UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): October 09, 2024

Lexeo Therapeutics, Inc.

(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-41855**	**85-4012572**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

345 Park Avenue South, Floor 6 **New York, New York**	**10010**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's Telephone Number, Including Area Code: 212 547-9879

N/A
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	LXEO	Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events.

On October 9, 2024, Lexeo Therapeutics, Inc. (the "**Company**") posted on its website an updated corporate presentation (the "**Corporate Presentation**"), noting the Company expects to share Cohort 1 data from LX2020 for the treatment of PKP2-ACM in the late first quarter or the early second quarter of 2025 and that the Company plans to present data from LX1001 for the treatment of APOE4-associated Alzheimer's disease at the Clinical Trials on Alzheimer's Disease conference in October 2024. The Corporate Presentation will be used from time to time in meetings with investors and analysts. A copy of the Corporate Presentation is attached hereto as Exhibit 99.1 and is incorporated by reference herein.

Cautionary Note Regarding Forward-Looking Statements

This report contains certain forward-looking statements regarding the business of the Company that are not a description of historical facts within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include statements regarding the Company's expected plans with respect to clinical trials of the Company's gene therapy candidates and the timing for announcement of data from such trials. Actual results could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, which include, without limitation, expectations regarding the initiation, progress, and expected results of the Company's preclinical studies, clinical trials and research and development programs, the unpredictable relationship between preclinical study results and clinical study results, delays in submission of regulatory filings or failure to receive regulatory approval and liquidity and capital resources. Additional risks and uncertainties that could cause actual results to differ materially from those contemplated by the forward-looking statements are included in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2023, Quarterly Report on Form 10-Q for the quarter ended June 30, 2024 and subsequent future filings the Company may make with the Securities and Exchange Commission from time to time that are available at www.sec.gov.

You are cautioned not to place undue reliance on forward-looking statements which are current only as of the date hereof. Except as required by applicable law, the Company undertakes no obligation to revise or update any forward-looking statement, or to make any other forward-looking statements, whether as a result of new information, future events or otherwise.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Corporate Presentation, dated October 9, 2024
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Lexeo Therapeutics, Inc.

Date: October 9, 2024

By: /s/ R. Nolan Townsend
R. Nolan Townsend, Chief Executive Officer

Exhibit 99.1

Lexeo Therapeutics Corporate Overview

October 2024

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 timing, progress and results of preclinical and clinical trials of Lexeo's gene therapy product candidates, the anticipated benefits of its current product candidates and expected cash runway. 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: 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; 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 Annual Report on Form 10-K for the year ended December 31, 2023, filed with the SEC on March 11, 2024, Quarterly Report on Form 10-Q for the quarter ended June 30, 2024, filed with the SEC on August 12, 2024, 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 Team

Management Team & Key Advisors

R. Nolan Townsend
Chief Executive Officer
Pfizer · Lehman Brothers

Eric Adler, M.D.
Chief Medical Officer and Head of Research
UC San Diego School of Medicine Division of Cardiology · Boston University

Sandi See Tai, M.D.
Chief Development Officer
Pfizer · Wyeth

Jenny R. Robertson
Chief Business and Legal Officer
Pfizer · Hogan Lovells

José Manuel Otero, Ph.D.
Chief Technical Officer
Auregen BioTherapeutics · Turnstone Biologics · Merck

Rajiv Patni, M.D.
Senior Advisor to the CEO and Board of Directors
Reata Pharmaceuticals · GBT · Portola

Chair and Scientific Founder

Steven Altschuler, M.D.
Chairman
The Children's Hospital of Philadelphia · Spark Therapeutics

Ronald Crystal, M.D.
Founder & Chief Scientific Adviser
Weill Cornell Medicine Genetic Medicine

Professor and Chairman, Weill Cornell Medicine
Director, Belfer Gene Therapy Core Facility

Former Chief, Pulmonary Branch
NIH National Heart, Lung, and Blood Institute

Founder / Co-founder
Adverum Biotechnologies · GenVec · XyloCor Therapeutics

Management team with broad leadership experience in gene therapy and rare disease

LEXEO therapeutics

Revolutionizing Genetic Medicines for Cardiovascular Diseases and APOE4-

Attractive Disease Area Strategy

- Genetically-defined cardiovascular and APOE4-associated Alzheimer's disease
- Well established biomarkers potentially allowing for early signs of clinical activity

