Lexeo Therapeutics Announces Positive Interim Phase I/II Data for LX2020 for the Treatment of PKP2-Associated Arrhythmogenic Cardiomyopathy

January 12, 2026

LX2020 generally well tolerated across ten participants with no clinically significant complement activation

LX2020 transduction, transcription, and increased protein expression observed across participants with dose-dependent response; mean increase in PKP2 protein of 93% in low-dose cohort and 162% in high-dose cohorts

Arrhythmia burden stabilized or improved in majority of participants with dose-dependent response in non-sustained ventricular tachycardia and premature ventricular contractions

Company to host webcast today at 8:00 AM ET / 5:00 AM PT

NEW YORK, Jan. 12, 2026 (GLOBE NEWSWIRE) -- Lexeo Therapeutics, Inc. (Nasdaq: LXEO), a clinical stage genetic medicine company dedicated to pioneering novel treatments for cardiovascular diseases, today announced preliminary data from the HEROIC-PKP2 Phase I/II clinical trial of LX2020 for the treatment of PKP2-associated arrhythmogenic cardiomyopathy (PKP2-ACM). Across dose cohorts, LX2020 was generally well tolerated and led to robust transduction, increased PKP2 protein expression, and clinically meaningful improvement or stabilization in measures of arrhythmia burden in the majority of participants.

“These interim data from ten participants reinforce the favorable safety profile of LX2020 and demonstrate promising trends in transduction, protein expression, and reduction in arrhythmia burden at the high dose,” said R. Nolan Townsend, Chief Executive Officer of Lexeo Therapeutics. “We are encouraged by these preliminary results and look forward to advancing development of LX2020 given its therapeutic potential and ability to address the underlying cause of cardiac dysfunction and disease progression in PKP2-ACM.”

LX2020 Interim Update

Ten participants have been dosed in the HEROIC-PKP2 Phase I/II clinical trial, including three participants in Cohort 1 at the low dose ($2x10^{13}$ vg/kg) and seven participants in Cohorts 2 and 3 at the high dose ($6x10^{13}$ vg/kg). Safety data are summarized for all ten participants dosed; efficacy data are inclusive of those participants with at least 6 months of follow-up as of the January 7, 2026 data cutoff date. Cardiac biopsy data are available for seven participants, as one participant in Cohort 1 declined post-dose biopsy.

Interim Safety Update (n=10)

- LX2020 generally well tolerated across ten participants dosed
- No clinically significant complement activation
- Elevations in liver function tests (LFT) observed in five participants at the high dose, treated successfully with re-introduction of low-dose prednisone in three participants and increased prednisone and sirolimus in two participants per the trial protocol. All elevations resolved without complication, hospitalization or other treatment
- No participants discontinued from the HEROIC-PKP2 Phase I/II study
- One previously disclosed Grade 3 serious adverse event of sustained ventricular tachycardia (VT) was observed three months after dosing in a single participant at the high dose and assessed as possibly treatment related. This event is consistent with the natural course of PKP2-ACM and its known clinical manifestations. The participant was successfully treated with anti-arrhythmic medication and discharged with no additional intervention required

PKP2 Transduction and Expression (n=7 with post-treatment cardiac biopsies at 3 months)

- Mean increase in PKP2 protein expression of 93% in the low-dose cohort (n=2) and 162% in the high-dose cohorts (n=5), assessed by western blot
- Mean exogenous mRNA of 7.9E+04 copies per microgram of nucleic acid in the low-dose cohort (n=2) and 2.7E+05 copies per microgram in the high-dose cohorts (n=5)
- Mean vector copy number (VCN) of 1.5 in the low-dose cohort (n=1) and 3.3 in the high-dose cohorts (n=5); insufficient cardiac biopsy tissue available for participant 1 in low-dose cohort for VCN analysis
- Appropriate PKP2 colocalization observed at cardiac intercalated discs via immunofluorescence staining

Clinical Data (n=8 with ≥ 6 months of follow up)

- Non-sustained ventricular tachycardia (NSVT) reduced or stabilized in the majority of participants; 22% mean improvement in high-dose cohorts at latest visit (n=5)
- Premature ventricular contractions (PVCs) reduced or stabilized in the majority of participants; 14% mean improvement in high-dose cohorts at latest visit (n=5)
- 4 of 5 participants in high-dose cohorts report improvement relative to baseline on the Patient Global Impression of Change (PGIC) scale, a patient-reported outcome measure
- Participants stable across other clinical measures including QRS duration, T-wave inversion, right ventricular ejection

fraction (RVEF) and New York Heart Association (NYHA) Class

Next Steps

- HEROIC-PKP2 enrollment completed in Q4 2025; biopsy results pending for participants 9 and 10
- 12-month data available for all high-dose participants in Q4 2026
- Regulatory engagement expected in 2026

Corporate Webcast Details
Lexeo Therapeutics will host a webcast at 8:00 AM ET / 5:00 AM PT today, January 12, 2026. 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 the call.

About LX2020
LX2020 is an AAV-based gene therapy candidate for the treatment of plakophilin-2-associated arrhythmogenic cardiomyopathy (PKP2-ACM). Mutations in the PKP2 gene are the most common genetic cause of ACM, responsible for approximately 50% of cases and estimated to affect approximately 60,000 people in the United States. PKP2 deficiency in ACM can lead to myocardial cell death, fibrosis, heart dysfunction, rhythm abnormalities, and sudden cardiac death. LX2020 is designed to systemically deliver a functional, full-length PKP2 gene within an adeno-associated viral capsid, AAVrh10, to cardiomyocytes to restore the desmosomal complex and cell-to-cell adhesion. LX2020 is being evaluated in the single-arm, open-label, multi-center HEROIC-PKP2 Phase I/II clinical trial (NCT06109181). LX2020 has been granted Orphan Drug and Fast Track designations by the FDA.

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 in Friedreich ataxia (FA) cardiomyopathy, LX2020 in 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 anticipated benefits of its current product candidates. 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: 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 September 30, 2025, filed with the SEC on November 5, 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:
Ashley Kaplowitz
akaplowitz@lexeotx.com