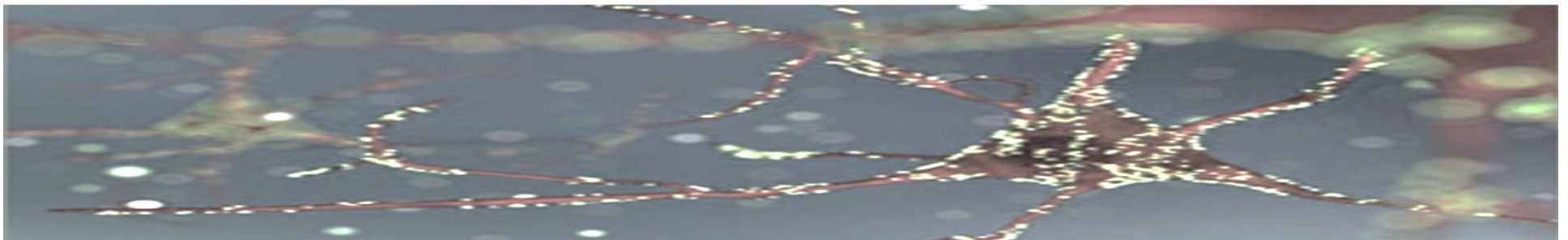


NEURALSTEM INC.

March 2016

Corporate Presentation



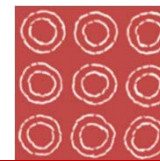
NEURALSTEM, INC.

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. For links to SEC documents please visit the company's Web site: neuralstem.com.

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Proprietary Neural Stem Cell Technology



Neural Stem cell CNS platform

Small Molecule Screening

Cell Therapy

Safe, Novel
MOA

Multiple
Targets

Continuous
Screening

High unmet
medical need

Outsourced
Funding

Lead Candidate: NSI-189 Phase II MDD

Lead Candidate: NSI-566
ALS (orphan), Stroke, cSCI

Pipeline



Compound / Indication	Preclinical	Phase I	Phase II	Phase III	Status
Small Molecule					
NSI-189 US Major Depression Disorder					Phase II start 1Q16
NSI-189 Exploratory					Data 2016
Cell Therapy (outsourced funding)					
NSI-566 US Amyotrophic Lateral Sclerosis					Phase II Completion
NSI-566 US Chronic Spinal Cord Injury					Phase I data 1Q16
NSI-566 China Ischemic Stroke					Phase I ongoing

Clinical Corporate Goals



NSI-189

- MDD Ph II Trial, Data 2H 2017
- Exploration of additional safety studies

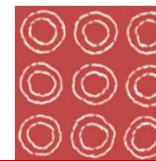
NSI-566

- Partnerships for continuing clinical development
- Expedite regulatory pathways

Corporate

- Expansion of clinical & regulatory personnel
- Business development initiatives

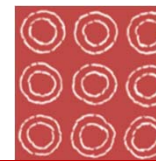
NSI-189 Scientific Advisory Board



World Class Psychiatric, Clinical and Regulatory Experts

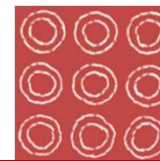
Dr. Maurizio Fava	Harvard, MGH, Executive Vice Chair, Dept. of Psychiatry Principal Investigator: NSI-189 Phase 2 MDD clinical trial
Dr. Michael Thase	Univ. of Pennsylvania, Chief, Division of Mood and Anxiety Disorders Treatment and Research Program
Dr. Mark Frye	Mayo Clinic, Chair, Psychiatry and Psychology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

NSI-189 Target Product Profile



Indication	<u>Monotherapy</u> and <u>Adjunctive</u> treatment of Major Depressive Disorder (MDD), with improvement of cognition
Efficacy <ul style="list-style-type: none">• <u>Primary:</u> MADRS• <u>Key secondary:</u> Onset of effect, sustained effect, cognitive symptom improvement	Superiority vs. active comparator at day 28 and sustained for 90 days & post-dosing durability
Tolerability <ul style="list-style-type: none">• Based on clinical wellness	<ul style="list-style-type: none">• Safe and well tolerated• No major adverse events: body weight gain or sexual dysfunction
Safety: <ul style="list-style-type: none">• Warnings & Precautions	Standard suicidality warning
Administration	Oral, 4-12 weeks episodic course of treatment
Health Outcome Measures (Payer requirement)	<ul style="list-style-type: none">• Economic modelling for reduced cost to payer• Patient reported outcomes - reduction in symptoms of depression, durability, and cognitive improvement