Evolving Regulatory Environment	Shift towards surrogate endpoints could circumvent need for large cardiovascular outcome trials
Targeted Delivery Platform	Improvements in modern AAV delivery technology, including AAVrh10 allows for greater targeting of the heart
Increased Genetic Screening	Increased screening has potential to expand awareness and increase opportunity
Lower Efficacy for APOE4 Patients(1)	APOE4 homozygotes demonstrated lower efficacy results compared to heterozygotes and noncarriers
Higher Risk of ARIA-E(1)	APOE4 homozygotes were associated with a higher incidence of ARIA-E compared to heterozygotes and noncarriers

Focused on genetically-defined cardiovascular diseases with data from Alzheimer's disease driving business development

Note: ARIA-E = amyloid-related imaging abnormalities characterized by edema and effusion.
(1) Van Dyck, et al. New England Journal of Medicine, 2022. Sims, et al. JAMA, 2023.

LEXEO therapeutics

Lexeo Investment Highlights

Clinical-stage genetic medicine company addressing larger-rare and prevalent patient populations

Cardiac Portfolio

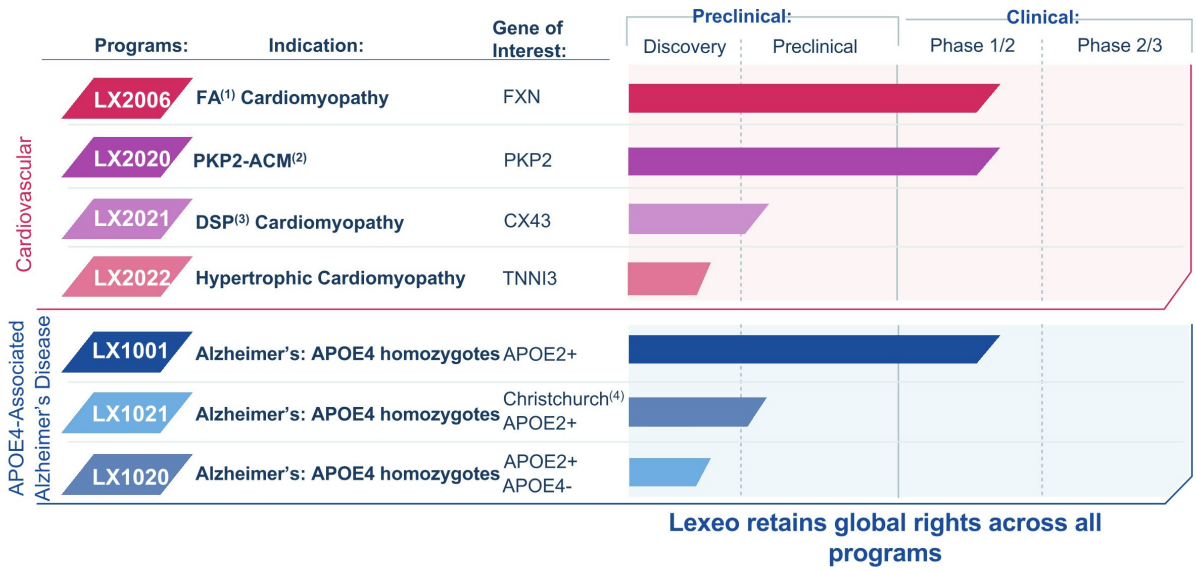
- Ongoing Phase 1/2 trial for **Friedreich ataxia cardiomyopathy** with interim clinical results shared in July 2024
  - **Mean reduction in LVMI of 11.4%** at 12 months in participants with elevated LVMI at baseline (n=4)
  - Clinically meaningful **reductions in LV wall thickness and hs-troponin I**
  - Increased **post-treatment frataxin expression above baseline** in all participants evaluated via myocardial biopsy
- Ongoing Phase 1/2 trial for the treatment of **arrhythmogenic cardiomyopathy caused by mutations in the PKP2 gene (PKP2-ACM)**

APOE4 Alzheimer's Portfolio

- **Significant optionality on portfolio of approaches to treat the genetics underlying APOE4-associated Alzheimer's disease**; estimated 900,000 E4 homozygotes in the US
- **Observed a decline in CSF biomarkers** in initial clinical data from Cohort 1 of ongoing Phase 1/2 clinical study of LX1001
- Phase 1/2 data readout to be shared at the CTAD conference in October 2024 **potentially driving business development**

