

NEURALSTEM INC.

Neural Stem Cell Technology Platform
Cell Therapy and Pharmaceuticals

February 2012

NYSE Amex: **CUR**

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.

Neuralstem, Inc.

Investment Highlights

- ❑ Proprietary Patented Neural Stem Cell Platform Serves as Foundation for Cell Therapy and Small Molecule Programs
 - ❑ NIH-discovered platform; Fully characterized, regionally specific neural stem cells
- ❑ Positive Human Data for Neural Stem Cell Therapy in ALS Patients; Cervical Phase
 - ❑ Reported data from 12 ALS patients showing the procedure and therapy were safe and well-tolerated with promising early indications of a treatment effect; cervical transplantation phase commenced Nov. 2011
- ❑ First-in-class Neurogenic Small Molecule Drug Program NSI-189 Advances to Phase Ib
 - ❑ Patented oral neuroregenerative compound completed Phase Ia trial and approved by FDA in Dec. 2011 to move into Phase Ib in major depressive disorder in 1Q12
- ❑ World-class Team
 - ❑ Leaders in their fields working with the company include Karl Johe, Ph.D., discoverer and developer of neural stem cell technology; independent ALS researchers Eva L. Feldman, M.D., Ph.D., Jonathan D. Glass, M.D., and Nicolas M. Boulis, M.D., and small molecule trial expert Maurizio Fava, M.D.
- ❑ Capital Efficient Business Model

Neuralstem, Inc.

The Promise of Stem Cell Therapeutics 15 Years in the Making

☐ Founded 1996

☐ Committed Partnership: Karl Johe, PhD and Richard Garr, JD

- ☐ Scientific breakthroughs begun while at NIH
- ☐ Private sector research opportunities
- ☐ U.S. DOD funding
- ☐ New discoveries
- ☐ Neuralstem's patented and proprietary:
 - ☐ Platform Technology
 - ☐ Nature of Cells
 - ☐ Delivery of Cells

☐ IPO 2006

- ☐ CUR chosen as ticker symbol to reflect corporate commitment to research and development of treatments that could lead to cures for neurodegenerative and neuropsychiatric disorders

Neuralstem, Inc.

