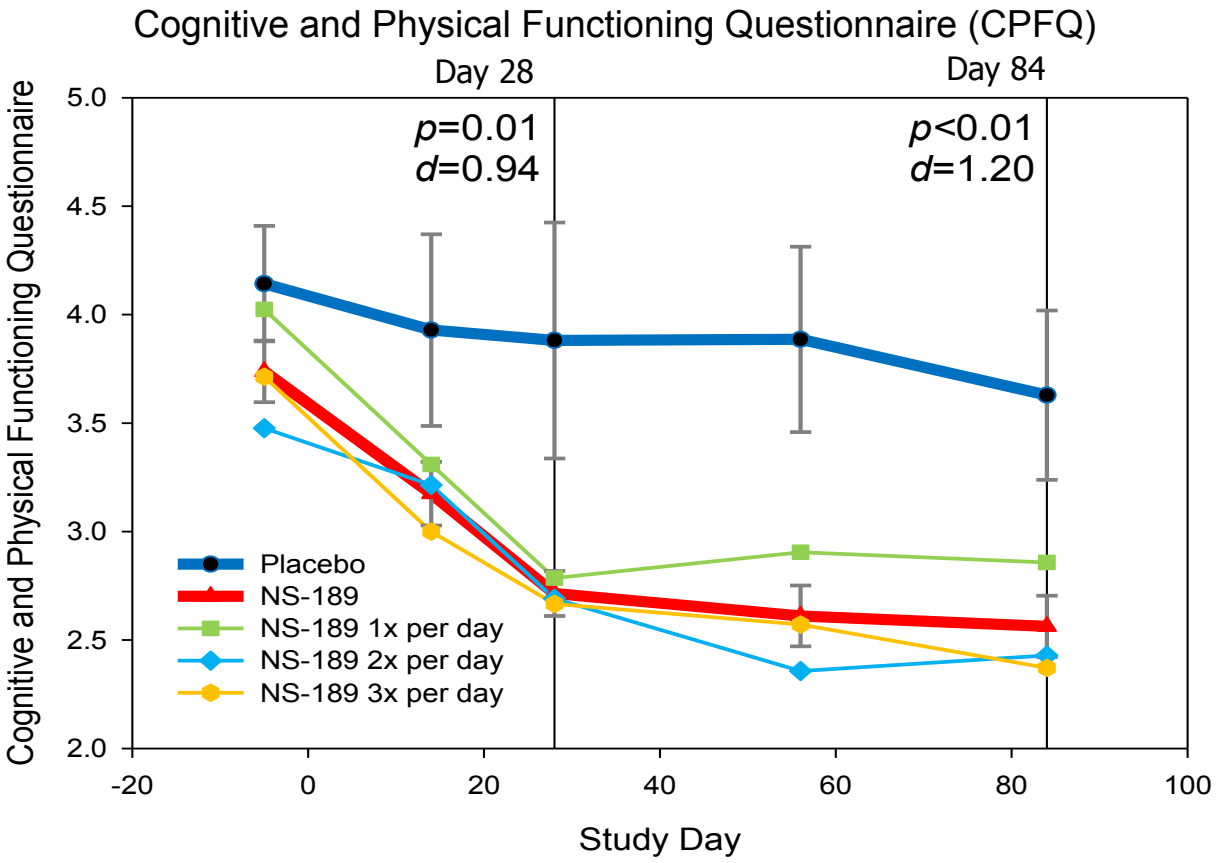




- Large effect size (d = 0.95) MADRS
- Responder (≥50% reduction in MADRS): 10/18 or 56%;
- Remission (≤10 score in MADRS): 9/18 or 50%
- Encouraging durable effect

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.

