CERE-110 for Alzheimer’s Disease
RECOMBINANT DNA ADVISORY COMMITTEE (RAC)
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Number of Person in US over age 65

~37 Million
Alzheimer’s Disease is an incurable, slowly progressive, degenerative brain disease that causes:

- Progressive loss of memory and other cognitive abilities
  - memory, language, attention, visuospatial ability
- Behavioral and affective disturbances
  - Psychotic symptoms, eg, hallucinations, misperceptions, delusions; agitation and aggression,
  - Depression
- Motoric
  - Parkinsonian signs, e.g., gait disturbance, and weight loss
- Caregiver distress and lost productivity
- Institutionalization
- Death

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Cholinergic basal forebrain neurons (Nucleus basalis of Meynert)

- 5 treatments approved by FDA
  - first 4 modulate this cholinergic system
- All symptomatic therapy
- None known to affect biology of disease

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CERE-110 for Alzheimer’s Disease


Key Personnel, Rush University Medical Center
David A Bennett, MD – Principal Investigator (RADC)
Zoe Arvanitakis, MD – Co-Principal Investigator (RADC)
Jean Arzbaecher, MS, APN – Nurse Practitioner (CINN)
Roy Bakay, MD - Neurosurgeon (CINN)
Debra Fleischman, PhD – Neuropsychologist (RADC)
Danielle Mele, APN – Nurse Practitioner, Coordinator (RADC)
Gail Ruderman, RPh - Pharmacist
Phase I: Objectives

Primary

• To assess the safety and tolerability of two doses of CERE-110 administered stereotactically to subjects with mild to moderate Alzheimer’s disease.

• To provide preliminary safety data from two doses of CERE-110 to support a Phase II clinical trial.
Phase I: Objectives

Secondary

• To determine the biodistribution of CERE-110 in serum and urine by PCR.
• To evaluate immunogenicity of the AAV vector and NGF by determining the antibody response to AAV and NGF.
• To obtain preliminary clinical outcome data, primarily to power further trials (e.g., ADAS-COG, ADCS-CGIC, CDR, MMSE, ADCS-ADL, Dementia Quality of Life-DQoL scales).
Two dose levels, 3-6 subjects each

- **First dose:** $8 \times 10^9$ vector genomes 3 subjects
  - If no adverse events (grade 3, 4, or SAE), go to Second dose
    - If 1 adverse event, add up to 3 more subjects
    - If no additional adverse events, go to Second dose
- **Second dose:** $4 \times 10^{10}$ vector genomes
- A period of 1 month will transpire between the procedure on each subject.
- Data on all participants will be collected, analyzed, reviewed by an independent Data and Safety Monitoring Board.
Methodology and Procedures

CERE-110 will be administered
  • to the cholinergic neurons in the basal forebrain (Nucleus basalis of Meynert)
  • using 4 injections (10 µL each); two on each side

  • Study duration: 24 months. Subjects are asked to return for annual follow-up thereafter.
Inclusion Criteria

- Males or females (2 years postmenopausal), 50 to 80 years old.
- A diagnosis of Alzheimer’s disease according to the (NINCDS/ADRDA) criteria.
- A score between 16 and 24 on the Mini-Mental State Examination [MMSE].
- On a stable dose of an acetylcholinesterase inhibitor for at least 6 months.
Inclusion Criteria (cont.)

- Good health with no clinically significant medical or psychological conditions.
- Informed Consent document signed by a competent and willing participant.
- In addition, an informed Consent document signed by;
  - a surrogate identified by the participant, or
  - a legally authorized power of attorney for Health Care, or
  - a family member identified according to the Illinois Health Care Surrogate Act.
Exclusion Criteria

- Any significant systemic illness that could put the subject at risk during the study or affect study compliance.
- Subjects who cannot undergo MRI or PET scanning (e.g., claustrophobia, metal implants, pacemaker).
- Subjects who have received any investigational agent or been exposed to investigational devices for 30 days prior to enrollment.
- Subjects with a history of receiving gene transfer products of any kind.

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