

Overcoming Challenges in Ataxia Trials, Regulatory Approvals, & HTAs

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LX2006: Overview

- LX2006 (AAVrh10hFXN) is an investigational gene therapy that 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
- Currently being studied in the Lexeo-sponsored Phase 1/2 clinical trial (SUNRISE-FA) and the Weill Cornell Medicine investigator-initiated Phase 1A trial for the treatment of Friedreich ataxia cardiomyopathy
- The Lexeo-sponsored CLARITY-FA natural history study is currently enrolling to learn about how heart disease develops and worsens in individuals with FA (no drug is administered in this study)

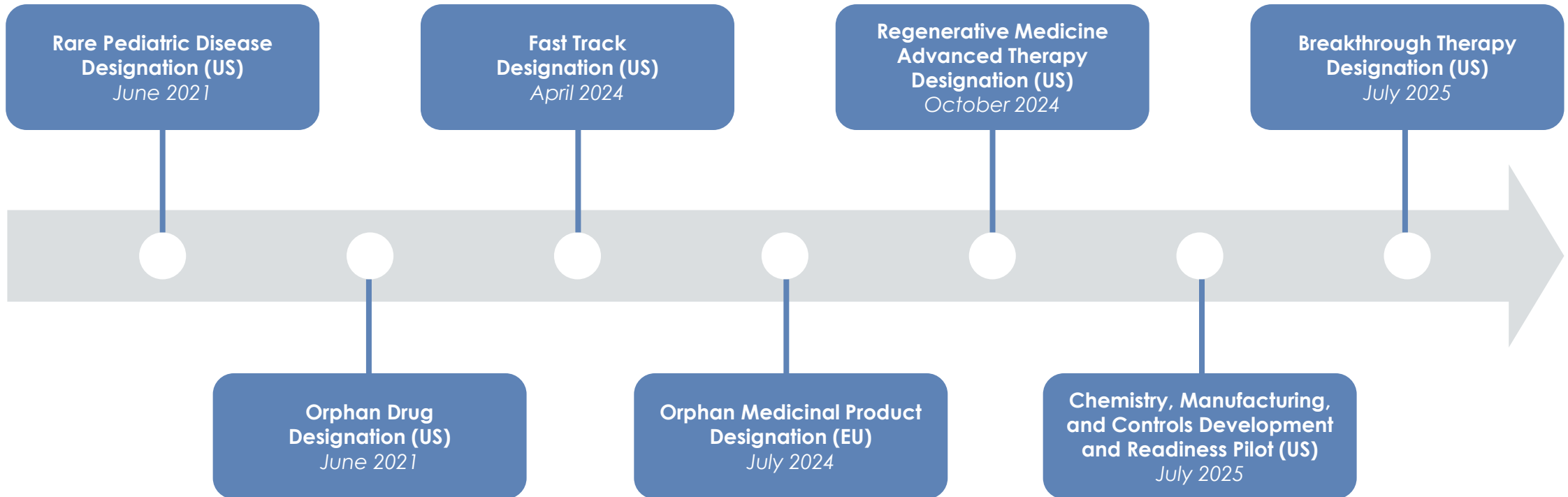


SUNRISE FA



CLARITY FA

LX2006: Our Path To Date



Overcoming Challenges in Ataxia Trials

LX2006: FDA Feedback to Date

Co-primary Endpoints in Pivotal Study for Accelerated Approval

LVMI

- Lexeo has had multiple interactions with the FDA to explore leveraging data from the Phase 1/2 studies for a Biologics License Application (BLA)
- FDA has agreed to evaluate LVMI co-primary endpoint at time point earlier than 12 months
- >10% reduction remains target threshold; Phase 1/2 results exceeding threshold at 6 and 12 months

Frataxin Protein Expression

Change from baseline in expression, which will be assessed using a validated assay, remains target threshold for planned pivotal study

Discussions with FDA included:



Use of LVMI and frataxin protein expression as co-primary endpoints to support Accelerated Approval



Planned inclusion of both children and adolescents in the study



Potential use of natural history data as a comparator arm

Overcoming Challenges in Ataxia Trials Through Partnership

- **Support from the patient community** has been critical in our discussions with regulatory authorities
 - FARA has been included in our meetings with the FDA to date and has provided essential input
- We continue to **LISTEN & LEARN** and incorporate the patient voice in our planning and to highlight the unmet need in FA
 - Through in-person events, webinars, our FA Cardiac Advisory Council, ongoing relationships with Advocacy Groups



How do we work with the FA community?

1. Early Engagement: Lived experiences of FA families has shaped our understanding of feasibility and patient experience.



2. Listening & Learning: Each conversation with the FA community provides unique insights shared with leadership to guide program direction.



FA Community Partnership

Continuous collaboration driving every aspect of our clinical program's design and execution.

3. Inclusive Research Design: Pediatric cohorts (ages 6–17) included in the natural history study



6. Strategic Co-Creation: Established an FA Cardiac Advisory Panel for long-term strategic input and to ensure community perspectives shape our future programs.



4. Collaborative Advocacy: Partnered with FARA in FDA meetings to represent the unmet need in FA-CM and emphasize the urgency for innovative treatments.



5. Community Feedback Loops: Town Halls and focus groups informed Phase 2 trial design, including schedule of assessments, participation willingness, and education areas.



Want to Learn More About Our Recent Program Updates?



Scan here to read our recent news on interim clinical data for the LX2006 program!



<https://trials.lexeotx.com>

Thank you!

