# Lexeo Therapeutics Announces Positive Interim Phase 1/2 Clinical Data of LX2006 for the Treatment of Friedreich Ataxia Cardiomyopathy

July 15, 2024

*Achieved mean reduction in left ventricular mass index (LVMI) of 11.4% at 12 months and 18.3% at 18 months in participants with elevated LVMI at baseline*

*>10% reduction in LVMI at 12 months in 75% of participants with elevated LVMI at baseline*

*Sustained and consistent improvements in other key measures of cardiac status, including left ventricular wall thickness and troponin I, in majority of participants at 12 months*

*Increased post-treatment frataxin expression above baseline in all participants evaluated via myocardial biopsy to date*

*LX2006 was well tolerated with no treatment-related serious adverse events to date; proceeding to Cohort 3 in SUNRISE-FA, with one participant dosed in this cohort to date*

*Company to host webcast today at 8:00 AM ET*

NEW YORK, July 15, 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 data of LX2006 for the treatment of Friedreich ataxia (FA) cardiomyopathy. Across both the Lexeo SUNRISE-FA Phase 1/2 clinical trial (NCT05445323) and the Weill Cornell Medicine investigator-initiated Phase 1A trial (NCT05302271), LX2006 was well tolerated with no treatment-related serious adverse events, and clinically meaningful improvements in cardiac biomarkers were observed with increasing improvement over time.

"We are very encouraged by these data and the potential of LX2006 to treat FA cardiomyopathy, a devastating and fatal condition with no currently approved therapies," said Dr. Eric Adler, Chief Medical Officer and Head of Research at Lexeo Therapeutics. "Based on the favorable safety profile and clinical benefits observed to date, we are excited to explore expedited clinical development of LX2006, including potential for accelerated approval of this possibly life-saving treatment."

"The interim data shared today demonstrate clinically meaningful improvements across multiple cardiac biomarkers of hypertrophy, a hallmark of FA cardiomyopathy," said Dr. Sandi See Tai, Chief Development Officer at Lexeo. "Together with the increases in frataxin protein expression observed in SUNRISE-FA cardiac biopsies to date, these results further highlight the potential of LX2006 to positively impact outcomes for people with FA cardiomyopathy. I would like to thank the participants, caregivers, and investigators participating in these trials who have helped to achieve this important milestone."

FA cardiomyopathy is a devastating, rare, and progressive disorder caused by loss of function mutations in the frataxin gene. Thus far in participants in the SUNRISE-FA trial with cardiac biopsies, low levels of frataxin have been found in the heart at baseline, estimated to be 2% or less of normal. In terms of clinical presentation, FA cardiomyopathy is typically characterized by left ventricular hypertrophy ultimately progressing to heart failure, and cardiac dysfunction is the cause of death in up to 80% of individuals with FA. A new natural history subset analysis conducted by Lexeo showed elevated left ventricular mass index (LVMI) in adults with FA cardiomyopathy, and LVMI remained stable or increased with age without spontaneous improvement. Elevated LVMI is an indicator of left ventricular hypertrophy and correlated with mortality in multiple cardiovascular conditions including FA cardiomyopathy.

**Interim Safety Results**

- LX2006 was well tolerated with no treatment-related serious adverse events to date in either study
- No signs of complement activation or other immunogenicity observed
- No cardiac or hepatic safety signals observed
- All adverse events were transient and resolved
- No participants discontinued from either study

**Interim Clinical Results (from 8 participants with ≥ 6-months of follow-up)**

- Left ventricular mass index (LVMI): Of participants with elevated LVMI at baseline, 75% achieved >10% reduction at 12 months (n=4). Of all participants, 50% achieved >10% reduction in LVMI at 12 months (n=6).
    - Among the participants with elevated LVMI at baseline, mean reduction in LVMI was 11.4% at 12 months (n=4) and 18.3% at 18 months (n=2).
- Left ventricular (LV) lateral wall thickness: wall thickening, an early indicator of left ventricular hypertrophy, was reduced by 13.6% on average in all participants at 12 months (n=6).
- High-sensitivity Troponin I (hsTnI): troponin I, a biomarker of myocardial injury, was reduced by 53.3% on average in all participants at 12 months (n=5).
- Frataxin protein expression evaluated via myocardial biopsy: observed increased frataxin levels compared to baseline following treatment with LX2006 in all participants evaluated to date utilizing two distinct measurements:
    - LCMS: frataxin increase observed in 3 of 3 evaluable participants.
    - IHC: frataxin increase observed in 2 of 2 evaluable participants.

**Dosing Update and Next Steps**

- As of July 15, 2024, 13 participants dosed to date across two trials:
  - Cohort 1 ($1.8x10^{11}$vg/kg): n=6
  - Cohort 2 ($5.6x10^{11}$ vg/kg): n=6
  - Cohort 3 ($1.2x10^{12}$ vg/kg): n=1
- SUNRISE-FA independent Data and Safety Monitoring Board endorsed proceeding to Cohort 3 dose level ($1.2x10^{12}$vg/kg). This cohort has started enrollment with 1 participant dosed to date and will include at least 3 participants.
- The Weill Cornell investigator-initiated trial is currently enrolling in Cohort 2.
- Lexeo expects to share further details of these interim results, including an additional cardiac biopsy from Cohort 2, at a scientific conference in Fall 2024.

**Corporate Webcast Details**
Lexeo Therapeutics will host a webcast at 8:00 AM ET today, July 15, 2024. Analysts and investors can participate by accessing the webcast live here or 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 the completion of the call.

**About the Clinical Studies**
SUNRISE-FA is a Lexeo-sponsored, multicenter, 52-week, open-label trial evaluating the safety and preliminary efficacy of LX2006 in people who have FA cardiomyopathy, with three ascending-dose cohorts. Investigators at Weill Cornell Medicine are conducting a Phase 1A study of AAVrh.10hFXN, known as LX2006 at Lexeo, in a single-site, 52-week, open-label trial evaluating the safety and preliminary efficacy in people who have FA cardiomyopathy, in two ascending-dose cohorts with five participants per cohort.

**About LX2006**
LX2006 is an AAV-based gene therapy candidate delivered intravenously for the treatment of FA cardiomyopathy, the most common cause of mortality 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. In preclinical studies, LX2006 reversed the cardiac abnormalities in FA disease models and showed improvement in cardiac function and survival while demonstrating a favorable safety profile. The FDA has granted Rare Pediatric Disease designation, Fast Track designation, and Orphan Drug designation to LX2006 for the treatment of FA cardiomyopathy.

**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 of LX2006 for the treatment of Friedreich ataxia cardiomyopathy 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 March 31, 2023, filed with the SEC on May 9, 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.

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