Message to the Friedreich Ataxia Community

October 7, 2025

Dear Advocacy Partners and FA community members,

This morning, we were pleased to share positive interim clinical data for LX2006, our investigational gene therapy, that includes both cardiac and neurological outcome measures. LX2006 (AAVrh10hFXN) is currently being studied in the Lexeo-sponsored SUNRISE-FA Phase 1/2 clinical trial and the Weill Cornell Medicine investigator-initiated Phase 1A trial for the treatment of Friedreich ataxia cardiomyopathy.

LX2006 aims to treat the root cause of Friedreich ataxia by delivering the *FXN* gene to cells in order to increase frataxin protein levels, which is needed for organs and tissues to function properly. While LX2006 is intended to be delivered to heart cells, it is possible for the gene therapy to go to other cells in the body. Both trials collected information on the modified Friedreich Ataxia Rating Scale (mFARS) scores to see if there is any neurological effect. This latest update included data from 16 participants with at least 6 months of follow-up across the two trials.

We are thrilled to share this exciting update for our program, which we believe supports advancement towards a future marketing application.

The full press release can be found here on the Lexeo website.

Highlights include:

- Participants who began the trial with an abnormal or increased left ventricular mass index (LVMI) (n=6) experienced an average improvement of 18% within 6 months and 23% within 12 months of treatment. LVMi is a measure of the size and thickness of the heart. An abnormally thick heart can lead to serious heart complications, and reducing LVMi can potentially improve health outcomes

- 11 of 16 participants had reduced or stable mFARS scores at their latest visit, compared to baseline. Without any treatment, natural history suggests that most people would experience an increase in mFARS score of 1-2 points per year[1]. A 2.0-point mean improvement in mFARS from baseline at the latest visit was seen across all 16 participants with at least 6-months of follow-up. This shows clinically meaningful improvement in the mFARS, which is indicative of slowed disease progression and improved function.

- LX2006 continues to be generally well tolerated by study participants, with no signs of clinically significant over-activation of the immune system (complement activation) and no significant elevations in liver function tests. Last fall, Lexeo reported one participant had an adverse event of asymptomatic myocarditis, one year after dosing which was considered to be possibly related to the study treatment. This individual continues to be monitored. Expert opinion has suggested that the individual may be experiencing intermittent episodes of myocarditis on top of progression of FA cardiomyopathy.

- Lexeo has shared these data with the FDA, and the FDA is open to considering a development approach that could potentially accelerate LX2006 approval.

Next steps for the LX2006 program:

We are excited to continue testing LX2006 in the next phase of our clinical program.

- Lexeo plans to start our registrational or pivotal study in the first half of 2026. This will be an interventional trial (i.e., participants will be given the investigational gene therapy LX2006). We will provide updates to this community on all ongoing and future trials.

- Our CLARITY-FA natural history study (LX2006-02) is currently enrolling. The goal of this natural history study is to learn about how heart disease develops and worsens in individuals with FA.
    - Information gained from participation in this study will provide valuable data about heart disease in FA and will help advance our gene therapy research.
    - It is important to note that participants in the CLARITY-FA natural history study will not receive any investigational study drug (i.e., gene therapy).

- For more information on the CLARITY-FA trial, visit https://trials.lexeotx.com
- For any additional 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 our partnership with the Friedreich ataxia community as we work to help address the devastating effects of this disease and unmet need in Friedreich ataxia cardiomyopathy.

The Lexeo Team

1. https://onlinelibrary.wiley.com/doi/10.1002/acn3.332