

An Update on Friedreich Ataxia Cardiomyopathy Gene Therapy Clinical Programs

Euro-Ataxia Patient Conference
October 28, 2025



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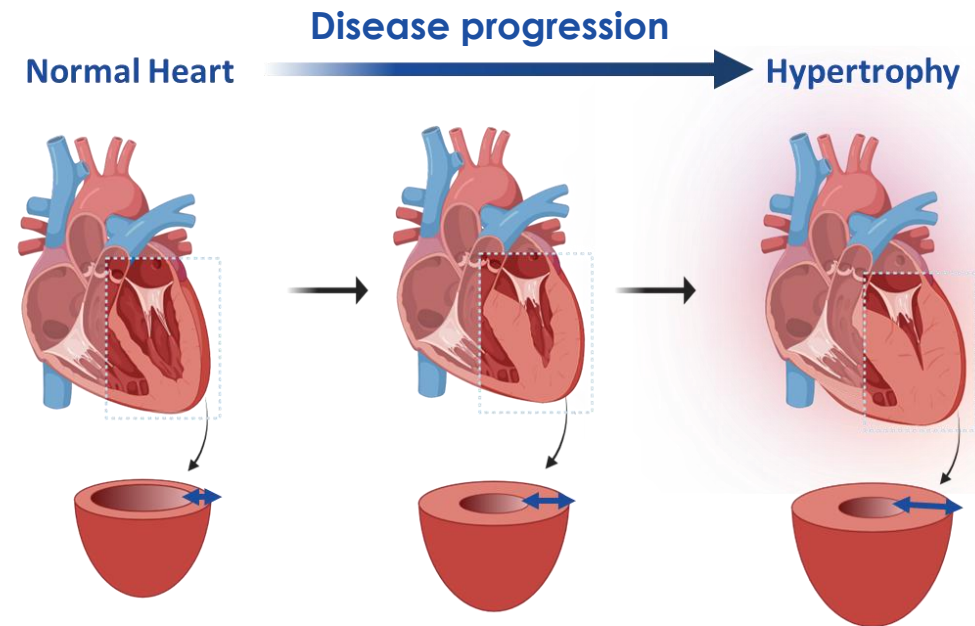
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Why Does the Heart Matter in Friedreich Ataxia (FA)?

Heart disease is the leading cause of death in people with FA

Without frataxin protein...

- The mitochondria in heart cells do not work properly, and the heart has to work harder to make up for it
- This added stress on the heart leads to the walls of the heart to thicken (**hypertrophy**), which can result in a “heavy heart”
- This can also cause the heart to become stiff and less flexible, making it harder for the heart to pump blood
 - This is known as heart muscle disease, or **cardiomyopathy**
- **Up to 80% of people with Friedreich ataxia develop cardiomyopathy**

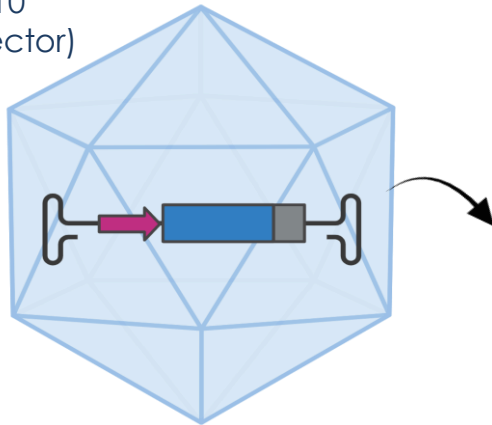


Follow Your Heart

Having a cardiologist as a part of your care team is important to monitor and understand your heart health

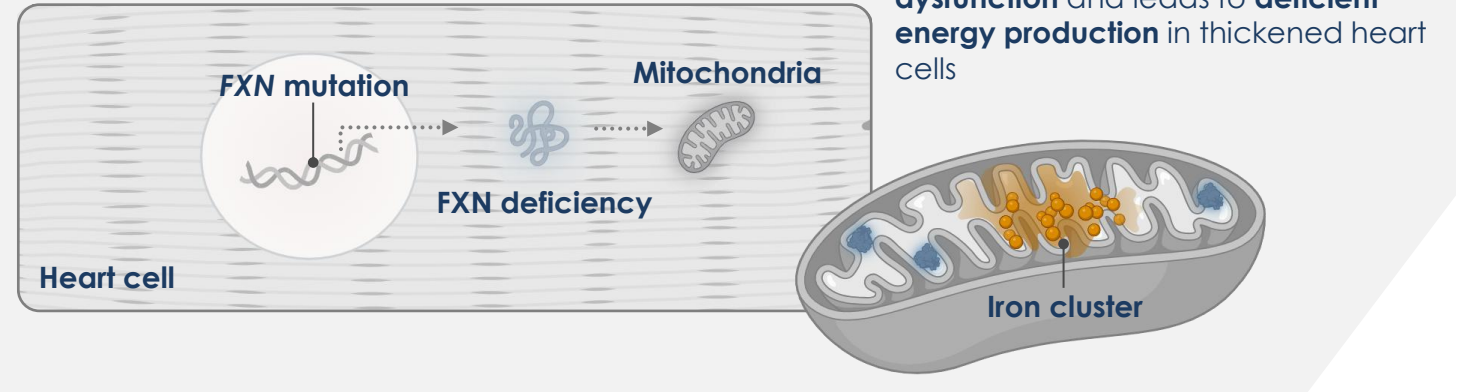
LX2006 Has the Potential to Treat the Root Cause of FA Cardiomyopathy: The Significant Decrease in Frataxin in the Heart

