Lexeo Therapeutics Announces Positive Interim Data for LX1001, First-Ever Gene Therapy to Impact the Underlying Genetic Cause of APOE4-Associated Alzheimer's Disease, at the Clinical Trials on Alzheimer's Disease (CTAD) Conference

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Dose-dependent increase in neuroprotective APOE2 expression in all participants with ongoing durability at 12 months

Consistent reductions across CSF tau biomarkers and tau PET in majority of participants

LX1001 well tolerated across all dose cohorts with no reports of amyloid-related imaging abnormalities (ARIA)

Company to host webcast today at 7:00 AM ET

NEW YORK, Oct. 30, 2024 (GLOBE NEWSWIRE) -- Lexeo Therapeutics, Inc. (Nasdaq: LXEO), a clinical stage genetic medicine company dedicated to pioneering treatments for genetically defined cardiovascular diseases and APOE4-associated Alzheimer's disease, today announced positive interim results from the Phase 1/2 study of LX1001 (NCT03634007) for the treatment of APOE4-associated Alzheimer's disease (AD). Treatment with LX1001 led to dose-dependent increases in APOE2 protein expression and improvements in AD-associated tau biomarkers, measures which have been closely correlated with cognitive outcomes. LX1001 also demonstrated a favorable safety profile with no reports of ARIA[1]. The data were presented today in a late-breaking oral presentation at the Clinical Trials on Alzheimer's Disease (CTAD) conference in Madrid, Spain and expand the body of evidence on LX1001 as a potential therapy for the more progressive course of Alzheimer's seen in APOE4 homozygotes.

"APOE4 homozygotes are approximately 15 times more likely to develop Alzheimer's disease than the general population, have faster disease progression, and have an increased risk of ARIA with currently available therapies that can cause serious complications," said Dr. Kim Johnson, Division Chief, Memory Disorders at the Department of Neurology of Duke University School of Medicine and a principal investigator in the Phase 1/2 study. "Today's results suggest the potential of LX1001, which based on available data is well tolerated without reports of ARIA. The study also resulted in notable reductions in tau biomarkers, which suggest a possible effect on Alzheimer's disease pathology."

LX1001 is an AAVrh10-based gene therapy candidate designed to deliver the protective APOE2 allele into the central nervous system of APOE4 homozygous patients, who have two copies of the toxic APOE4 allele. APOE2 is associated with a significantly lower risk of Alzheimer's onset and slower disease progression. In the Phase 1/2 study, which completed enrollment in Q4 2023, fifteen patients with mild cognitive impairment (MCI) or mild or moderate AD were dosed with LX1001 in four dose-ascending cohorts. The study's primary objective was to assess safety and tolerability, with secondary outcomes including cerebrospinal fluid (CSF) APOE2 protein expression and change in tau and amyloid biomarkers.

"In light of the rapid progression of Alzheimer's disease in this population, these data highlight the therapeutic potential of delivering APOE2, which can impact multiple mechanisms of Alzheimer's disease upstream of any specific pathway and thereby meaningfully alter the devastating course of this complex disease," said Dr. Sandi See Tai, Chief Development Officer of Lexeo Therapeutics. "These data are highly encouraging and provide clinical evidence of the unique and targeted mechanism of LX1001 to potentially treat Alzheimer's disease."

The interim Phase 1/2 data include follow-up through 12-months for dose Cohorts 1 through 3 and follow-up through 6-months for dose Cohort 4, demonstrating:

- CSF APOE2 protein expression in all participants, with dose- and time-dependent increases in expression and durability out to 12 months
- Stabilization of amyloid pathology in the majority of participants, with minimal change from baseline in Aß42/40 ratio and amyloid PET
- Consistent reductions across CSF tau biomarkers including CSF T-tau, P-tau181, P-tau217[2] and P-tau231[2], in over two thirds of participants relative to baseline and natural history
- Reductions at 6 months in global tau PET[3] SUVR in 5 of 6 participants and in regional SUVR in a majority of participants across all brain regions
- Participants with moderate AD (n=4) generally demonstrated the most improvement across various biomarker endpoints
- Four SAEs were reported, with three deemed unrelated to treatment and one event of mild-moderate sensorineural hearing loss assessed as possibly related to treatment with repeat audiometry pending.