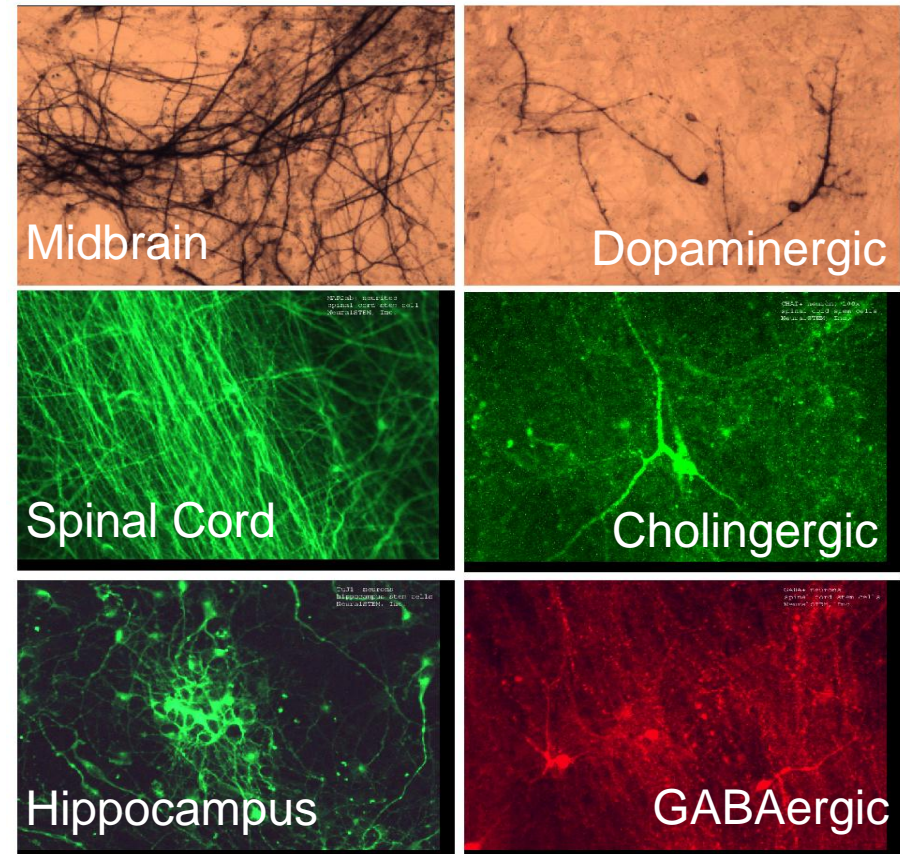
Executive Management

- ❑ Karl Johe, PhD **Co-founder, Chairman of the Board, and Chief Scientific Officer, 1997-present**
 - ❑ Discoverer and developer of Human Neural Stem Cell Technology
 - ❑ Staff Scientist at the NIH Laboratory of Molecular Biology of the National Institute of Neurological Disorders and Stroke in Bethesda, 1993-1997
 - ❑ Post Doctoral, Molecular Genetics, University of California San Francisco; PhD, Biochemistry, Albert Einstein College of Medicine
- ❑ Richard Garr, JD **Co-founder, Director, President and CEO, 1996-present**
 - ❑ Focused on the business of science for 15 years; corporate legal, regulatory and patent experience
 - ❑ Previous corporate and commercial law practice: Beli, Weil & Jacobs, the B&G Companies, and Circle Management Companies
 - ❑ JD, Columbus School of Law, The Catholic University of America; BA, Psychology, Drew University; Co-founder and Director, First Star Foundation; Mid-Atlantic Chapter Co-founder, The Starlight Foundation; Former Honorary Chairman, Brain Tumor Society
- ❑ Thomas G. Hazel, PhD **Vice President, Research, 2008-present**
 - ❑ Previously served as Neuralstem's Stem Cell Discovery Program Director, 2000-2004; Sr. Scientist, 1998-2000
 - ❑ Staff Scientist at the NIH Laboratory of Molecular Biology of the National Institute of Neurological Disorders and Stroke in Bethesda, 1996-1998; IRTA fellow, 1993-1996
 - ❑ PhD, Genetics, University of Illinois College of Medicine
- ❑ John Conron **CFO, 2007-present**
 - ❑ More than 30 years of experience in corporate finance; previous CFO positions included Loral's Cyberstar, Inc., Transworld Telecommunications, and Mercury Communications, the European subsidiary of Cable & Wireless
 - ❑ Certified Public Accountant; BSBA, Accounting, Georgetown University

Neuralstem Technology

Stem Cells of the Brain and the Spinal Cord

- ❑ Platform technology
- ❑ Numerous cell therapy products
 - ❑ Regionally specific CNS stem cells
 - ❑ cGMP manufacturing
- ❑ Patented
 - ❑ Issued and re-affirmed worldwide
- ❑ Fully characterized
 - ❑ Expanded under defined conditions: no animal-derived reagents, serum or feeder cells
 - ❑ Reproducible differentiation: constitutive behavior of cells
 - ❑ Physiologically relevant neurons: 50%