Clinical Results from NSI-189 Phase Ib



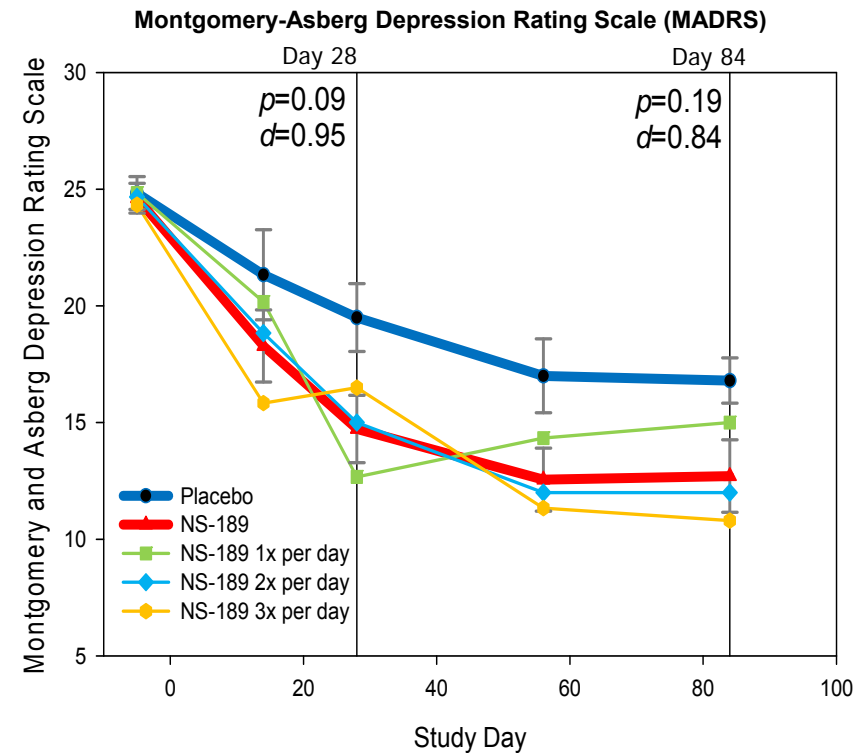
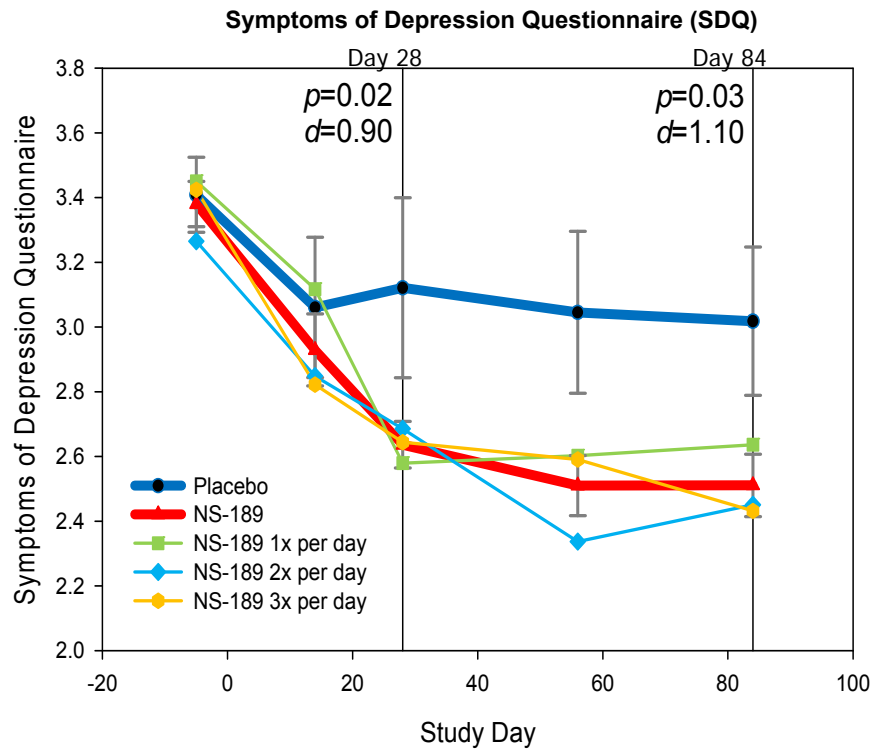
NSI-189 Phase Ib double-blind, randomized, placebo-controlled, multiple-dose study assessing safety and tolerability

