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

Clinical Update
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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: $8 \times 10^9$ vg/subject
  • High dose: $4 \times 10^{10}$ 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)

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<th>Exposure (Weeks post-op)</th>
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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
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Neurosurgeon

Steven H. Ferris, Ph.D.
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