Lexeo Therapeutics
LX2006 Regulatory Update

June 15, 2026

Forward Looking Statements

This presentation contains “forward-looking statements” within the meaning of the federal securities laws, including, but not limited to, statements regarding Lexeo’s expectations and plans regarding its current product candidates and programs, including statements regarding the structure of and timelines for completion of any current or additional clinical trials required by the U.S. Food and Drug Administration (FDA), the timing for receipt and announcement of data from any such clinical trials, and the timing and likelihood of potential regulatory developments, trial design changes and approval. 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: the outcome of ongoing discussions with the FDA regarding the design of our pivotal trial for accelerated approval pathway and the design of our confirmatory study for obtaining full approval; risks and uncertainties related 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; topline data and final results from our pivotal trial; 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 March 31, 2026, filed with the SEC on May 11, 2026, 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.

LEXEO therapeutics

Dedicated to **reshaping heart health** by applying pioneering science to fundamentally change how cardiovascular disease is treated

Individuals and families impacted by Friedreich ataxia

LEXEO therapeutics

- **Genetic medicine leader with rare cardiac disease focus**
- **Proven experience in the clinic**
- **Platform designed for safety and scalability**

Finalized pivotal study protocol for LX2006, with potential BLA submission in 1H 2028

Pivotal Protocol for Accelerated Approval

- Finalized LX2006 pivotal study and statistical analysis plan to support BLA for LX2006 under accelerated approval pathway
- Study initiation on track for Q2 2026, topline data readout expected in 2H 2027, and potential BLA submission in 1H 2028

Key Study Details

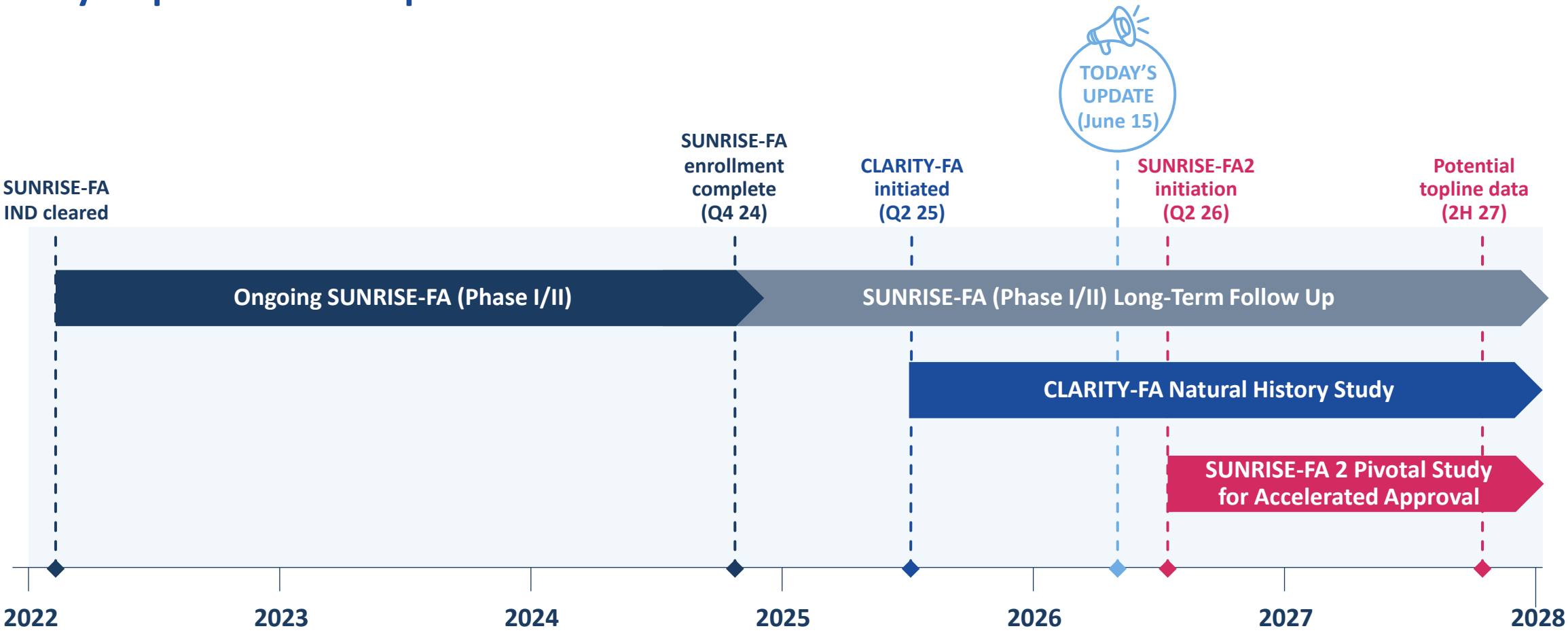
- Open-label trial with 13 participants aged 16+ who will receive a single IV administration of high-dose LX2006 compared with 13 participants untreated with LX2006 (no placebo or sham procedure)
- Primary endpoint is LVMI at 6-months post-treatment
- Key secondary endpoints include mFARS, KCCQ, hs-troponin I, and lateral wall thickness
- Lexeo remains in ongoing FDA discussions regarding the confirmatory evidence strategy