*NEURONAL
Differentiation*

Subtypes

Neuralstem Technology

Published Papers

- ❑ Human neural stem cell grafts in the spinal cord of SOD1 transgenic rats: differentiation and structural integration into the segmental motor circuitry.
 - ❑ Xu L, Ryugo DK, Pongstaporn T, Johe K, Koliatsos VE, Department of Pathology, Division of Neuropathology, The Johns Hopkins Medical Institutions, Baltimore
 - ❑ *The Journal of Comparative Neurology*, 2009 Jun 1;514(4):297-309.
- ❑ Extensive neuronal differentiation of human neural stem cell grafts in adult rat spinal cord.
 - ❑ Yan J, Xu L, Welsh AM, Hatfield G, Hazel T, Johe K, Koliatsos VE, Department of Pathology, Division of Neuropathology, The Johns Hopkins Medical Institutions, Baltimore
 - ❑ *PLoS Medicine*, 2007 Feb;4(2):e39.
- ❑ Combined immunosuppressive agents or CD4 antibodies prolong survival of human neural stem cell grafts and improve disease outcomes in amyotrophic lateral sclerosis transgenic mice.
 - ❑ Yan J, Xu L, Welsh AM, Chen D, Hazel T, Johe K, Koliatsos VE, Department of Pathology, Neuropathology Division, The Johns Hopkins University School of Medicine, Baltimore
 - ❑ *Stem cells (Dayton, Ohio)*, 2006 Aug;24(8):1976-85. Epub 2006 Apr 27.
- ❑ Functional recovery in rats with ischemic paraplegia after spinal grafting of human spinal stem cells.
 - ❑ Cizkova D, Kakinohana O, Kucharova K, Marsala S, Johe K, Hazel T, Hefferan MP, Marsala M, Institute of Neurobiology, Centrum of Excellence, Slovak Academy of Science, Kosice, Soltesovej 4, Slovakia.
 - ❑ *Neuroscience*, 2007 Jun 29;147(2):546-60. Epub 2007 May 23.

Neuralstem Technology

U.S. Patents Issued and Re-affirmed Worldwide

- ❑ U.S. Pat. No. 8,030,492 (October 2011)
 - ❑ Compositions to effect neuronal growth
- ❑ U.S. Application No. 12/939,897 (Allowed July 2011; patent number pending)
 - ❑ Compositions to effect neuronal growth
- ❑ U.S. Pat. No. 7,691,629 (April 2010)
 - ❑ Transplantation of human neural cells for treatment of neurodegenerative conditions
- ❑ U.S. Pat. Nos. 7,560,553 and 7,858,628 (July 2009, December 2010)
 - ❑ Use of fused nicotinamides to promote neurogenesis (div)
- ❑ U.S. Pat. No. 7,544,511 (June 2009)
 - ❑ Stable neural stem cell line methods
- ❑ U.S. Pat. No. 6,284,539 (September 2001)
 - ❑ Method for generating dopaminergic cells derived from neural precursors
- ❑ U.S. Pat. No. 6,040,180 (March 2000)
 - ❑ In vitro generation of differentiated neurons from cultures of mammalian multipotential CNS stem cells
- ❑ U.S. Pat. Nos. 5,753,506 and 6,040,180 (May 1998)
 - ❑ Isolation propagation and directed differentiation of stem cells from embryonic and adult central nervous system of mammals (div)

Neuralstem Cell Therapy Surgical Device

Exclusive Worldwide License

- ❑ Spinal Platform and Floating Cannula
 - ❑ Proprietary breakthrough medical device
 - ❑ Designed specifically by ALS trial neurosurgeon, Nicholas M. Boulis, MD, for the world's first intraspinal delivery of neural stem cells
 - ❑ To be utilized to deliver Neuralstem cells in the spinal cord safely and effectively for myriad diseases and injuries
 - ❑ Neuralstem holds exclusive worldwide license:
 - ❑ Allowed U.S. Patent Application No. 12/418,170 (October 2011)
 - ❑ Spinal Platform and Method for Delivering a Therapeutic Agent to a Spinal Cord Target
 - ❑ Issued & Pending Patents: U.S. Pat. No. 7,833,217 (November 2010); U.S. Application No. 12/913,527
 - ❑ Floating Spinal Cannula and Method of Use

Neuralstem Platform

Cell Therapeutics' Commercialization and Platform Roll-out

Neuralstem Technology Platform



Cell Therapy

Direct Injection /
Transplantation Into
the Spinal Cord or
Brain

Amyotrophic
Lateral Sclerosis

Chronic Spinal
Cord Injury

Chronic Stroke

Huntington's
Disease

Brain Cancer

Ischemic Spastic
Paraplegia

Pharmaceuticals

Small Molecule
Discovery /
Development Enabled
by Proprietary Stem
Cell-based Screening