AAVrh.10
(viral vector)

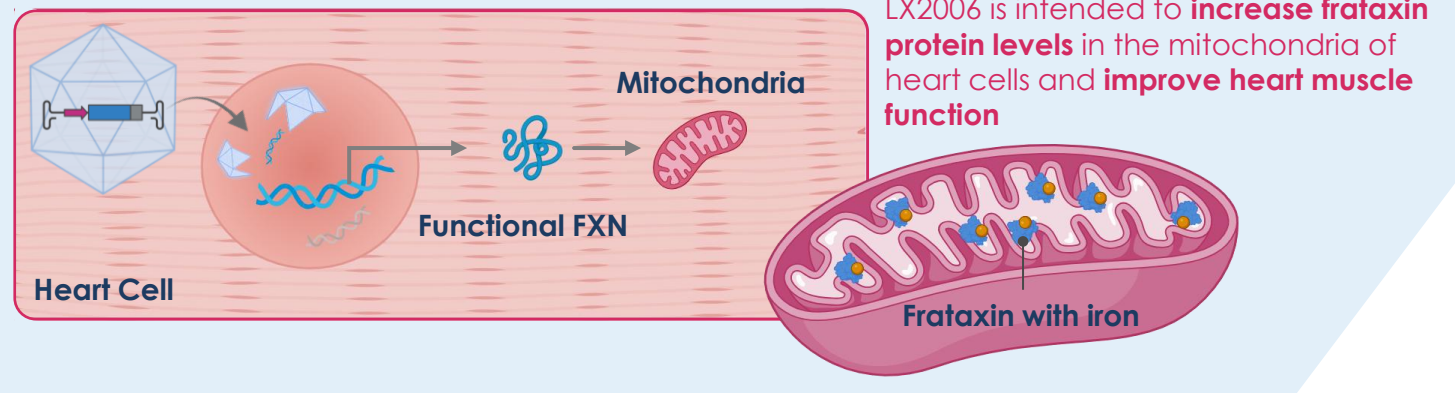


LX2006 (AAVrh.10hFXN) is given by intravenous (IV) infusion into the circulation

FA Cardiomyopathy



LX2006 Mechanism



Lexeo's Investigational Gene Therapy Program for FA Cardiomyopathy

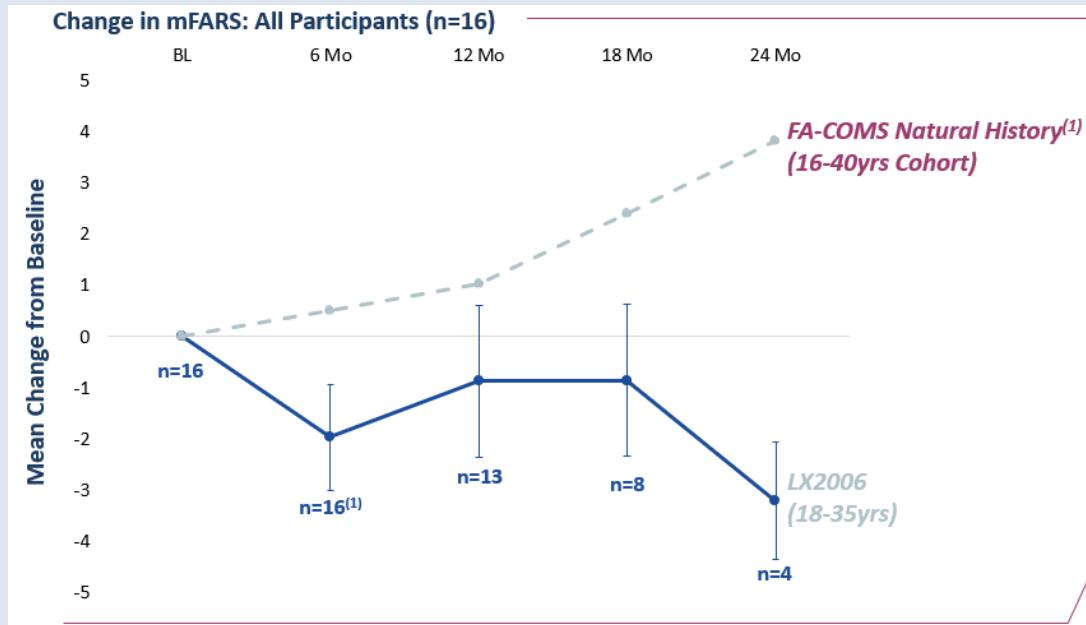
LX2006 Has Been Tested in SUNRISE-FA

- Lexeo **completed enrollment** of a Phase 1/2 trial, called **SUNRISE-FA**, to study the **safety and efficacy** of investigational gene therapy LX2006
- The trial included participants between the **ages 18-50** with a **diagnosis of FA and evidence of cardiomyopathy** (heart muscle disease)
- The trial was conducted in the U.S.
- All trial participants received a one-time IV infusion of LX2006
- **Key Measurements:**
 - Safety
 - Amount of frataxin protein in the heart
 - Measures of heart health
 - Other measures of function and reported outcomes
- **Study Length:** 52 weeks (1 year) / Study follow-up: 4 years

Our Recent News Update

- 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 was any neurological effect.
- Data from 16 participants with at least 6 months of follow-up across the two trials.

mFARS



11 of 16 participants had **reduced or stable mFARS scores** at their latest visit, compared to baseline

LVMI

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** of treatment
- **23%** within **12 months** of treatment

Safety

- Generally well tolerated
- No signs of clinically significant over-activation of the immune system (complement activation)
- No significant elevations in liver function tests
- One adverse event of asymptomatic myocarditis (possibly related to study treatment)

LVMI, left ventricular mass index; mFARS, modified Friedreich Ataxia Rating Scale.

1. "Lexeo Therapeutics Announces Progress in FDA Discussions for Accelerated Approval Pathway and Positive Interim Clinical Data for LX2006 in Friedreich Ataxia Cardiomyopathy." Lexeo Therapeutics, Inc. 07 October 2025. Press release.



CLARITY FA

CLARITY-FA Natural History Study

About the CLARITY-FA Natural History Study

- The goal of the Lexeo-sponsored CLARITY-FA natural history study is to learn about how heart disease develops and worsens in individuals with FA
- This is important because even though the **majority of people with FA exhibit heart issues, which account for up to 80% of deaths**, researchers currently do not know much about how the heart is impacted in FA