The Company has initiated engagement with FDA on these data and expects to provide an update on regulatory interactions and further LX1001 development plans in 2025.

Conference Call Information
Lexeo will host a webcast today at 7:00 AM ET to review these data and next steps for the program. To register for and access the conference call and webcast presentation, please visit https://ir.lexeotx.com/news-events/events. The webcast presentation includes slides with further analysis of the LX1001 interim data. The on-demand webcast presentation may be accessed under the News & Events tab in the Investors section of the Company's website, and a replay will be available following the presentation.

About LX1001
LX1001 is an AAVrh10-based gene therapy candidate for the treatment of APOE4-homozygous Alzheimer's disease. Individuals homozygous for APOE4, an allele of the gene APOE, are approximately 15 times more likely to develop Alzheimer's disease than the general population, and it is estimated that there are approximately 900,000 APOE4 homozygous patients with Alzheimer's disease in the United States. Conversely, individuals

homozygous for the APOE allele APOE2 are 40% less likely to develop Alzheimer's disease than the general population. LX1001 is designed to express the protective APOE2 gene in the central nervous system of APOE4 homozygous patients, potentially slowing or halting the progression of Alzheimer's disease. LX1001 has been granted Fast Track designation by the FDA.

About Lexeo Therapeutics
Lexeo Therapeutics is a New York City-based, clinical stage genetic medicine company dedicated to transforming healthcare by applying pioneering science to fundamentally change how genetically defined cardiovascular diseases and APOE4-associated Alzheimer's disease are treated. Using a stepwise development approach, Lexeo is leveraging early proof-of-concept functional and biomarker data to advance a pipeline of cardiovascular and APOE4-associated Alzheimer's disease programs.

Cautionary Note Regarding Forward-Looking Statements
Certain statements in this press release may constitute "forward-looking statements" within the meaning of the federal securities laws, including, but not limited to, our expectations and plans regarding our current product candidates and programs, including statements regarding the potential benefits and safety of LX1001 for the treatment of Alzheimer's disease and the timing for receipt and announcement of data from its clinical trials, and the timing and likelihood of potential regulatory approval. Words such as "may," "might," "will," "objective," "intend," "should," "could," "can," "would," "expect," "believe," "design," "estimate," "predict," "potential," "develop," "plan" or the negative of these terms, and similar expressions, or statements regarding intent, belief, or current expectations, are forward-looking statements. While Lexeo believes these forward-looking statements are reasonable, undue reliance should not be placed on any such forward-looking statements. These forward-looking statements are based upon current information available to the company as well as certain estimates and assumptions and are subject to various risks and uncertainties (including, without limitation, those set forth in Lexeo's filings with the U.S. Securities and Exchange Commission (SEC)), many of which are beyond the company's control and subject to change. Actual results could be materially different from those indicated by such forward looking statements as a result of many factors, including but not limited to: risks and uncertainties related to global macroeconomic conditions and related volatility; expectations regarding the initiation, progress, and expected results of Lexeo's preclinical studies, clinical trials and research and development programs; the unpredictable relationship between preclinical study results and clinical study results; delays in submission of regulatory filings or failure to receive regulatory approval; liquidity and capital resources; and other risks and uncertainties identified in Lexeo's Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2024, filed with the SEC on August 12, 2024, and subsequent future filings Lexeo may make with the SEC. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Lexeo claims the protection of the Safe Harbor contained in the Private Securities Litigation Reform Act of 1995 for forward-looking statements. Lexeo expressly disclaims any obligation to update or alter any statements whether as a result of new information, future events or otherwise, except as required by law.

[1] Amyloid-related imaging abnormalities (ARIA) refer to MRI findings observed in patients receiving anti-amyloid therapies for Alzheimer's disease. ARIA is most commonly observed as brain swelling and/or microhemorrhages and has a higher incidence in patients who are APOE4 allele carriers.

[2] CSF P-tau217 and P-tau231 collected only in Cohorts 2, 3 and 4; all Cohort 4 samples, including 6 month and 12 month, pending analysis

[3] Tau PET performed only in Cohorts 3 and 4; Cohort 4 12-mth visits pending analysis

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