Clinical Results from NSI-189 MDD Phase Ib



- Large effect size (d=0.94) in cognitive function improvement
- Persistent improvement over the drug-free 8 weeks in CPFQ

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: Adverse Events

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%)	-

Biomarker Results from NSI-189 MDD Phase Ib

Blood biomarker panel:

- Blood panel analysis correlates to MADRS response rate
- MDD panel was developed based on SSRIs activity profile
- Rapid and persistent efficacy

Response Rate	Partial Responder (<14) +Responders (≥ 50%)	Responder (≥ 50%)	Remission (≤ 10)
By MADRS	13/18 (72%)	10/18 (56%)	9/18 (50%)
By Blood Panel	13/18 (72%)		

10 Biomarkers:

- A1AT
- ApoC3
- BDNF
- Cortisol
- EGF
- MPO
- Prolactin
- Resistin
- TNFR2
- TSH

Biomarker Profiling of NSI-189 Phosphate, a Neurogenic Compound, in Patients with Major Depressive Disorder (MDD) during a Phase Ib Randomized Double-Blind, Placebo-Controlled Trial JA. Bilello1, X. Feng1, LM.Thurmond1 , L. Gertsik2, BA. English3, L. Ereshefsky3, M. Fava4, B. Hoeppner4, M. Flynn4, D. Mischoulon4, G. Kinrys4, M. Freeman4, and K. Johe5

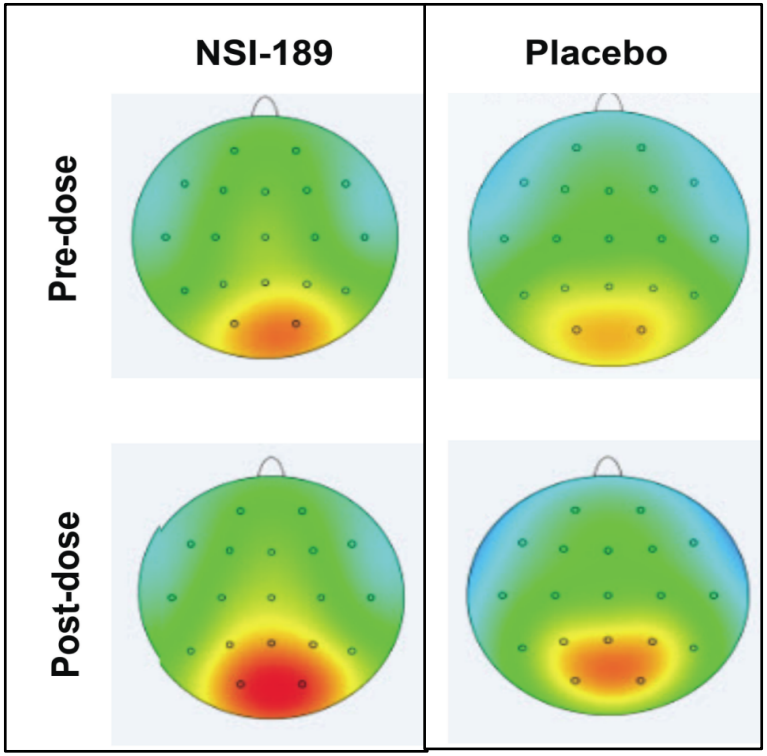
Biomarker Results from NSI-189 MDD Phase Ib

Quantitative EEG (qEEG) biomarker:

- Increases coherence activity between prefrontal cortex and hippocampus
- Two coordinating brain centers utilized for depression and cognition

qEEG

Topographs of High Frequency alpha (10-12 Hz): Day 28 from Baseline



Left posterior temporal (T5) (t=2.45, p=0.02)
Left parietal regions (P3) (t=3.31, p=0.004)

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.

Building the Case for MOA

Extensive screening showed novel MOA vs. currently marketed therapies

Screening:

- 52 neurotransmitter related receptors/ion channels/enzymes

  Novoscreen: Adenosine, GABA, Glutamate, Histamine, Muscarinic, Nicotinic, norepinephrine, opioid, or and serotonin receptors, Ca++, Cl-, K+ channels, PKA, PKC, CRF, MAO-A/B, or CREB and ERK pathways (related to BDNF release)

- 900 other kinases

NSI-189 Binding Activities ≥ 50% at 10μM

Target	IC50 (μM)
Dopamine Transporter (h)	14.2
Norepinephrine Transporter (h)	1.1
5-HT Transporter (h)	>30
5-HT3 Receptor	2.1
5-HT7 Receptor (h)	11.1
Opioid mu Receptor (h)	15.7
Opioid delta 1 Receptor	12.7