CLARITY-FA Natural History Study

- CLARITY-FA natural history will provide supportive evidence on the untreated disease course for both accelerated and full approval
- Enrollment is progressing well; CLARITY-FA shares identical inclusion criteria and patients enrolled are eligible to participate in SUNRISE-FA 2
- First patient expected to enroll from CLARITY-FA into SUNRISE-FA 2 by end of June

BLA = biologics license application, LVMI = left ventricular mass index, mFARS = modified Friedreich Ataxia Rating Scale, KCCQ = Kansas City Cardiomyopathy Questionnaire, Hs = high sensitivity.

Today's update and the path forward for LX2006



Today We Are Providing a Regulatory Update Regarding the SUNRISE-FA 2 Pivotal Study

LEXEO therapeutics

LX2006 for the Treatment of Friedreich Ataxia

Cardiac complications are the leading cause of death in Friedreich Ataxia

FA is a **rare, progressive and devastating multisystem disease** caused by a loss of function mutation in the FXN gene[1].

With a typical age of onset between 5 and 15 years[2], individuals with FA experience a combination of cardiac and neurological manifestations, with **cardiac complications accounting for up to 80% of deaths**[1]

Cardiac dysfunction in FA is associated with a multitude of symptoms but ultimately presents as **cardiac hypertrophy and subsequent heart failure**[1]; **hypertrophy in childhood** is potentially associated with a **more severe phenotype**, with earlier progression to end-stage disease[3]

The only approved disease-specific treatment for FA demonstrated efficacy on neurological measures but was not evaluated for the treatment of cardiac dysfunction in clinical trials, **leaving significant unmet need within FA cardiomyopathy**[4]

~5,000
individuals affected by FA in the U.S.[2]

~15,000
individuals affected by FA worldwide[2]

Cardiac complications account for **up to 80%** of deaths in those with FA, with an average life expectancy of 35–40 years[1,5]

Up to 40% of adults with FA have left ventricular hypertrophy as defined by abnormal LVMI[6,7]

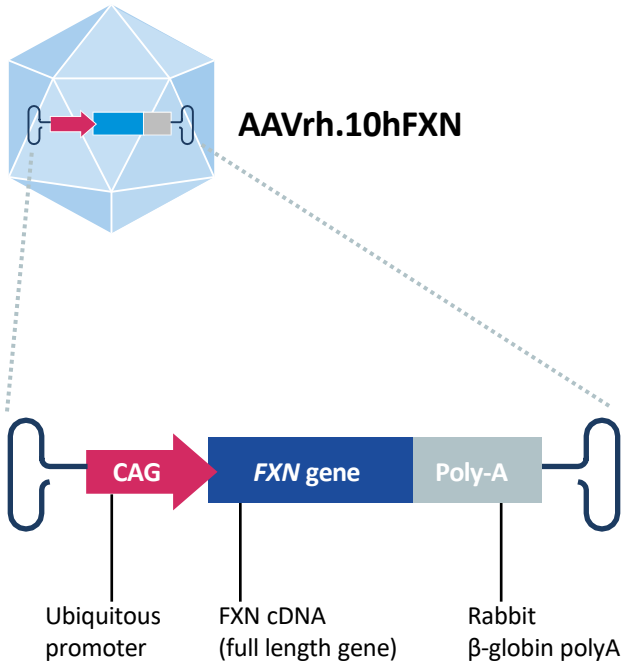
FA - Friedreich Ataxia;
FXN - Frataxin;
LVMI - Left Ventricular Mass Index.