Major Depressive
Disorder

Bipolar Disorder

Anxiety

Alzheimer's
Disease

PTSD

Schizophrenia



Neuralstem ALS Trial

ALS Phase I Trial Design

- ❑ **Primary Endpoint**
 - ❑ Safety
- ❑ **Secondary Endpoints**
 - ❑ Attenuation of motor function loss
 - ❑ Maintenance of respiratory capacity
 - ❑ Stabilization of ALS functional rating scale
 - ❑ Reduction of spasticity/rigidity if present
 - ❑ Graft survival at autopsy upon mortality
- ❑ **World-Class Clinical Investigators**
 - ❑ Principal Investigator: Eva L. Feldman, M.D., Ph.D., Professor of Neurology & Director A. Alfred Taubman Medical Research Institute of the University of Michigan Medical School; President of American Neurological Association
 - ❑ Site Principal Investigator: Jonathan D. Glass, M.D., Professor of Neurology & Director Emory ALS Center Emory University
 - ❑ Co-Investigator & Neurosurgeon: Nicholas M. Boulis M.D., Assistant Professor Neurosurgery Emory University

Group A: Non-ambulatory

Patients #1 – 3:
Five injections at Lumbar Cord (Unilateral)

Patients #4 – 6:
Ten Injections at Lumbar Cord (Bilateral)

January 2010 – August 2010

Group B/C: Ambulatory - Lumbar

Patients #7 – 9 (Group B):
Five injections at Lumbar Cord (Unilateral)

Patients #10 – 12 (Group C):
Ten Injections at Lumbar Cord (Bilateral)

October 2010 – April 2011

Group D/E: Ambulatory - Cervical

Patients #13 – 15 (Group D):
Five injections at Cervical Cord

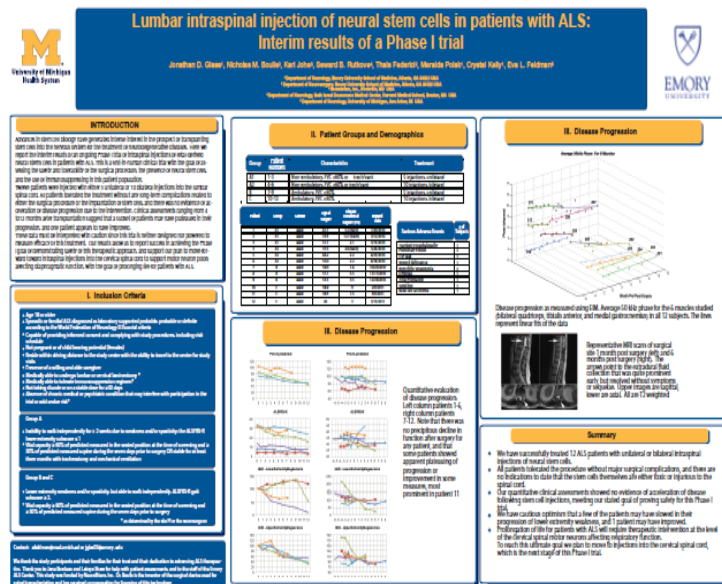
Patients #16 – 18 (Group E):
Five Injections at Cervical Cord

November 2011 – Late 2012

Neuralstem ALS Trial

ALS Phase I Patient Summary

- Poster titled “Lumbar intraspinal injection of neural stem cells in patients with ALS: Interim results of a Phase I trial”
- Presented at American Neurological Association Annual Meeting, September 2011



PATIENT	GROUP	GENDER	AGE AT SURGERY	DISEASE DURATION AT SURGERY (Yrs)	IMPLANT DATE
1	A1	Male	61.7	5.2 (trach)	1/20/2010
2	A1	Male	43.4	12.7 (trach)	3/12/2010
3	A1	Male	51.1	2.1	4/14/2010
4	A2	Male	37.5	2.0 (trach)	5/26/2010
5	A2	Male	66.2	2.2	6/23/2010
6	A2	Male	55.0	2.2	8/18/2010
7	B	Male	59.0	1.6	10/20/2010
8	B	Male	41.1	5.5	11/17/2010
9	B	Male	54.5	3.5	12/29/2010
10	C	Male	48.9	11	2/9/2011
11	C	Male	39.4	1.5	3/9/2011
12	C	Male	65	3	4/13/2011