Pipeline Update & MOA insight

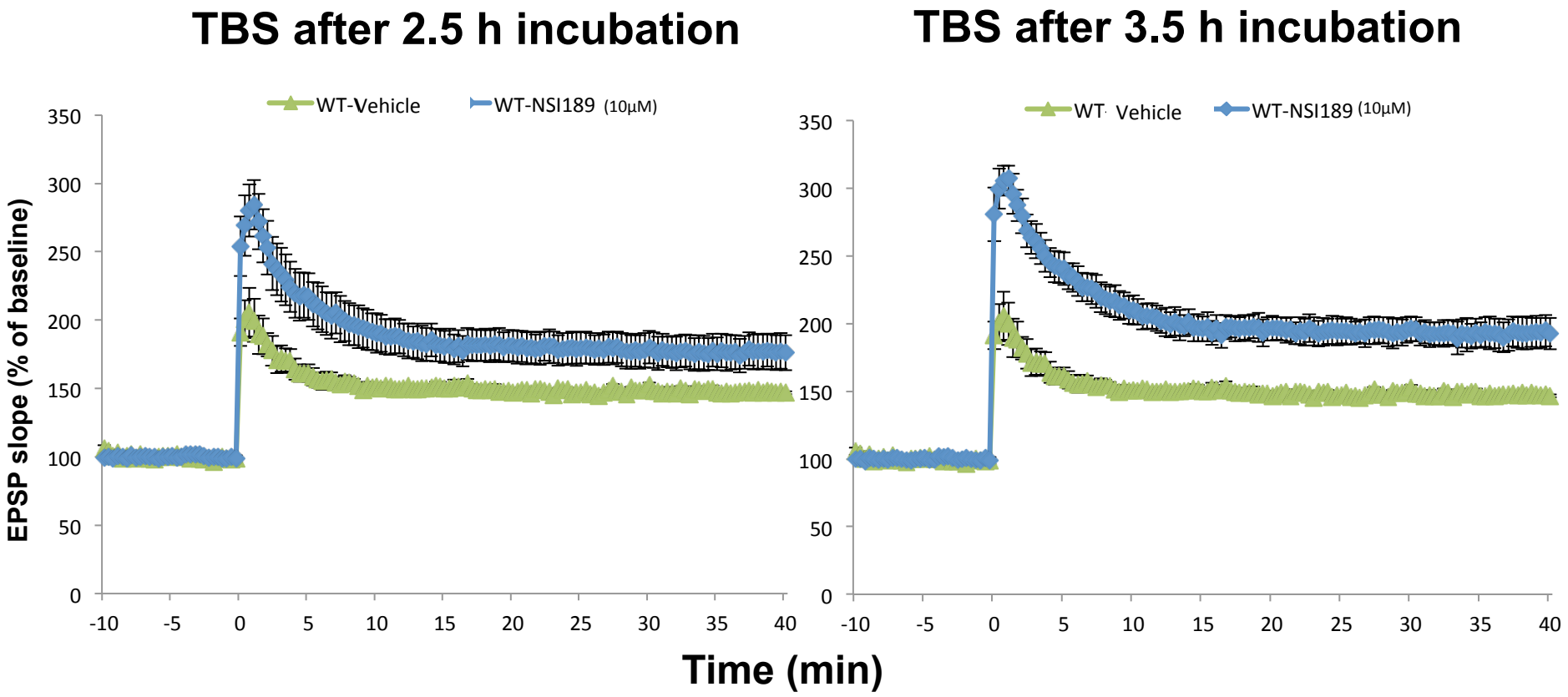
Compound / Indication	Preclinical	Phase I
NSI-189 Small Molecule		
NSI-189 Angelman Syndrome (orphan)		
NSI-189 LTP Enhancement		
NSI-189 Irradiation-induced cognition		
NSI-189 Diabetes-related neuropathy		
NSI-189 MCAO Stroke		

- Upcoming preclinical data presentation in 2H 2016
- MOA: Enhances short-term and long-term potentiation in normal mice
- Restores LTP in Angelman Syndrome mouse

Understanding LTP and Memory

- For mechanistic studies: cognition = memory
- LTP is a cellular biomarker of memory
  - repetitive, high-frequency stimulus leads to long-lasting synaptic transmission
  - increased LTP means enhanced memory, decreased LTP means memory deficit.
- LTP occurs in hippocampus (memory), amygdala (emotion), cortex (attention), and striatum (motor)
- AMPA-receptor dependent Ca++ influx ultimately triggers the neuron firing.
  - Several different pathways can change responsiveness of this trigger - NMDAR, BDNF, Reelin, CaMKII, etc.

