LEXEO Therapeutics Announces Positive Initial Data from Ongoing Phase 1/2 Clinical Trial of AAV-based Gene Therapy Candidate LX1001 in Patients with Alzheimer's Disease

– In the initial clinical data from low-dose cohort of the ongoing trial, we observed that LX1001 expressed the protective APOE2 protein in the CNS and decreased core Alzheimer's disease-related biomarkers –

– No serious adverse events reported to date, indicating an emerging favorable tolerability profile –

– Initial data from mid-dose cohort, with additional 12-month follow-up data from low-dose cohort, expected in the second half of 2022 –

NEW YORK – March 2, 2022 (GLOBE NEWSWIRE) – LEXEO Therapeutics (LEXEO), a clinical-stage gene therapy company advancing a deep and diverse pipeline of adeno-associated virus (AAV)-based gene therapy candidates for genetically defined cardiovascular and central nervous system (CNS) diseases, announced today positive initial expression and biomarker data from the low-dose cohort (cohort 1) of its ongoing Phase 1/2 clinical trial of LX1001. LX1001 is an AAV-based investigational gene therapy designed to deliver the protective apolipoprotein *E2 (APOE2)* gene into the CNS of *APOE4* homozygous Alzheimer's disease patients to halt or slow disease progression.

"Initial data have shown meaningful *APOE2* target engagement and declines in cerebrospinal fluid biomarkers, which support our belief that LX1001 has therapeutic potential for *APOE4*-associated Alzheimer's disease," said Jay A. Barth, M.D., Executive Vice President and Chief Medical Officer of LEXEO. "There is an urgent need for new treatments for this devastating condition, and we are extremely grateful to patients, their families and caregivers, as well as investigators who are participating in the trial."

"LX1001 is the lead program in our Alzheimer's disease gene therapy portfolio. These encouraging data support our unique approach to target the genetics of Alzheimer's disease with multiple gene therapy candidates," said R. Nolan Townsend, Chief Executive Officer of LEXEO. "We will continue to advance this clinical stage program and others at the preclinical stage which are on the cutting edge of today's Alzheimer's disease research."

The Phase 1/2 clinical trial is an open-label, dose-ranging study evaluating the safety and tolerability of LX1001 in approximately 15 Alzheimer's disease patients 50 years of age or older who each have two copies of the *APOE4* allele (*APOE4* homozygous patients). The trial consists of three dose-ascending cohorts. Secondary endpoints include evaluation of the conversion of the cerebrospinal fluid (CSF) from the *APOE4* homozygous profile to an *APOE4/E2* profile and CSF biomarkers. This trial is enrolling patients with clinical diagnoses ranging from mild cognitive impairment to mild or moderate dementia. Patients must also have evidence of amyloid plaques and CSF biomarkers consistent with Alzheimer's disease to be included in the trial.

Below are key initial results from four evaluated patients in cohort 1 of the Phase 1/2 clinical trial:

- Expression of the protective *APOE2* protein in the CSF in all evaluated patients with follow-up data at three months or longer (two patients with data through the month-3 visit, and two patients with data through the month-12 visit)
    - Increases in CSF *APOE2* levels from baseline, relative to their respective CSF *APOE4* levels in all evaluated patients with follow-up data at the month-3 visit

- Increases in CSF *APOE2* levels from baseline, relative to their respective CSF *APOE4* levels in the two patients with follow-up data at the month-12 visit
- Declines in CSF core biomarkers total tau (T-tau) and phosphorylated tau (P-tau) protein levels relative to baseline in the two patients with data through the month-12 visit
  - T-tau and P-tau protein levels are widely accepted biomarkers that reflect key pathological changes in the brain of Alzheimer's disease patients, such as accumulation of tau proteins that occur during the neurodegenerative process
- Generally well-tolerated with no serious adverse events to date

Initial data from the mid-dose cohort (cohort 2) and additional 12-month follow-up data from cohort 1 are expected in the second half of the year and will be presented at a future medical conference.

About LX1001
LX1001 is an AAV-based gene therapy candidate designed as a one-time treatment delivering a protective *APOE2* gene into the CNS for the treatment of *APOE4*-associated Alzheimer's disease. LX1001 is designed to express the protective *APOE2* gene in the CNS of *APOE4* homozygous patients to potentially halt or slow the progression of Alzheimer's disease. LX1001 is being evaluated in an ongoing open-label, dose-escalation Phase 1/2 clinical trial and has been granted Fast Track designation by the U.S. Food and Drug Administration.

About *APOE4*-Associated Alzheimer's Disease
Alzheimer's disease is the leading cause of cognitive decline in late adult life and characterized by complex underlying pathology in the CNS. Currently, there are no treatments approved as disease-modifying for Alzheimer's disease. Apolipoprotein E, or APOE, a lipid transport protein, is the major transporter of cholesterol in the brain. The prevalent APOE alleles include *APOE4, APOE3* and *APOE2*, with the *E4* allele increasing risk and reducing the age of onset and the *E2* allele decreasing risk and markedly delaying the age of onset of the disease. *APOE4* homozygous patients, individuals who have two copies of the *E4* allele, are at the highest risk and are approximately 15 times more likely to develop Alzheimer's disease than the general population.

About LEXEO Therapeutics
LEXEO Therapeutics is a New York City-based, clinical-stage gene therapy company focused on addressing some of the most devastating genetically defined cardiovascular and central nervous system diseases affecting both larger-rare and prevalent patient populations. LEXEO's foundational science stems from partnerships and exclusive licenses with leading academic laboratories at Weill Cornell Medical College and the University of California, San Diego, two preeminent institutions on the cutting edge of gene therapy research. LEXEO is advancing a deep and diverse pipeline of AAV-based gene therapy candidates in rare cardiovascular diseases, *APOE4*-associated Alzheimer's disease, and CLN2 Batten disease, and is led by pioneers and experts with decades of collective experience in genetic medicines, rare disease drug development, manufacturing and commercialization. For more information, please visit www.lexeotx.com or LinkedIn.

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