1 - Payne R.M. JACC Basic Transl Sci, 2022;13;7(12):1267-1283.
2 - Friedreich's Ataxia Research Alliance, 2024.
3 - Norrish G., et al. Arch Dis Child, 2022;107(5), 450–455.
4 - Reetz, K., et al. Lancet Neurol, 2025;24(7):614-624.
5 - Indelicato, E., et al. Mov Disord, 2024;39(3), 510–518.
6 - Clinical Management Guidelines for Friedreich Ataxia. Chapter 4. The heart and cardiovascular system in Friedreich ataxia. 2022.
7 - Lexeo Therapeutics, Data on File, 2025.

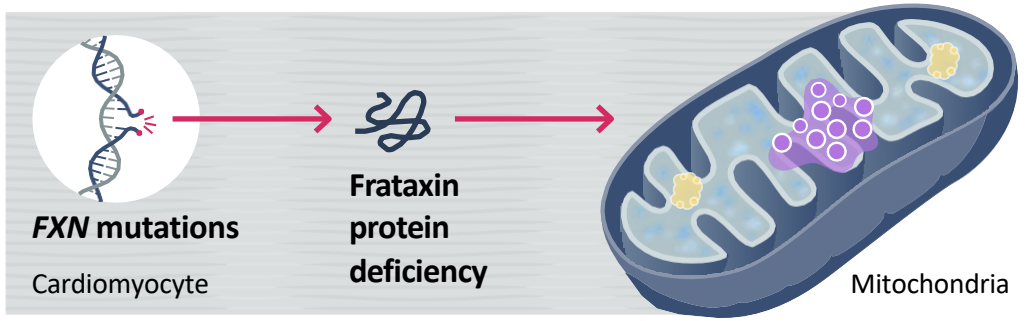
LEXEO therapeutics

LX2006 has the potential to treat the root cause of FA cardiomyopathy: significant decrease in frataxin in the heart

LX2006 construct:

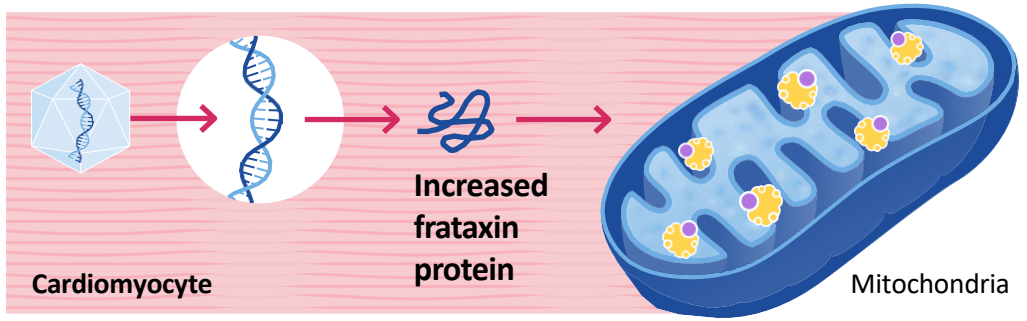


FA cardiomyopathy:



Frataxin deficiency results in **mitochondrial dysfunction** and leads to **deficient energy production** in hypertrophic cardiomyocytes

LX2006 mechanism:

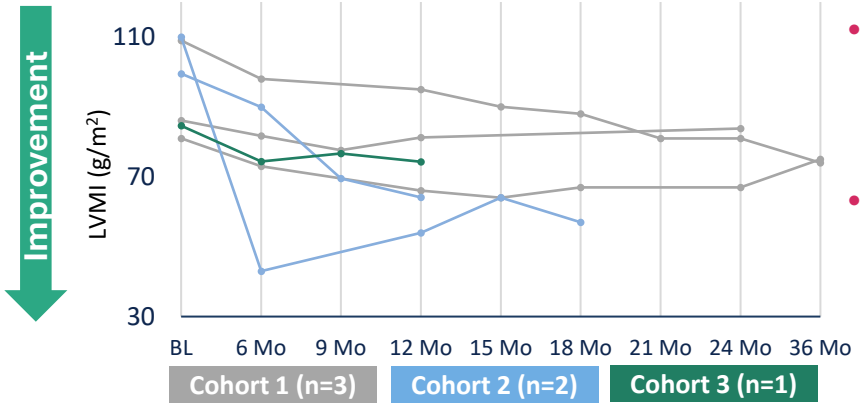


Transfer of *FXN* gene to cardiomyocytes is intended to **increase frataxin levels** in the mitochondria and **improve cardiac muscle cell function**