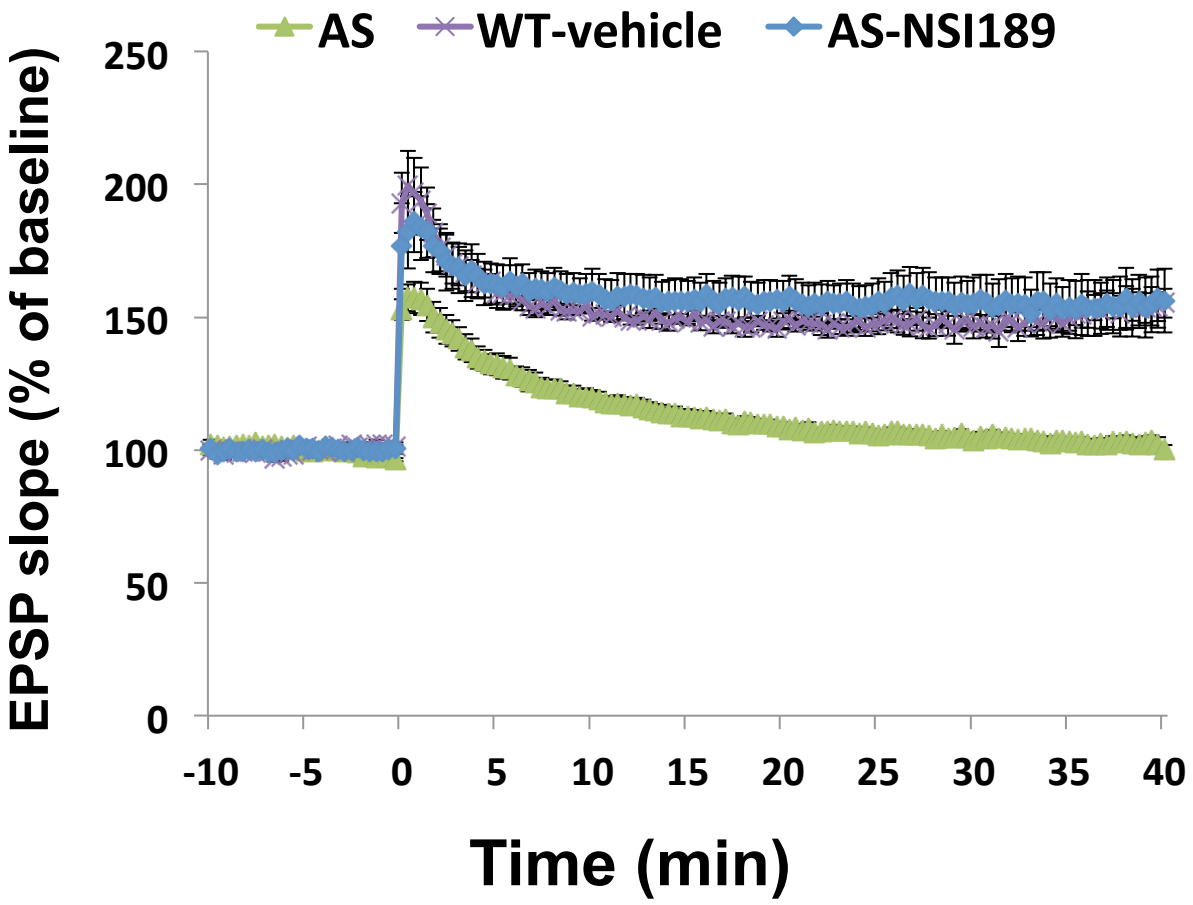
NSI-189 enhances LTP magnitude



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

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

NSI-189 restores STP & LTP from Angleman Syndrom mice



