Message to the Arrhythmogenic Cardiomyopathy Community

January 14, 2026

Dear Advocacy Partners and ACM community members,

Earlier this week, we were pleased to share positive interim clinical data for LX2020, our investigational gene therapy for the treatment of arrhythmogenic cardiomyopathy associated with mutations in the *PKP2* gene (PKP2-ACM). This update included data from 10 participants treated in the Lexeo-sponsored HEROIC-PKP2 Phase 1/2 clinical trial, including 8 participants with at least 6 months of clinical follow up in the trial. 3 participants were treated with a lower dose of LX2020, while 7 received a higher dose. We are excited to share this update for our program, and the full press release can be found here on the Lexeo website.

Highlights include:

- LX2020 has been generally well tolerated by the 10 study participants. Last fall, Lexeo reported one participant had a serious adverse event (SAE) of sustained ventricular tachycardia (VT) which was considered possibly treatment related. The SAE was treated successfully with anti-arrhythmic medication and has since been resolved without other complications.
    - 5 participants experienced increased levels in liver function tests, which can occur following any gene therapy treatment. All increases were treated successfully with appropriate medications and have since been resolved without other complication or hospitalization
- 3 months after gene therapy treatment, all study participants showed evidence of LX2020 treatment reaching the heart when looking at LX2020 levels with heart biopsy (n=7).
    - The average increase in PKP2 protein expression was 93% in the low-dose cohort (n=2) and 162% in the high-dose cohorts (n=5) compared to beginning expression levels.
    - One participant declined the post-treatment biopsy, and biopsy results from the last two participants treated are still pending.
- Premature ventricular contractions (PVCs), a type of arrythmia, were reduced or stable in the majority of participants at their latest follow up visit (n=8), with a 14% improvement on average among participants treated with the LX2020 high dose (n=5)
- Non-sustained ventricular tachycardia (NSVT) events, a more severe type of arrythmia, were reduced or stable in the majority of participants (n=8), with a 22% improvement on average among participants treated with the LX2020 high dose (n=5)
- 4 of 5 participants treated with the LX2020 high dose reported feeling improvement relative to baseline on the Patient Global Impression of Change (PGIC) scale, a questionnaire designed to assess patient perceptions about their condition
- Participants were stable across other clinical measures related to ACM

Next steps for LX2020:

- Enrollment was completed last fall for the Phase 1/2 HEROIC-PKP2 study; no additional participants will be enrolled for treatment at this time
- More clinical and heart biopsy data will be available from this study by the end of 2026, once all participants reach at least one year of follow-up

- Lexeo expects to meet with the Food and Drug Administration (FDA) in 2026 to discuss these data and potential next steps in terms of future studies in PKP2-ACM

For more information or any questions, please contact clinicaltrials@lexeotx.com. We thank our study investigators and the courageous trial participants and caregivers who have helped us get to this point. We appreciate your partnership as we work to help address the unmet need in PKP2-ACM.

The Lexeo Team