AAV, Adeno-Associated Virus; CAG, Chicken Beta-Actin; cDNA, Copy DNA; FA, Friedreich Ataxia; FXN, Frataxin; Poly-A, Poly Adenosine.

LX2006 clinical data show sustained or deepening improvements across cardiac measures of FA; LX2006 generally well tolerated

Cardiac MRI: LVMI (n=6; abnormal at baseline)



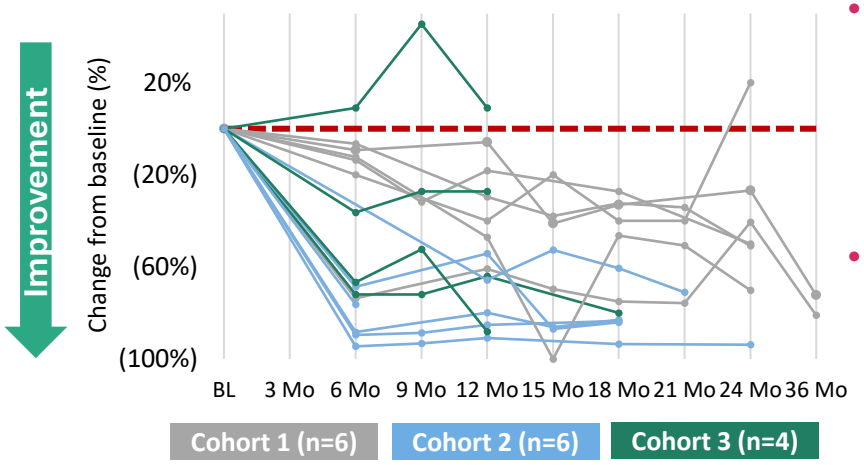
- Majority of participants reach or remain in normal LVMI range at latest visit
- **Durable LVMI improvement maintained out to three years following treatment**

Cardiac MRI: LVMI

Mean LVMI Change	
Participants at 12-mo visit *(n=6)*	**-23%**
Participants at 6-mo visit[1] *(n=6)*	**-18%**
Cohorts 2 and 3 at 12-mo visit *(n=3)*	**-33%**
Cohorts 2 and 3 at 6-mo visit[1] *(n=3)*	**-28%**

Among participants with abnormal baseline LVMI (key inclusion criteria for pivotal study; n=6):

Biomarkers: High-Sensitivity Troponin I (n=17)



- **16 of 17 participants have significantly reduced or stable troponin I,** excluding participant with myocarditis[2]
- Highly specific, blood-based marker of myocardial injury

LX2006 generally well tolerated

- LX2006 generally well tolerated across 17 participants dosed with no Grade 3 treatment-related SAEs to date
- No clinically significant complement activation
- Minimal, transient LFT elevations
- No signs of frataxin over-expression observed in cardiac tissue
- One previously disclosed, possibly treatment-related Grade 2 event of asymptomatic myocarditis observed one year after dosing

(1) Participant 11 6-month visit not conducted due to hurricane; 3-month visit used for mean calculations. (2) Participant 10 not included in Hs-TNI chart due to scale. Values are +29% at 6M, +45% at 9M, +2,702% at 12M, +1,857% at 18M, +1,620% at 21M, and +1,458% at 24M as of most recent safety monitoring.
Note: Data as of December 2025.