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)
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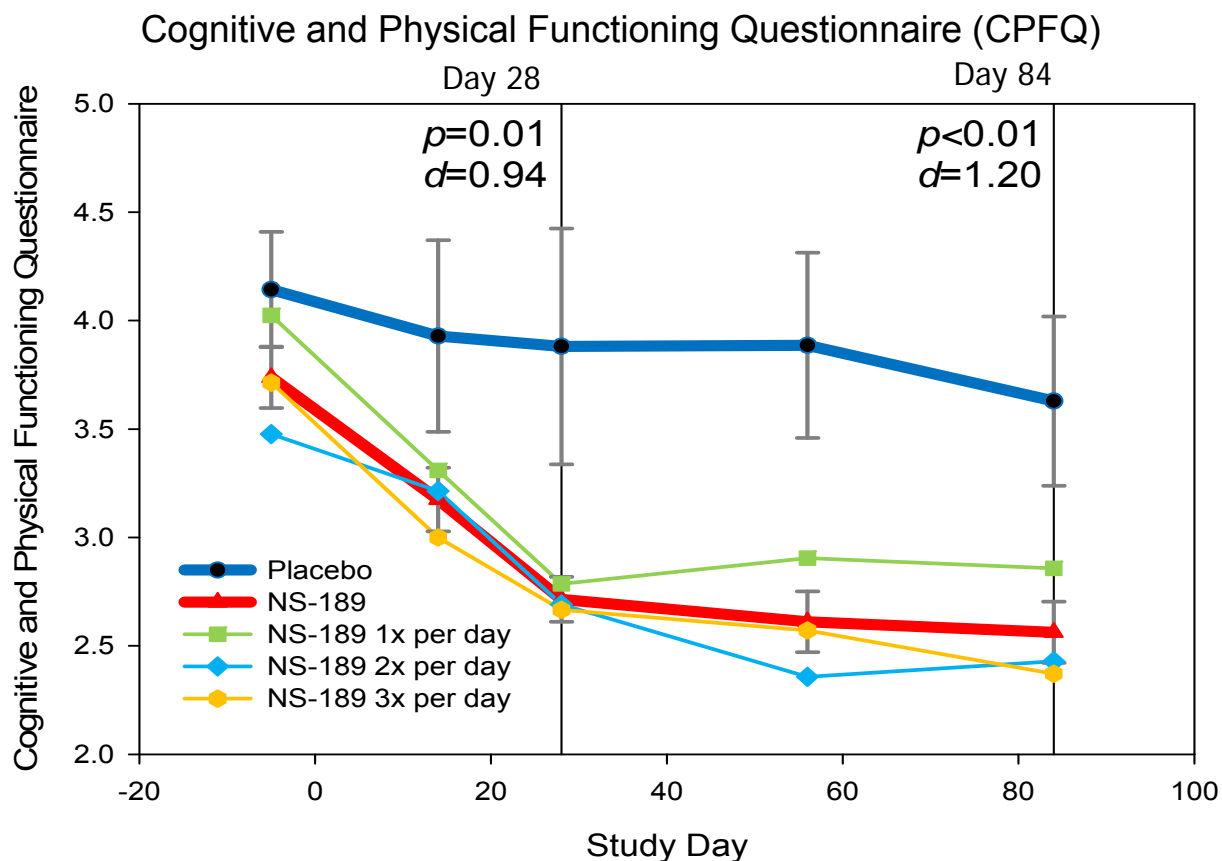
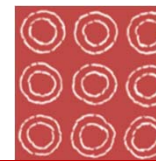
- Patients at screening could be taking an antidepressant medication(s), or have a history of taking antidepressant medication(s) in the past for their depressive disorder
- At least two prior depressive episodes (including current episode)

Clinical Results from NSI-189 MDD Phase Ib



- Statistically significant improvement, $p=0.02$, by SDQ
- Large effect size of Cohen's $d = 0.95$ by MADRS
- Responder ($\geq 50\%$ reduction in MADRS): 10/18 or 56%; Remission (≤ 10 score in MADRS): 9/18 or 50%

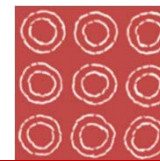
Clinical Results from NSI-189 MDD Phase Ib



- Significant ($p=0.01$) and 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 Hoepfner, Ph.D., Martina Flynn, David Mischoulon, M.D., Ph.D., Gustavo Kinrys, M.D., and Marlene Freeman, M.D.

