Lexeo Therapeutics Announces Positive Interim Phase 1/2 Data for LX2006 in Friedreich Ataxia Cardiomyopathy Supporting Advancement to Registrational Study

April 7, 2025

Participants with abnormal left ventricular mass index (LVMI) at baseline achieved 25% mean reduction in LVMI by 12 months or sooner

Clinically meaningful improvements in majority of participants across cardiac biomarkers and functional measures

All SUNRISE-FA participants achieved meaningful increases in frataxin expression at 3-months post treatment; 115% average cardiac frataxin expression increase in high dose cohort, demonstrating dose response

Frataxin expression and LVMI improvement exceed co-primary target thresholds for planned registrational study

LX2006 generally well tolerated with no signs of complement activation or other immunogenicity to date

Company to host webcast today at 8:00 AM ET

NEW YORK, April 07, 2025 (GLOBE NEWSWIRE) -- Lexeo Therapeutics, Inc. (Nasdaq: LXEO), a clinical stage genetic medicine company dedicated to pioneering novel treatments for cardiovascular diseases, today announced positive interim data across all dose cohorts of LX2006 for the treatment of Friedreich ataxia (FA) cardiomyopathy. In both the Lexeo-sponsored SUNRISE-FA Phase 1/2 clinical trial (NCT05445323) and the Weill Cornell Medicine investigator-initiated Phase 1A trial (NCT05302271), treatment with LX2006 was associated with clinically significant improvements in cardiac biomarkers and functional measures, and increased frataxin protein expression was observed in all participants with cardiac biopsies.

“These data provide strong evidence that LX2006 is acting as a beneficial disease-modifying treatment candidate, supporting its continued development as a potential first- and best-in-class therapy for FA cardiomyopathy,” said Dr. Eric Adler, Chief Medical Officer and Head of Research at Lexeo Therapeutics. “Cardiac dysfunction is the leading cause of death for people with FA, and the clinical and functional improvements we’ve observed across these studies could be transformational to the standard of care. Participants have experienced clinically meaningful improvements across multiple measures, as well as increased frataxin expression in the heart, all of which underscore the potential of LX2006 to positively impact outcomes for people with FA cardiomyopathy.”

“We believe these data show LX2006 exceeding the thresholds aligned with the U.S. Food and Drug Administration (FDA) to support accelerated approval in the planned registrational study,” said Dr. Sandi See Tai, Chief Development Officer at Lexeo. “We are eager to advance this promising candidate as quickly as possible to support adults and children living with the devastating and fatal impacts of FA cardiomyopathy, and we expect to initiate a registrational study by early 2026. I would like to thank the participants, caregivers, and investigators who have helped to advance this important research.”

Lexeo has obtained alignment with the FDA on key parameters related to the LX2006 planned registrational study, including co-primary endpoints of LVMI, with a target threshold of >10% improvement at 12 months, and frataxin expression, with a target of any increase from baseline at three months.

Trial Design
SUNRISE-FA and the Weill Cornell Medicine investigator-initiated trial are 52-week, ascending dose, open-label trials evaluating the safety and preliminary efficacy of LX2006 in participants with FA cardiomyopathy. LX2006 is administered as a one-time intravenous infusion. While the two studies share similar designs, myocardial biopsies were conducted only in the SUNRISE-FA Phase 1/2 trial. Evidence of cardiomyopathy is required for study inclusion but participants vary in the severity of baseline hypertrophy as measured by LVMI. As of the data cutoff on March 25, 2025, a total of 16 participants have been dosed across the two studies, six of whom had cardiac hypertrophy with abnormal LVMI (at least two standard deviations above the mean in healthy volunteers). SUNRISE-FA enrollment was completed in Q4 2024.

Interim Clinical Update (n=12 participants with ≥ 6-months of follow-up)

Left ventricular mass index (LVMI):

- Among participants with abnormal baseline LVMI (a key inclusion criteria for planned registrational study; n=6):
  - 5 of 6 participants achieved >10% improvement by 12-month visit or sooner
  - 5 of 6 participants achieved LVMI measurements within the normal range as of latest visit
  - 27% mean improvement in LVMI as of latest visit
  - 25% mean improvement in LVMI by 12-month visit or sooner
  - Participants treated in Cohorts 2 and 3 (mid- and high-dose) demonstrate greater, dose-dependent improvement at earlier time points relative to Cohort 1 (low-dose)
- Among participants with normal baseline LVMI (n=6), the majority demonstrated LVMI improvement or stabilization over time

Secondary cardiac biomarkers, functional measures and patient-reported outcomes:

- 10 of 12 participants achieved reduction in lateral wall thickness (LWT) at latest visit
- 11 of 12 participants achieved >25% reduction in high-sensitivity troponin I at latest visit
- Majority of participants showed improvements across functional measures including the modified Friedreich Ataxia Rating Scale (mFARS) and Kansas City Cardiomyopathy Questionnaire (KCCQ-12)

Cardiac frataxin expression (assessed in SUNRISE-FA trial only: n=8):

- All participants achieved increases in frataxin protein expression at 3 months
- Dose-dependent increases observed across cohorts on average, with 115% mean increase in Cohort 3 (n=4)

Interim Safety Update (n=16 participants)

- Treatment with LX2006 has been generally well tolerated with no Grade 3+ SAEs to date
- No signs of complement activation or other immunogenicity
- No signs of frataxin over-expression observed in cardiac tissue
- No participants discontinued from either study
- One previously disclosed, possibly treatment-related Grade 2 event of asymptomatic myocarditis observed one year after dosing

Registrational Study and Next Steps

- In Q2 2025, Lexeo expects to begin enrollment in a prospective natural history study serving as a concurrent external control arm for the registrational study
- Expect to initiate registrational study by early 2026 with a potential efficacy readout in 2027
- Registrational study will assess co-primary endpoints of frataxin protein expression and LVMI

Corporate Webcast Details
Lexeo Therapeutics will host a webcast at 8:00 AM ET today, April 7, 2025. Analysts and investors can participate by accessing the webcast live on the News & Events page in the Investors section of Lexeo's website, www.lexeotx.com. The webcast will be archived on the company's website following completion of the call.

About LX2006
LX2006 is an AAV-based gene therapy candidate for the treatment of FA cardiomyopathy, the leading cause of death in individuals with FA affecting approximately 5,000 people in the United States. LX2006 is designed to target the cardiac manifestations of FA by delivering a functional frataxin gene to promote the expression of the frataxin protein and restore mitochondrial function in myocardial cells. LX2006 has been granted Rare Pediatric Disease designation, Fast Track designation, Orphan Drug designation and Regenerative Medicine Advanced Therapy designation by the FDA for the treatment of FA cardiomyopathy, and orphan medicinal product designation by the European Commission.

About Lexeo Therapeutics
Lexeo Therapeutics is a New York City-based, clinical stage genetic medicine company dedicated to reshaping heart health by applying pioneering science to fundamentally change how cardiovascular diseases are treated. The Company is advancing a portfolio of therapeutic candidates that take aim at the underlying genetic causes of conditions, including LX2006 for the treatment of Friedreich ataxia (FA) cardiomyopathy, LX2020 for the treatment of plakophilin-2 (PKP2) arrhythmogenic cardiomyopathy, and others in devastating diseases with high unmet need.

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, Lexeo's expectations and plans regarding its current product candidates and programs 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 Annual Report on Form 10-K for the annual period ended December 31, 2024, filed with the SEC on March 24, 2025 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.

Media Response:
Media@lexeotx.com

Investor Response:
Carlo Tanzi, Ph.D.
ctanzi@kendallir.com