Cardiac function improvement observed in individual with later stage cardiomyopathy

Effect of LX2006 on Cardiac Function

Majority of Participants (16/17)

- **Baseline LVEF:** Normal
- **Post therapy:** No change

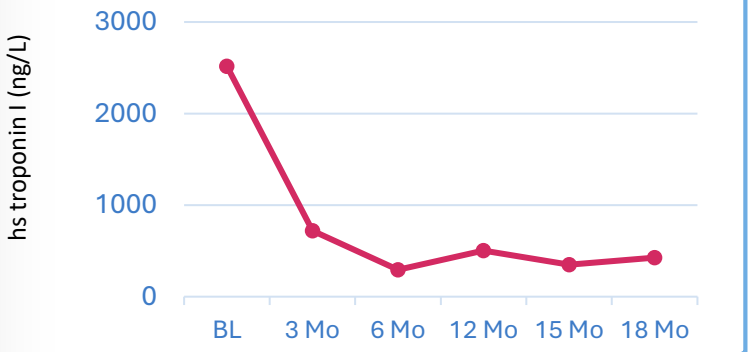
One Participant (#13) with later stage cardiomyopathy

- **Baseline LVEF:** Low (35%)
- **Post Therapy:** Significant improvements across all cardiac biomarkers

Cardiac Improvements 18 months Post LX2006 Treatment in Participant with Low Baseline LVEF