Biomarker Results from NSI-189 MDD Phase Ib



Quantitative EEG (qEEG) biomarker:

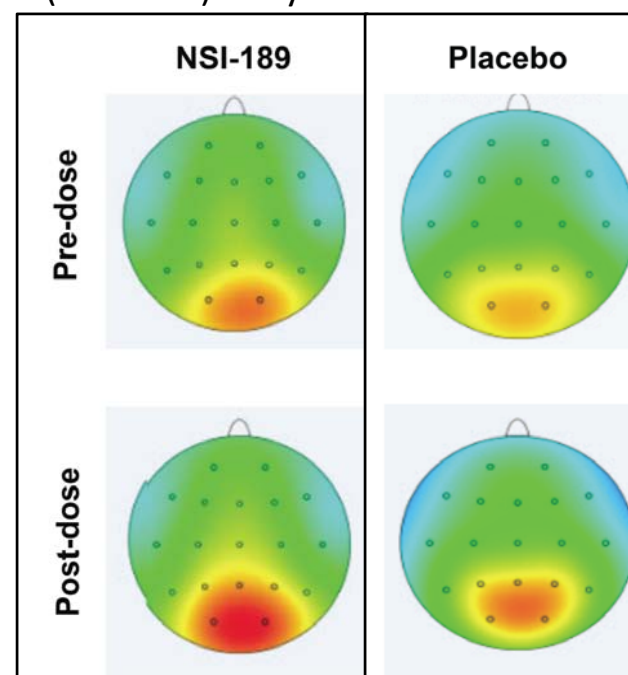
- Increases coherence activity between prefrontal cortex and hippocampus
- Two coordinating brain centers utilized for depression and cognition

Blood biomarker panel:

- Blood panel analysis (78%) correlates to MADRS response rate: (78%) partial responder (<14) + responders ($\geq 50\%$)

qEEG

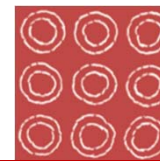
Topographs of High Frequency alpha (10-12 Hz): Day 28 from Baseline



Left posterior temporal (T5) ($t=2.45$, $p=0.02$)

Left parietal regions (P3) ($t=3.31$, $p=0.004$)

Favorable NSI-189 DMPK Characteristics



Human PK supports QD dosing in clinic

- $t_{1/2}$ is 17-20 hours
- Total clearance is low (less than hepatic blood flow)
- No gender difference in exposure profiles
- No difference in AUC and $t_{1/2}$ between fasted and fed states

Attractive metabolic profile

- Few metabolites, multiple pathways, no unique human metabolites (hepatocytes)

Attractive pharmaceutical properties

- Good solubility and high permeability, single crystalline polymorph, optimized salt form

NSI-189 Phase II MDD Trial



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

Study Objectives

- Primary: Montgomery-Asberg Depression Rating Scale (MADRS)
- Secondary: SDQ, HAMD17, CGI-S, CPFQ, SFI (sexual dysfunction), Cogscreen Battery (including Digit Symbol Coding Task), Cogstate Brief Battery

Innovative Study Design

- Independent, remote, confirmation of MADRS diagnosis by MGH
- Placebo-reducing prescreen process
- Fewer, quality MDD trial sites (n=12)
- Three arm: 40mg BID, 40mg QD, & placebo (n=220 randomized)
- Potential registration study if successful in either active arm
- Power: >80%, 2-sided $p \leq 0.05$; $d=0.5$