Confirmatory second model in a genetic disease

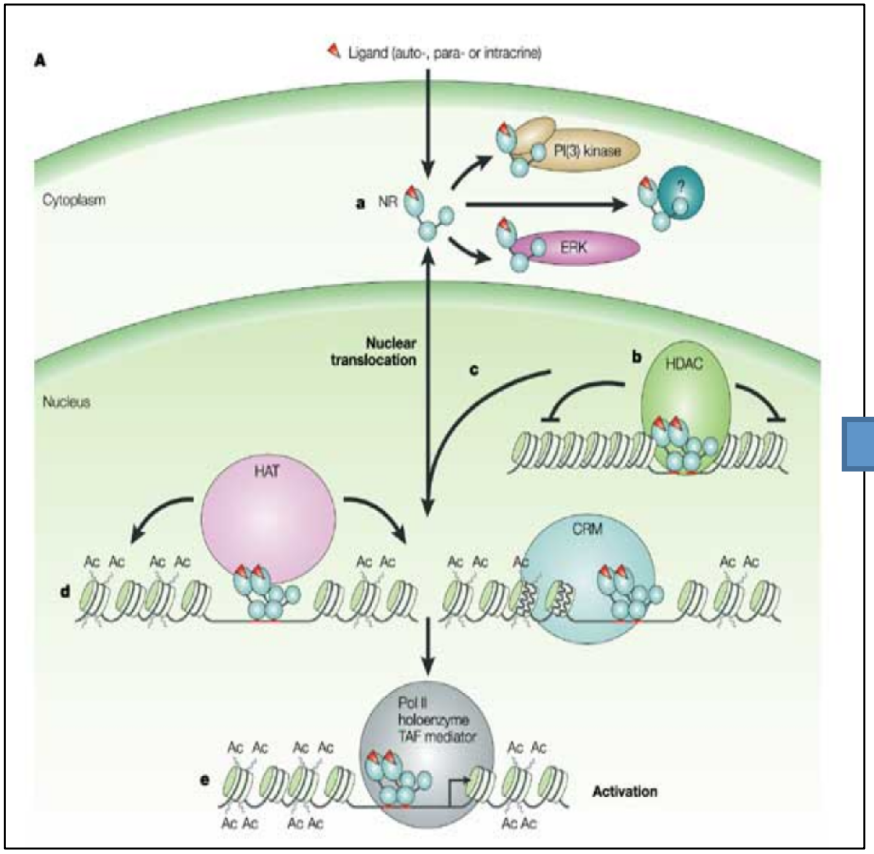
By courtesy of Yan Liu[1], Xiaoning Bi[1], Michel Baudry[1]
Western University of Health Sciences, Pomona, CA 91766