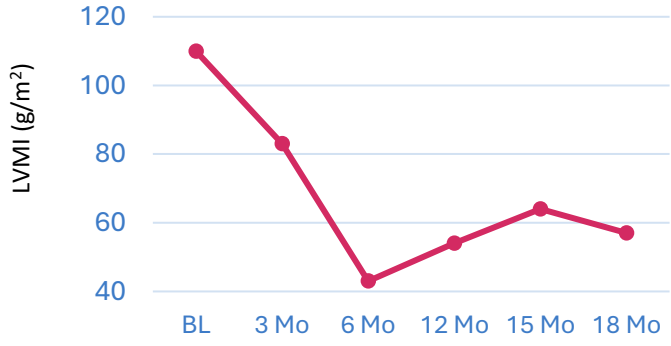
Biomarkers: High-Sensitivity Troponin I

83% reduction

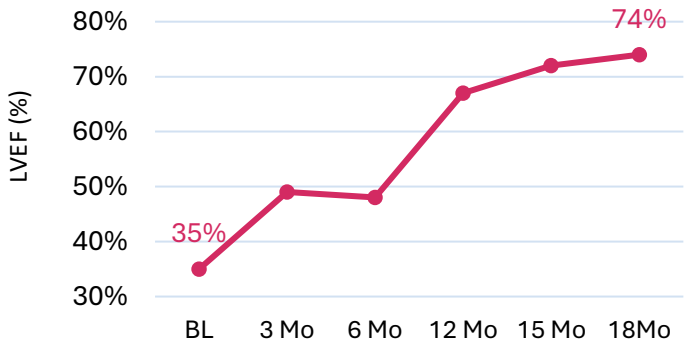


Cardiac MRI: LVMI

48% reduction



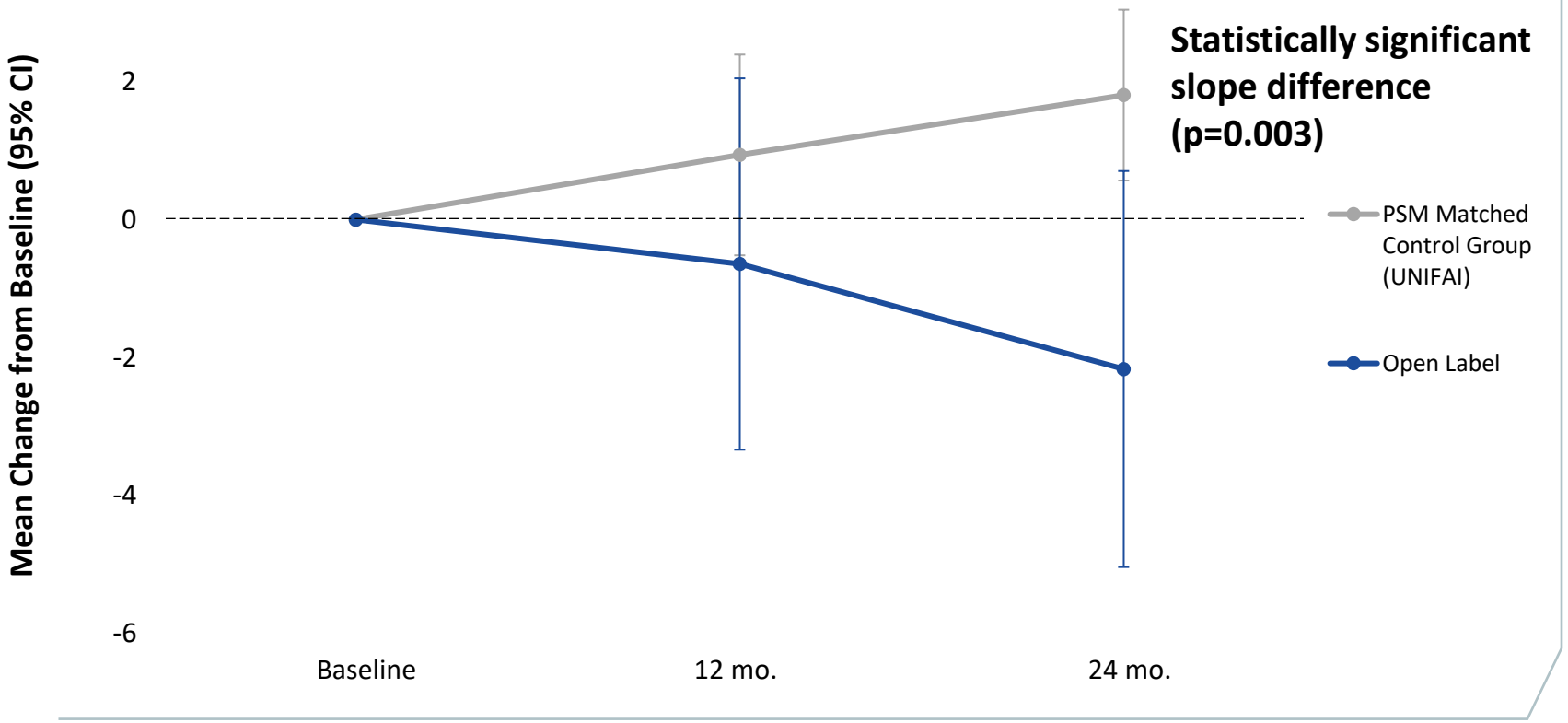
Cardiac MRI: LVEF



LVMI = left ventricular mass index, LVEF = left ventricular ejection fraction.
Note: Data as of December 2025.

Statistically significant improvement in mean mFARS scores for LX2006-treated participants compared to propensity-matched control cohort

Change in mFARS: Open Label Cohort (n=16) vs. UNIFAI Matched Control (n=45)



- ✓ mFARS validated clinical scale measures FA neurological progression; higher scores represent disease worsening
- ✓ Majority of LX2006-treated participants demonstrate mFARS improvement or stabilization at latest visit relative to baseline
- ✓ **New evidence of neurological functional improvement compared to propensity matched control, with annualized difference in progression of 2.3 points per year** (95% CI: 0.82-3.84)