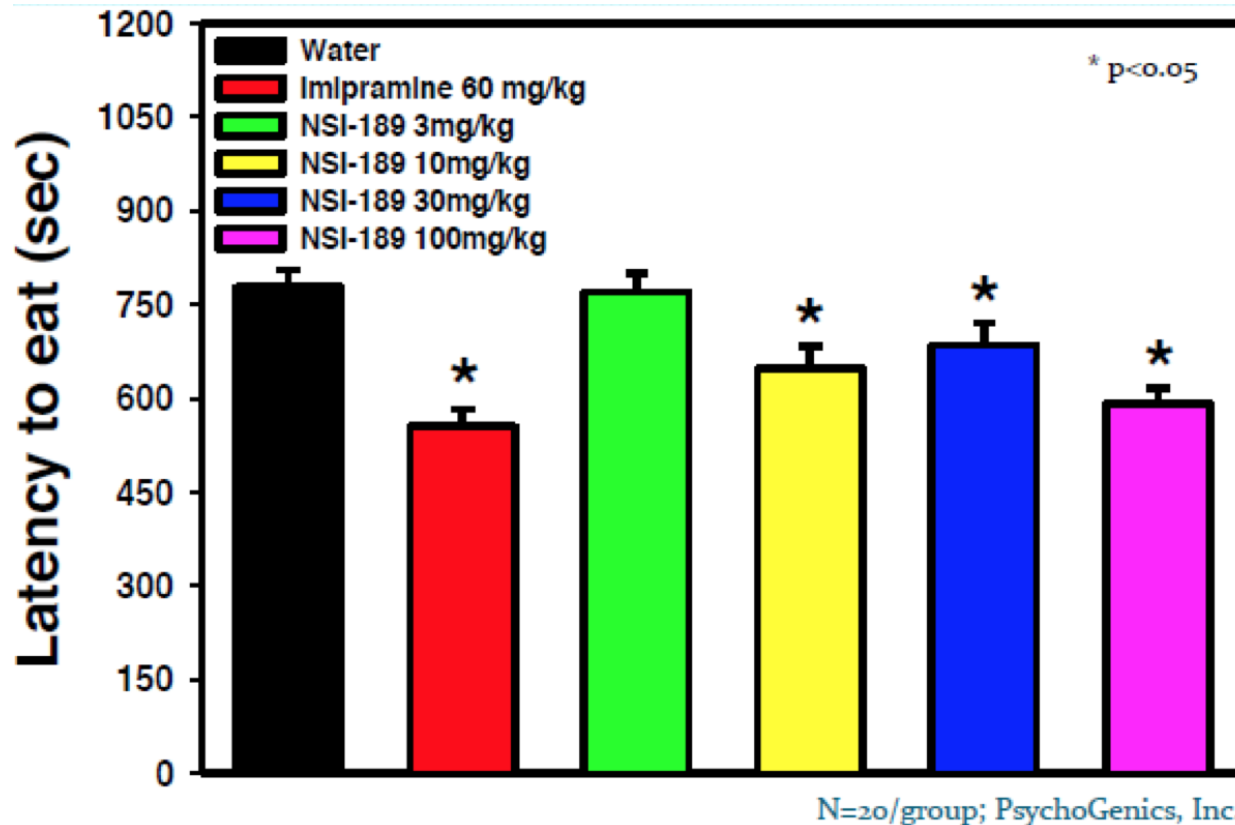
Principal Investigator: Maurizio Fava, M.D. Slater Family Professor of Psychiatry at Harvard Medical School, Massachusetts General Hospital

Preclinical Data



- Orally active, neurogenic, neuroregenerative, compound for the treatment of depression, cognitive impairment, and neurodegeneration
- A new chemical entity with novel mechanism of action, molecular target yet unknown, but not mediated by SSRI or SNRI or by BDNF release or via any known GPCRs, kinases, or channels
- Stimulates hippocampal neurogenesis and increases hippocampal volume in young, healthy, normal mouse
- Shows antidepressant effects in mouse models of depression