Neuralstem ALS Trial

ALS Phase I Safety Data: First 12 Patients

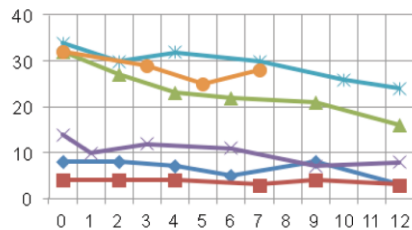
Phase I Data Key Findings:

- ❑ Successfully treated 12 ALS patients with unilateral or bilateral intraspinal injections
- ❑ All patients tolerated the procedure without major surgical complications
- ❑ No indications to date that the stem cells themselves are either toxic or injurious to the spinal cord
- ❑ No evidence of acceleration of disease following stem cell injections
- ❑ Several of the patients may have slowed in their progression of lower extremity weakness, and one patient may have improved

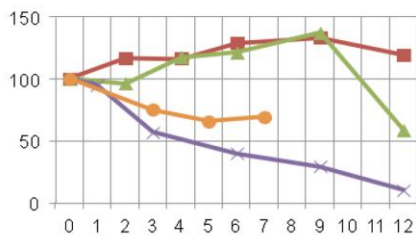
Disease Progression Data

Patients 1 - 6

ALSFRS-R

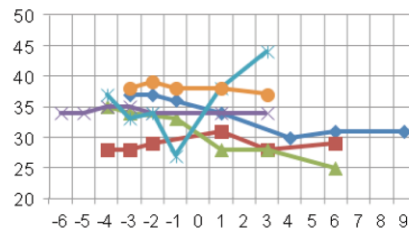


HHD - LowerExtremityMegascors

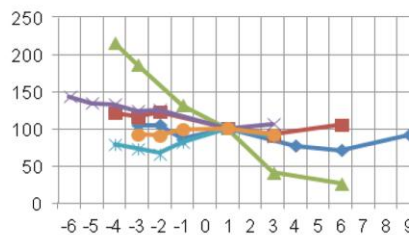


Patients 7 - 12

ALSFRS-R

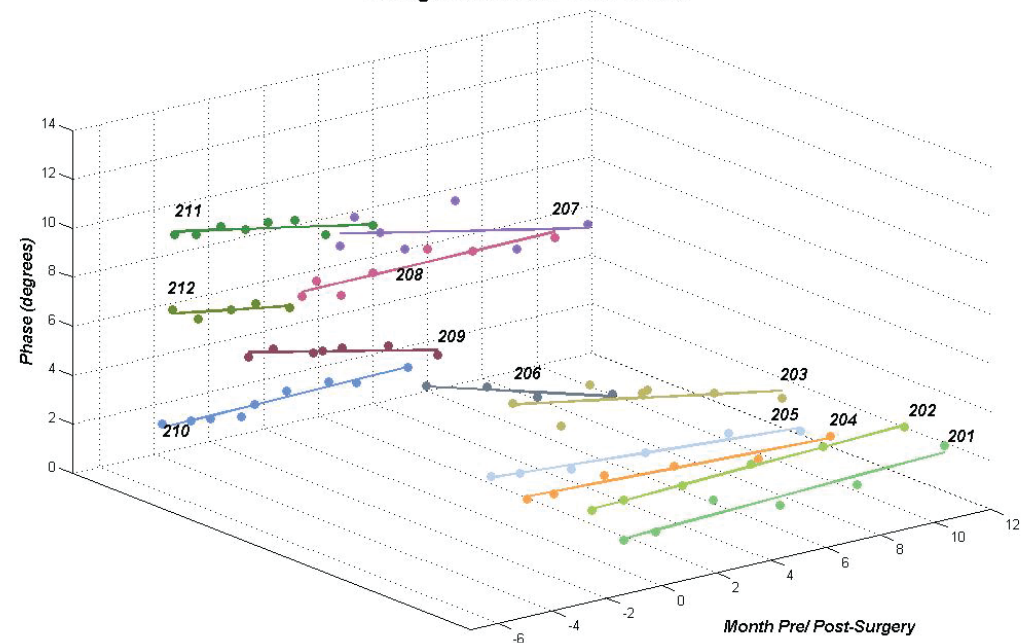


HHD - LowerExtremityMegascors



Disease Progression EIM⁽¹⁾ Measurements of Lower Extremity Muscles

Average 50kHz Phase For 6 Muscles



Neuralstem Cell Therapy Program (U.S.)