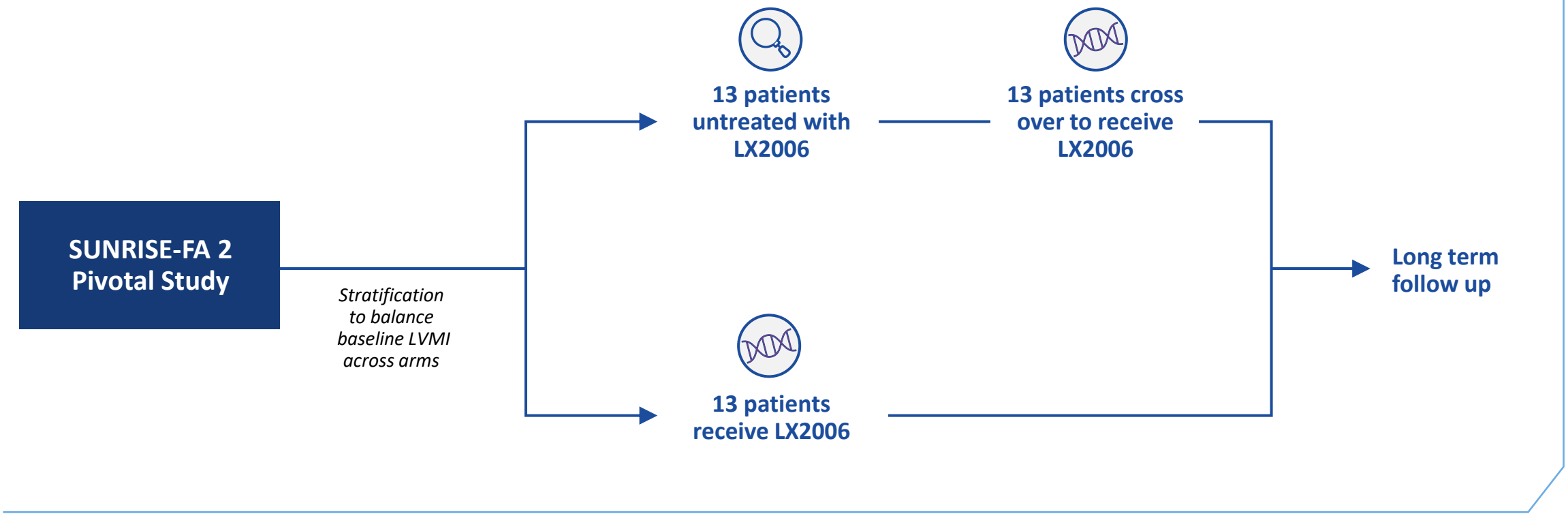
PSM, propensity score matched.
Note: Data as of December 2025. 16 patients treated with LX2006 in the Open Label study were matched to a control group of individuals in the Friedrich Ataxia Global Clinical Consortium UNIFIED Natural History Study of Friedrich's Ataxia (UNIFAI) in a 3:1 ratio. While some patients did not have 2 years of follow up, this model is using every patient's earlier visits to inform the rate-of-change estimate for mFARS (an annualized slope). Analysis performed by Christian Rumney in partnership with FARA.

LEXEO therapeutics

SUNRISE-FA 2 pivotal study design

SUNRISE FA2

Finalized Open-Label Study Design for LX2006



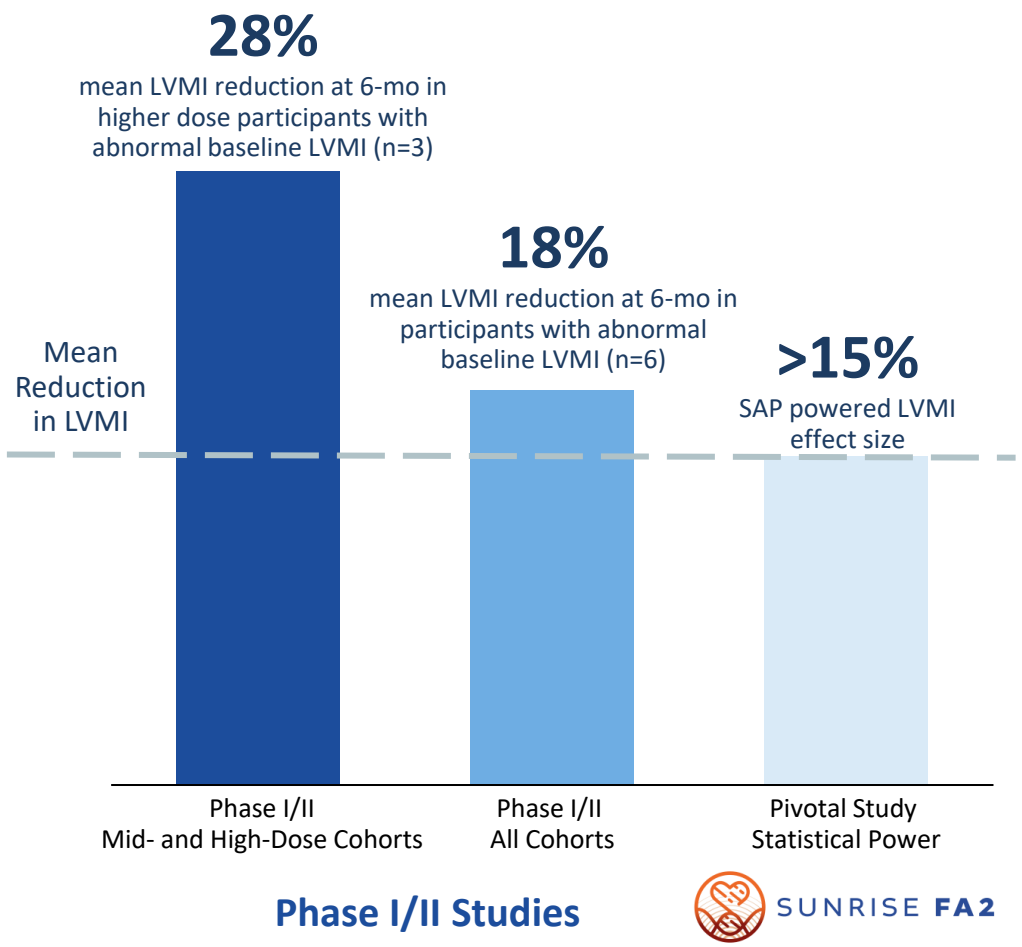
Eligible CLARITY-FA participants or new participants can enroll into the pivotal study[1]