- Information gained from participation in this study will provide **valuable data to learn more about heart disease in FA** and **help advance our gene therapy research**
- Additionally, data collected from CLARITY-FA may be used to compare the results collected in the new gene therapy study

The CLARITY-FA natural history study is currently enrolling

FA, Friedreich ataxia.

1. Perfitt TL. et al. *Am J Physiol Heart Circ Physiol.* 2024;326(2):H357-H369.
2. Payne RM. *JACC Basic Transl Sci.* 2022;7(12):1267-1283.



Who Is Eligible?



Open to individuals with **genetically confirmed FA diagnosis** and **evidence of cardiomyopathy** based on specific criteria



CLARITY-FA includes two age groups:

- Individuals who are at least 16 years of age
- Individuals who are between 6 and 15 years of age



Full eligibility criteria will be evaluated by the study doctor to determine if an individual is the right candidate for this study



This is a global study that has locations currently enrolling in the US & Canada



Participants taking Skyclarys® should be on a stable dose for at least 12 weeks prior to the baseline visit and remain at a stable dose throughout the study

CLARITY-FA Study Sites



Connecting with the FA Community

- At Lexeo, individuals with FA and their loved ones are at the heart of everything we do
- We are proud to partner with Euro-Ataxia and the community to support those impacted by FA
- Together, we can potentially push the boundaries of science and achieve shared goals to address unmet treatment needs



PATIENTS & COMMUNITY

Thank You!

Important Information

- This study is sponsored by Lexeo Therapeutics, Inc.
- Participation in the CLARITY-FA study is voluntary
- You may withdraw from the study at any time for any reason. If you refuse to participate or decide to withdraw, you will not suffer any penalty, loss of rights, or loss of benefits to which you are entitled
- You will receive no direct payment for taking part in the study
- All study-related assessments will be provided at no cost. Participants and their caregiver will be reimbursed for reasonable study-related expenses for travel (e.g., transportation, meals, and hotel, as appropriate)
- As with any clinical study or trial, there may be risks involved with participation. We encourage any individual considering participation in a clinical study or trial to consult with your physician or medical team

Learn More About Lexeo's Trials & Participation in CLARITY-FA:



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<https://trials.lexeotx.com>