ALS Phase I Continuation (Cervical)

- ❑ Continuation of Phase I Clinical Trial
 - ❑ Six patients scheduled to demonstrate the safety of cervical injections
- ❑ Timing
 - ❑ Single center (Emory)
 - ❑ Patients transplanted one per month
 - ❑ First patient transplantation: November 2011
 - ❑ Trial's Safety Monitoring Board review between Patient Groups D and E
 - ❑ Entire 18-patient trial concludes six months after final surgery

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Patients #16 – 18 (Group E):
Five Injections at Cervical Cord

November 2011 – Late 2012

Neuralstem Cell Therapy Program (U.S.)

Additional Indications

☐ Chronic Spinal Cord Injury (cSCI)

- ☐ IND filed August 2010, pending review of safety results from ALS patients
- ☐ Same cells and injection procedure as ALS trial

☐ Chronic Motor Disorders from Stroke

- ☐ Advanced preclinical program at University of Pittsburgh
- ☐ Intracerebral injections at peri-infarct sites through method previously shown to be safe
- ☐ Study planned in patients with chronic paralysis for at least four months

☐ Brain Cancer

- ☐ Engineer Neuralstem's cells to express various anti-cancer agents
- ☐ DOD funded program to develop and engineer neural stem cell technology through \$1.6 M award
- ☐ Goal is to submit therapeutic product for cancerous brain cells to the FDA by 2015

Neuralstem Cell Therapy Program (International)

Cell Therapy Product Status

☐ Neuralstem China: Stroke

- ☐ Trial expected to commence in second half of 2012
- ☐ Wholly owned subsidiary: Neuralstem China 神脑生物医药公司 (Suzhou Neuralstem Biopharmaceutical Company, Ltd.)
- ☐ BaYi Brain Hospital in Beijing, collaborator

☐ India: Spinal Cord Injury (chronic and acute)

- ☐ IND filing expected in 2012
- ☐ Company evaluating potential trial centers and collaborators

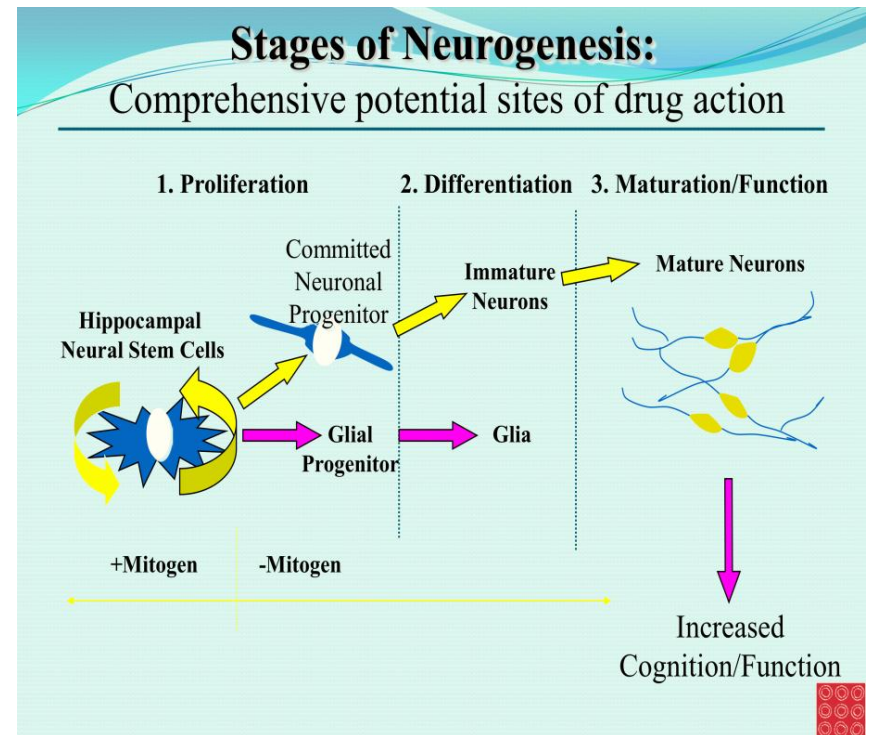
☐ South Korea, Indonesia, Malaysia, Philippines, Singapore and Vietnam