LTP-based assay for NSI-189's molecular pathway

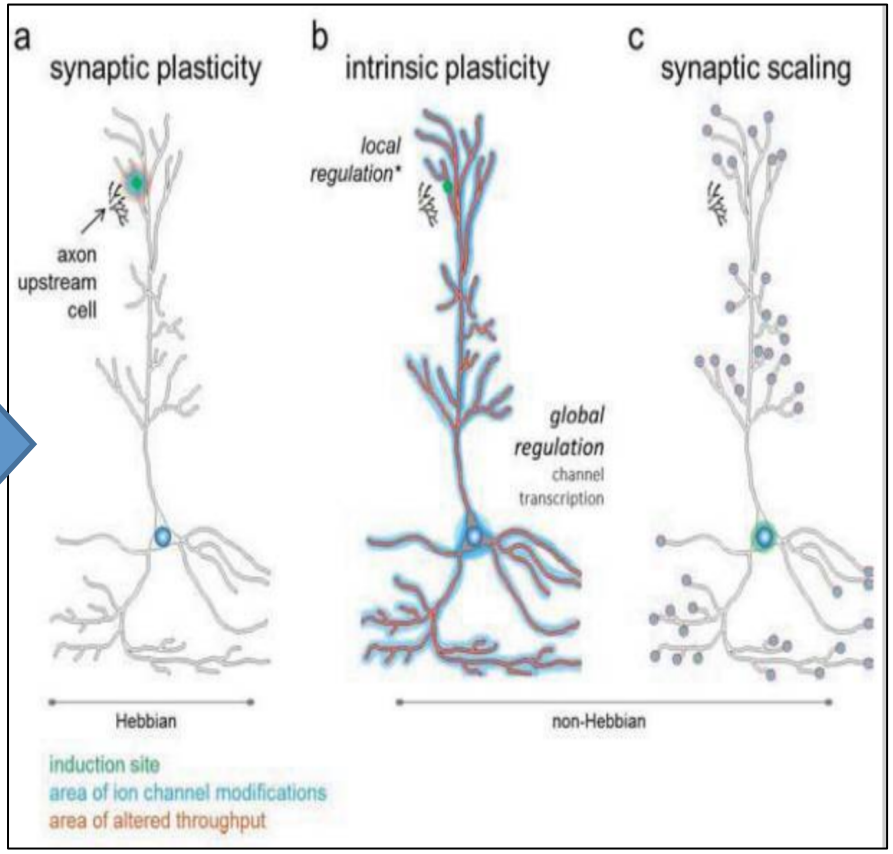
- NSI-189 increases LTP magnitude in a time-dependent and concentration-dependent manner.
  - This effect is not from increased synaptic transmission.
  - This effect is not from increased NMDA receptor properties
  - This effect occurs within 1-3.5 hours of treatment but not before.
  - The drug needs not be present during LTP.
- NSI-189 restores LTP in a mouse model of Angelman syndrome, a genetic disease
  - By 3.5 hours of pre-treatment in vitro.
- NSI-189 also increases neurogenesis, synaptic density, hippocampal volume in vivo.
- What is the common molecular pathway underlying all of these effects?

189 Mechanism of Action: Dynamic transcriptional enhancer?

Potential Molecular Pathways



Potential Cellular Outcome



Gronemeyer H, Gustafsson JA, Laudet V. Principles for modulation of the nuclear receptor superfamily. Nat Rev Drug Discov. 2004 Nov;3(11):950-64. Review. PubMed PMID: 15520817.

Guzman-Karlsson MC, Meadows JP, Gavin CF, Hablitz JJ, Sweatt JD. Transcriptional and epigenetic regulation of Hebbian and non-Hebbian plasticity. Neuropharmacology. 2014 May;80:3-17. Epub 2014 Jan 10. Review. PubMed PMID: 24418102

Limited epigenetic pathways

- DNA methylation & histone acetylation/deacetylation of DNA are dynamically regulated
  - leads to changes in protein synthesis and strength of neuronal connectivity
- mRNA regulation at pre/post-synaptic ending modulates synaptic scaling
  - changes neurotrophic factors, ion channels, neurotransmitter receptors, and synaptic structural proteins
  - results in long-lasting structural and functional changes in neuronal connectivity
- Necessary for learning and memory in vivo

NSI-189 Phase II MDD Trial

Randomized, Double-Blind, Placebo-Controlled, 2-Dose Study

Milestones:

- First Patient enrolled May 2016
- Phase 2 Results expected 2H17

Study Objectives

- Primary: Montgomery-Asberg Depression Rating Scale (MADRS)
- Secondary: SDQ, HAMD17, CGI-S, CPFQ, SFI, Cogscreen Battery, Cogstate Brief Battery

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

NSI-189 Phase II MDD Trial

Placebo-reducing, Study Design

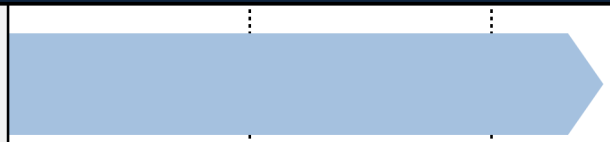
Innovative Trial Design

- Experienced MDD trial sites (n=12)
- Dual patient screening requirement
  - Secondary confirmatory screen: independent, remote MADRS diagnosis by MGH
- Placebo-reducing prescreen process, re-randomization