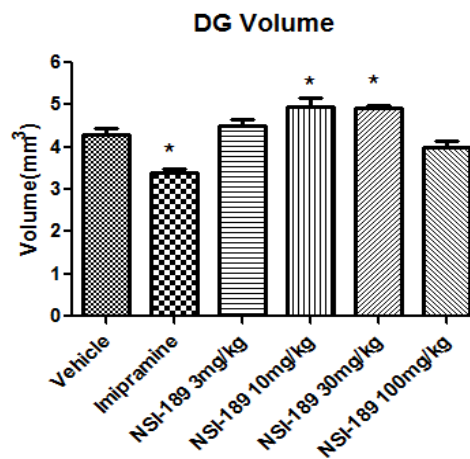
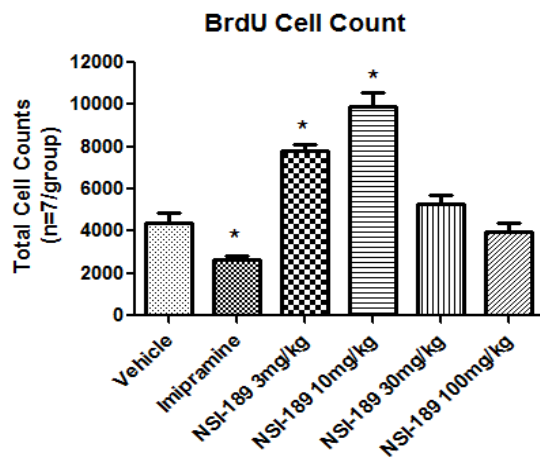
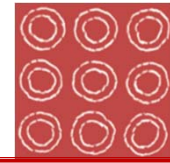
P-o-P Activity at Multiple Doses in Novelty Suppressed Feeding Model (Mouse)



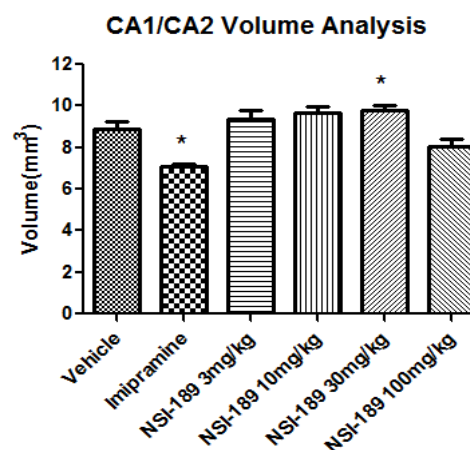
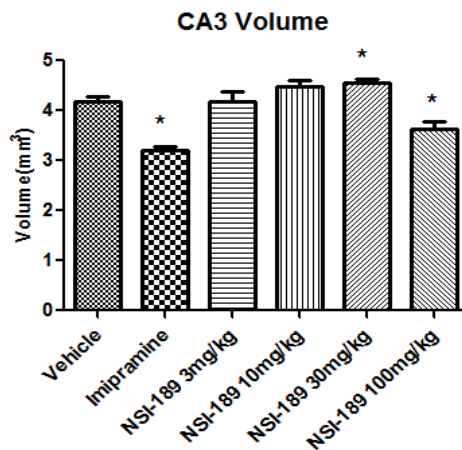
Doses: 10-100mg/kg

- NSI-189 (10-100mg/kg) and imipramine significantly decreased the latency to eat compared to vehicle (water) after 28 days of oral dosing but not 1 day (now shown)
- No significant treatment effects on either body weight or neurological observations

P-o-P Activity at Multiple Doses in Novelty Suppressed Feeding Model (Mouse)

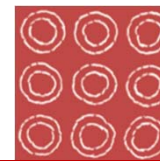


- 10mg/kg and 30mg/kg are the pharmacologically active concentrations.
- Bell-shaped dose-response curve: Higher dose may not necessarily yield larger effect.



Mouse brains from Novelty Suppressed Feeding Test (N=15/group)

Building the Case for MOA



No appreciable binding activity against 52 neurotransmitter related receptors/ion channels/enzymes

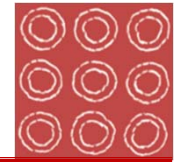
- Novoscreen: Adenosine, GABA, Glutamate, Histamine, Muscarinic, Nicotinic, norepinephrine, opioid, or and serotonin receptors, Ca⁺⁺, Cl⁻, K⁺ channels, PKA, PKC, CRF, MAO-A/B, or CREB and ERK pathways (related to BDNF release)

No binding or functional activities against 900 Other kinases
(DISCOVERX KinomeScan)