- ☐ Exclusive option agreement with partner CJ Cheil Jedang Corporation for cell therapy products in South Asian countries

Neuralstem Small Molecule Drug Program

First-in-class Neurogenic Small Molecule Drugs

- ❑ U.S. DOD-funded screening platform, viability demonstration, and the discovery of the class of drugs
- ❑ Patents issued for these new neuroregenerative small molecule drugs (first issued 2008)
- ❑ Neuralstem owns 100% of the commercialization rights for the drugs covered by the patents
- ❑ Molecules demonstrate neurogenic activity: the ability to stimulate neurogenesis of normal adult brain cells in the hippocampus



Neuralstem Small Molecule Drug Program

Overview

- ❑ NSI-189
 - ❑ First in this new class of compounds
 - ❑ Characteristics: molecular wt. <400, orally active, excellent brain penetration, key biological activity: enhanced neurogenesis and increased hippocampal volume
 - ❑ Major Depressive Disorder – leading indication
 - ❑ **Product Status:** Phase Ia human safety trial initiated in Feb. 2011
 - ❑ **Mechanism of Action:** Neurogenesis
 - ❑ **Route of Administration:** Oral
 - ❑ **Clinical lot:** 12 kg cGMP completed
 - ❑ **Timeline:** Phase Ia completed in Oct. 2011, and Ib expected to be completed in 3Q12
 - ❑ Other potential indications include:
 - ❑ Alzheimer's Disease
 - ❑ Anxiety
 - ❑ Bipolar Disorder
 - ❑ PTSD-Post-Traumatic Stress Disorder
 - ❑ Schizophrenia
 - ❑ Stroke

BioCentury, The BERNSTEIN REPORT ON BIOBUSINESS

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Product Discovery & Development

Neuralstem's new branch

By Tim Fulmer
Senior Writer

After 14 years spent working on neural stem cell therapies for neurological disorders, Neuralstem Inc. thinks it has found a second way to monetize its research investment. This quarter, the company plans to begin a Phase I trial of its first small molecule therapeutic discovered using the company's CNS stem cell lines.

Neuralstem was founded in 1996 to develop human CNS stem cell lines to treat neurological disorders such as amyotrophic lateral sclerosis (ALS) and spinal cord injury (SCI). The company's lead product, NSI-566RSC, is a human spinal cord-derived stem cell line in Phase I testing to treat ALS.

In 2000, the U.S. Department of Defense's Defense Advanced Research Projects Agency (DARPA) awarded Neuralstem a contract to use the company's human neural stem cell lines to screen for an orally available small molecule with activity in the hippocampus. The objective was to identify compounds that could trigger growth of hippocampal neurons to counteract the stress-induced hippocampal atrophy that is believed to cause impaired cognition and memory in soldiers.

While those screens did turn up a few small molecules that triggered neurogenesis in cultured human hippocampal neural stem cells, DARPA discontinued funding of the research following a change in priorities in the wake of the 9-11 terrorist attacks. Neuralstem set the small molecules aside and returned to moving its stem cell therapy pipeline forward.

Over time, multiple lines of evidence from animal models and patients have suggested a link between impaired growth of hippocampal neural stem cells and neuropsychiatric diseases. In particular, chronic depression has been associated with atrophy and shrinkage of the hippocampus.

Those findings, combined with the receipt of a U.S. patent covering the composition of matter and use of the small molecules to promote neurogenesis to treat CNS diseases, led Neuralstem to revisit the small molecule strategy in 2009.

Neuralstem scientists hypothesized that their small molecules might be able to stimulate growth of new neurons in the hippocampus to treat depression. To test that idea, the company chose NSI-189, the best of four small molecule nicotinamide derivatives at stimulating neurogenesis in cell culture and mice.

