

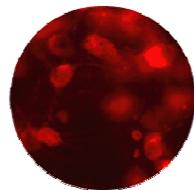
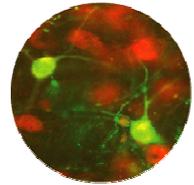


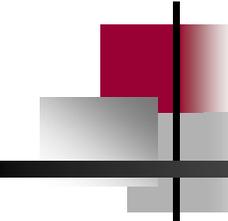
CERE-110 (AAV-NGF) for Alzheimer's Disease

Clinical Update

Raymond T. Bartus, Ph.D.

Senior V.P and COO, Ceregene, Inc.

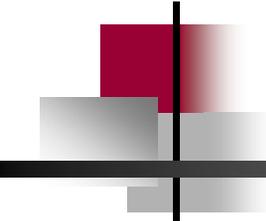




CERE-110 for Alzheimer's Disease

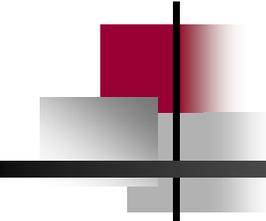
Protocol: CERE-110-01

- A Phase I, Dose –Escalating Study to Assess the Safety and Tolerability of CERE-110 (Adeno-Associated Virus (AAV)-based, Vector –Mediated Delivery of Beta-Nerve Growth Factor [β -NGF]) in Subjects with Mild to Moderate Alzheimer's Disease
- **BB-IND #: 11517**
- **NIH/OBA Protocol #: 0401-623**
- **Principle Investigator**
 - David Bennett, M.D.
Director, Rush Alzheimer's Disease Center



CERE-110-01: Protocol Summary

- **CERE-110** is a genetically engineered, adeno-associated serotype 2 (AAV2) virus with modified DNA that expresses NGF protein.
- **Phase I:**
 - Open-label, dose escalation
 - Two dose levels, 3 subjects each
 - Low dose: 8×10^9 vg/subject
 - High dose: 4×10^{10} vg/subject



CERE-110-01: Objectives

Primary

- To assess the **safety and tolerability** of two different doses of CERE-110 (AAV-NGF) when administered stereotactically to subjects with mild to moderate Alzheimer's disease

Secondary

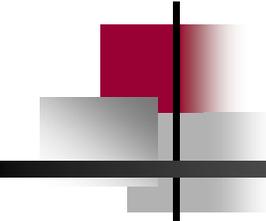
- To evaluate **efficacy** by measurements of cognitive function (ADAS-COG, CDR Scale, ADCS-CGIC and MMSE)
- To evaluate the outcomes of the **Activities of Daily Living** (ADCS-ADL) and quality of life (Dementia Quality of Life-DQoL) scales
- To determine the **biodistribution of CERE-110** in serum and urine by PCR
- To evaluate **immunogenicity** by determining the antibody response to AAV and NGF

CERE-110-01: Cohort 1 (Low Dose)

Subject	Age/Race/ Gender	Dose Date	Exposure (Weeks post-op)
101	64/W/M	27-Jul-04	33
102	73/W/M	7-Dec-04	14
104	64/W/F	11-Jan-05	9

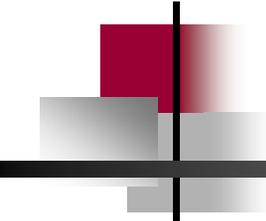
CERE-110-01: Initial Safety Data

- **No** concerning **adverse events**
 - No CERE-110-related adverse events
 - Primarily mild and transient surgery-related events
- Humoral **immune** response **anti-huNGF**
 - None detected at baseline or thereafter
- Humoral **immune** response **anti-AAV2**
 - Mild and transient increase in 1 patient
 - Day 28, only (returned to baseline at 3 and 6mo)
- CERE-110 **biodistribution** in serum and urine
 - All samples **negative**



CERE-110-01: Progress to Date

- Cohort 1 Dosing Completed, January 11, 2005
- DSMB Meeting, March 10, 2005
 - Cumulative review of all data
 - Recommended continuing study as planned
- Cohort 2 First Dose April, 2005
- Enrollment expected to be completed, 1st to 2nd quarter



CERE-110: DSMB Board Members

Kenneth L. Tyler, M.D.
Reuler-Lewin Family Professor
University of Colorado
Neurologist/Viral infection of CNS

G. Yancey Gillespie, Ph.D.
Professor of Surgery
University of Alabama
Neurovirologist/Neuroimmunologist

Robert L. Martuza, M.D.
Chief, Neurosurgery Service
Massachusetts General Hospital
Neurosurgeon

Steven H. Ferris, Ph.D.
Professor of Psychiatry
NYU School of Medicine
Alzheimer's Disease Expert