NSI-189 Binding Activities \geq 50% at 10 μ M

Target	IC50 (μ M)
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

Rapid Bioavailability in the Brain by Oral Administration



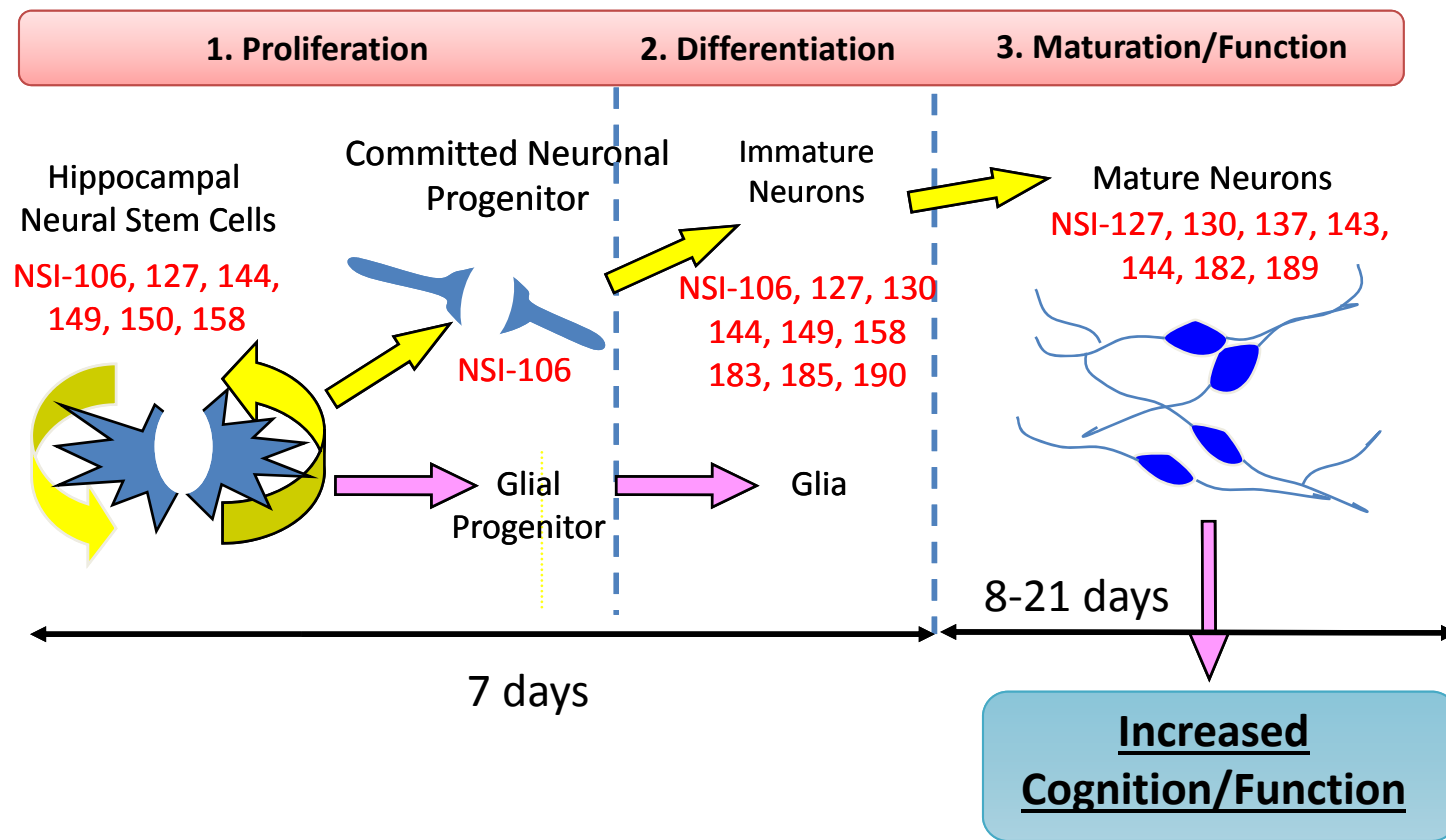
PK/ADME Results from Single Oral and IV Doses (mouse)