NSI-189 is now set to begin a two-part Phase I trial. If the safety endpoints are met in healthy volunteers, the second part will enroll depressed patients for a dose-escalation study. The entire trial is expected to last about one year, CSO and cofounder Karl Johe told BioCentury.

Meanwhile, the company will work on identifying the molecular target of NSI-189.

"Our screens are set up to identify compounds that enhance

the complex cellular process of neurogenesis, which involves a variety of different neural pathways that include many different potential targets. Thus, based solely on those screens, we cannot say what the molecular target of NSI-189 is," Johe said.

He hypothesized NSI-189 might reverse the disease process in depression by "triggering structural changes in the hippocampus, including formation of new synapses and increased hippocampal volume."

If that proves true, Johe said, the improvements achieved with NSI-189 would probably be longer-lasting than those achieved by marketed drugs such as selective serotonin reuptake inhibitors (SSRIs), which transiently alter serotonin levels.

Johe said the small molecule approach is complementary to the company's cell therapies.

"The small molecules would be ideal for triggering growth of endogenous stem cells to treat neuropsychiatric disorders."

Karl Johe, Neuralstem

"The small molecules would be ideal for triggering growth of endogenous stem cells to treat neuropsychiatric disorders, whereas the stem cell therapies are probably more geared toward indications like spinal cord injury," he said. "Looking very far ahead, we might speculate that the two approaches could be used together to treat some disorders — stroke, for example."

"Because the marketed antidepressants are orally active compounds, the invasive

surgical procedures necessary for neural stem cell transplant may seem impractical to doctors and regulatory agencies for most forms of depression," noted CEO Richard Garr.

Garr also thinks NSI-189 could be useful in Alzheimer's disease, as enhancing neurogenesis could lead to improvements in cognition and memory. "Depending on how the depression trial goes, we hope to be able to begin a clinical trial in AD sometime in 2011," he said.

NSI-189 is exclusively licensed from an undisclosed chemistry company that supplied some of the compound libraries originally screened under the DARPA project.

Garr said Neuralstem hopes to partner out the other small molecule nicotinamide derivatives identified by its screen, as the company's resources are sufficient to move only NSI-189 into the clinic.

"We are also interested in partnering out our stem cell discovery platform to identify whole new classes and families of compounds that could treat CNS disorders," he said.

According to Johe, "One area of interest might be multiple sclerosis (MS). Using our stem cell screen, it might be possible to identify compounds that promote differentiation of oligodendrocytes and myelination."

Neuralstem plans to continue to develop and commercialize its stem cell therapy pipeline on its own, Garr said.








COMPANIES & INSTITUTIONS MENTIONED




Neuralstem Inc. (NYSE-A:CUR), Rockville, Md.
U.S. Department of Defense, Washington, D.C.

Try the searchable BioCentury Archives.

Neuralstem, Inc.

Clinical Programs Plan for 2012

	<u>Pre-clin.</u>	<u>Phase I</u>	<u>Phase 2</u>	<u>Comments</u>
<i>Cell Therapy Programs</i>				
ALS				Data expected for patients 13 – 18 in 4Q12
Chronic Spinal Cord Injury				IND approval expected
				IND filing expected
Stroke (Chronic Motor Disorders)				Trials conducted in China, expected to commence in 3-4Q12
<i>Small Molecule Programs</i>				
NSI-189 (Major Depressive Disorder)				Data from Phase Ib trial expected in 3Q12

-  Completed Trials
-  Core U.S. Trials
-  Ex-U.S. Expansion Trials

Neuralstem, Inc.

2012 Catalysts

☐ Ongoing Clinical Trials

☐ ALS

- ☐ Phase I cervical-transplantations completion

- ☐ Phase II trial application

☐ NSI-189

- ☐ Phase Ib trial completion

- ☐ Phase IIa trial application in U.S.

☐ New Clinical Trials

- ☐ NSI-189 Phase II approval

- ☐ cSCI IND approval

- ☐ Stroke Phase I / II / III trials in China

- ☐ Chronic and acute SCI IND filing in India

☐ Business Milestones

- ☐ License of NSI-189 with a Japanese pharmaceutical company for Japanese market