LEXEO therapeutics

1. Eligible participants are those who test negative for neutralizing antibodies to AAVrh10 and meet the LVMI criteria (≥2SD above normal mean).

Phase I/II data showed clinically meaningful benefit in LVMI improvement

Phase I/II Results Exceed the Effect Size in LVMI Used to Power the SUNRISE-FA 2 Pivotal Study



SUNRISE FA2

Dose	• $1.2x10^{12}$ vg/kg, one-time IV infusion
Key Eligibility Criteria	• **Adults (16yrs+): Abnormal baseline LVMI**, ≥2SD above normal mean • Pediatric (6-15yrs): Abnormal baseline LV wall thickness, assessed via echocardiography. Pediatric cohorts assessed primarily for safety
Primary Endpoint (Adults)	• **LVMI**, via cMRI at 6 months
Key Secondary Endpoints	• mFARS, KCCQ, Hs-Troponin I, lateral wall thickness
Immune Suppression	• Corticosteroid use following LX2006 administration
Statistical Plan	• **Sample size:** 26 participants, 13 participants treated with LX2006 • Pivotal arms stratified to balance baseline LVMI • SAP powered for 15% or greater LVMI change at 6 months
Confirmatory Evidence Strategy	• Lexeo remains in ongoing discussions with the FDA • Potential use of certain secondary endpoints at the 12-month time point in SUNRISE-FA 2 to support full approval

SAP = statistical analysis plan, Vg/kg = vector genomes per kilogram, LVMI = left ventricular mass index, cMRI = cardiac magnetic resonance imaging, mFARS = modified Friedreich Ataxia Rating Scale, KCCQ = Kansas City Cardiomyopathy Questionnaire, Hs = high sensitivity.

LEXEO therapeutics

Summary: Finalized LX2006 pivotal study design with potential BLA filing in 1H 2028 under accelerated approval pathway

Finalized SUNRISE-FA 2 Pivotal Trial Protocol

Pivotal Study Design for Accelerated Approval

- **Primary endpoint with clinical relevance: LVMI**
- Evaluating LVMI at **6 months,** SAP powered for 15% or greater reduction
- Phase I/II data to be submitted for safety and comprehensive BLA review
- No need for frataxin assay or nonclinical murine bridging study

Statistical Analysis Plan

- **Open label design,** with no placebo or sham procedures
- 26 adult participants total, **13 adult participants treated with LX2006**
  - Pediatric cohorts (n≈6) will be assessed for safety following dosing in adults
- Random allocation of participants into LX2006 treatment arm or untreated control; **minimizes sources of bias without changing study size, duration or open-label design**

Manufacturing

- Approval to use optimized, high-yield Sf9-baculovirus manufacturing process to begin dosing patients in pivotal study
- **Clinical drug product already manufactured** at commercial scale and immediately available
- Anticipate FDA flexibility in PPQ, **supporting faster timelines to reach BLA filing**

BLA = biologics license application, LVMI = Left Ventricular Mass Index.

Strong path forward for LX2006

SUNRISE-FA 2 to be Initiated in Q2 2026, with First Patient Expected to be Enrolled by End of June

Phase I/II Results Exceed the Effect Size in LVMI Used to Power the Pivotal Study

Building Internal Commercial Capabilities to Support Successful Launch

Differentiated AAVrh10 Capsid and Commercial-Ready CMC Supply Chain

With Final SUNRISE-FA 2 Protocol, Lexeo Anticipates Potential Topline Data in 2H 2027 and BLA in 1H 2028

LEXEO therapeutics

LEXEO therapeutics

Thank you