Dose	10 mg/kg Oral		30 mg/kg Oral		100 mg/kg Oral	
	Plasma	Brain	Plasma	Brain	Plasma	Brain
C _{max} (ng/mL plasma; ng/g brain)	116	77.8	270	169.6	8100	2063.2
T_{max} (h)	0.5	0.5	0.25	0.3	0.133	0.1
AUC _{0-t} (h*ng*/mL plasma; h*ng/g brain)	105	258	420	425	4926	2549
AUC _{0-∞} (h*ng*/mL plasma; h*ng/g brain)	109.0	886	423.9	588	4936.6	2620
T _½ (h)	1.5	38.5	2.5	8.4	1.8	3.3
Dose	1 mg/kg IV		3 mg/kg IV		10 mg/kg IV	
	Plasma	Brain	Plasma	Brain	Plasma	Brain
C _{max} (ng/mL plasma; ng/g brain)	215.4	298.48	858	654.4	3014	2280
T_{max} (h)	N/A	0.133	N/A	0.133	N/A	0.133
AUC _{0-t} (h*ng*/mL plasma; h*ng/g brain)	172	165	625	522	2135	1278
AUC _{0-∞} (h*ng*/mL plasma; h*ng/g brain)	182	171	634	771	2141	1354
T _½ (h)	5.6	4.1	1.6	13.7	2.6	3.5

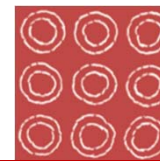
Proprietary Drug Screening Platform



- Based on human neural stem cell differentiation in vitro
- Captures large window of neurodevelopment: neurogenesis to synaptogenesis
- Multiple Potential Sites of Action During Stages of Neurogenesis



In-Licensed Compound Libraries



Neuralstem's Library Selection: Potentially CNS-Active Compounds

Libraries selected to target neurogenesis

- Kinases & phosphatases
- Nuclear receptors
- Peptide mimetics
- GPCRs

Five structural libraries chosen for diversity (scaffolds)

Selected ~2000 compounds per library

- Predict in advance for CNS-Availability
- Cover max chemical space within each library

Screening Path to NSI-189



10,269 Small Molecule Compounds through High Content Screen

↳ 16 Neurogenic Compounds *in vitro*

↳ 16 Tested for Acute Toxicity in Mice

↳ 15 Tested for Neurogenesis in Healthy, Adult Mice

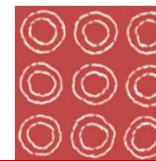
↳ 7 Orally Active Neurogenic Leads
(3 Structural Classes)

↳ 4 Leads Tested in 3 Mouse Depression Models



**1 Development Candidate Selected
NSI-189**

Neuralstem's Operational Team



CMC	Jim Zeller, Ph.D., API Process Chemistry	22 years in Warner-Lambert/Parke Davis/Pfizer, in Holland, MI, NDAs for gabapentin, atorvastatin, quinapril.; 12 years consulting –NDAs for carfilzomib, vismodegib, tedizolid phosphate, lifitegrast, obitecholic acid
	Sam McClintock, Ph.D., Drug Product Development/Analytical Chemistry	23 years in Merck, 9 years in biotech. Merck Key Contributor to approval & launch of Singulair, Vioxx, and Arcoxia
	Richard Pariza, Ph.D., Analog Chemistry	30 years in Abbott/Cedarburg
Pharm-Tox	Grace Furman, Ph.D. , Toxicology	25 years in Pfizer/Biotechs, NDA for DepoCyt (cytarabine liposomal), Sutent (sunitinib malate), Macugen (pegaptanib), Sivextro (tedizolid phosphate)
	Ronald Christopher, Ph.D., Metabolism/Clin. Pharmacology	25 years in Merck/Takeda/Biotechs, NDA for Ultram (tramadol), Nesina (alogliptin), and Belviq (lorcaserin)
	William Kramer, Ph.D., PK/PD/Clinical Pharmacology	11 years in Boehringer Mannheim/Schering-Plough, 18 years consulting.
	Dennis Fisher, M.D., Population PK	> 25 years in academia (UCSF) and industry consulting
Clinical Trials	Andrew Moniz, V.P.,	25 years in global CROs, special emphasis in CNS indications: 4 NDAs and 3 ANDAs in CNS
Strategic Marketing	Terry Frangiosa	20 years in Boehringer Mannheim /Janssen/J&J, Launched /prelaunch Risperdal (Bipolar), Invega Sustenna (Schizophrenia), Esketamine (Depression)