Study Design

- Three arm: 40mg BID, 40mg QD, & placebo (n=220 randomized)
- Power: >80%, 2-sided p≤ 0.05; d=0.5
  - Potential registration study
- 12 week study; 6 month follow-up study

Cell Therapy Program Update

Cell Therapy (outsourced funding)		
NSI-566 US Amyotrophic Lateral Sclerosis		P2a Completed
NSI-566 US Chronic Spinal Cord Injury		P1 follow-up
NSI-566 China Ischemic Stroke		P1 follow-up

- ALS Long-term Phase 1 / 2 follow up data will be presented at an upcoming scientific conference
- cSCI is currently evaluating 4 Phase 1 thoracic patients; 4 additional cervical patients to be dosed
- Phase I stroke completed dosing all 9 patients and currently evaluating safety

Key Highlights

- Experienced Management Team
- Implementation of Reorganization
- Lead Candidate: NSI-189 novel neurogenic small molecule
- New Chemical Entity; Protected IP: 2024-2034
- Near term milestones:
  - Phase II MDD trial; results expected 2H17
  - Preclinical publications; expected 2016
  - Cell therapy updates
- Compelling randomize, double blind, Phase Ib MDD data, large effect size
  - Supporting biomarker data
  - Potential disease modifying
- Cell therapy business development opportunities

Management

Richard Daly, CEO	• President, AstraZeneca Diabetes, US; President, BMS Diabetes, US; EVP, Takeda Pharmaceuticals; VP, Commercial Strategy, TAP Pharmaceuticals • Boards: Catalyst Pharmaceuticals; Synergy Pharmaceuticals • Education: MBA, Kellogg Graduate School of Management; BS, Microbiology, University of Notre Dame
Karl Johe Ph.D., CSO	• Co-founder, Chairman of the Board of Neuralstem; NIH/NINDS Staff Scientist • Education: Post-doctoral fellow, UCSF; Ph.D, Biochemistry, Albert Einstein College of Medicine; MA/BA, Biochemistry, University of Kansas
Jonathan Lloyd Jones, CFO	• Sr. Director, Corporate Development, Genzyme Corporation; V.P Finance, TransMolecular; CFO and V.P Corporate Development, TetraLogic; CFO, Columbia Laboratories, Inc.. • Education: MBA, University of Pennsylvania Wharton School of Business; BSc. Business Studies, University of Bradford
Andrew Moniz, Vice President, Global Clinical Trails Operations	• 22 years of experience in CNS drug development; VP, Global Neuroscience Operations World Clinicial Trials (WTC); Neuroscience Leadership team, i3 Research (Inventiv Health) • Education: Master of Science in Experimental Psychology from the University of Kentucky and a Bachelor of Arts in Psychology from Salve Regina University
Thomas Hazel Ph.D. Senior Vice President, Research	• Neuralstem's Stem Cell Discovery Program Director and Senior Scientist since 1998; Staff Scientist at the NIH Laboratory of Molecular Biology of the National Institute of Neurological Disorders and Stroke in Bethesda; and was a NIH IRTA fellow from 1993-1996. • Education: PH.D, Genetics, University of Illinois College of Medicine; BA, Biology, Kalamazoo College

NSI-189 Scientific Advisory Board

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

Intellectual Property

Small Molecule

11 US & 65 World Issued and Pending Patents

- 16 Neurogenic compounds (including 189), composition of matter, US (7,560,553) to 2024, Patent Extension to 2029.
- Assay method for screening neurogenic compounds, US (8,293,488) and Europe to 2023
- Synthesis method for NSI-189, World-wide to 2030
- Treatment of MDD, World-wide, pending (filing date 6/2015)

Neural Stem Cells

13 US & 63 World Issued and Pending Patents*

- Adherent neural stem cells, composition of matter (US 5,753,506) to 2016
- Stable neural stem cells, composition of matter (US 7,544,511) to 2016
- Method of culturing human neural stem cells (US 7,691,629) to 2025
- Method of expanding human neural stem cells (US 8,236,299) to 2025

* The Company also licenses 3 U.S. and 6 foreign patents related medical devices used in connection with the Company's stem cell therapies.