LEXEO therapeutics

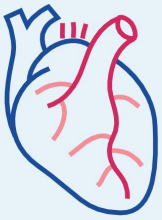
Advancing Genetic Medicines in Larger-Rare and Prevalent Patient Populations



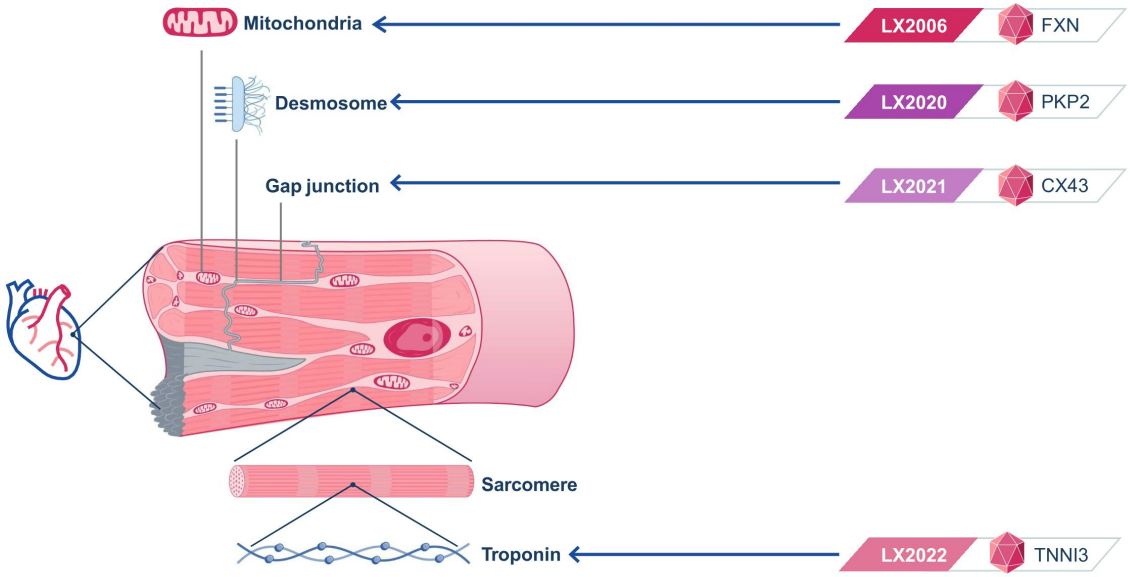
Lexeo retains global rights across all programs

(1) Friedreich Ataxia. (2) Plakophilin 2 Arrhythmogenic Cardiomyopathy. (3) Desmoplakin. (4) Christchurch Modified APOE2 gene.

Cardiovascular diseases



Several Targets in Cardiac Organelles that are Dysregulated in Cardiomyopathy; Potential Readthrough to Other Therapeutic Indications



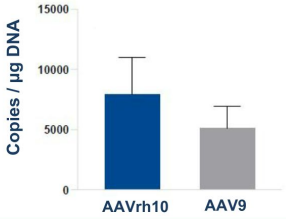
Utilizing AAVrh10 for Initial Genetic Cardiac Indications

- ✓ Observed ~1.5x to 2.0x greater biodistribution in the heart compared to AAV9 in multiple large animal models
- ✓ Observed greater trends of functional improvements in PKP2-murine model compared to AAV9
- ✓ AAVrh10 cardiac tropism may allow for lower doses compared to other vector serotypes while achieving targeted transgene biodistribution

Compelling Cardiac Tropism

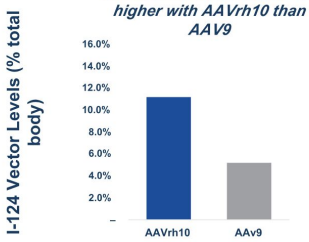
Yucatan Minipig Biodistribution(1)

Distribution to the heart ~1.5x higher with AAVrh10

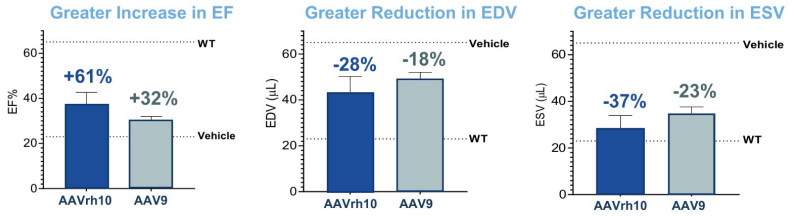


NHP Biodistribution(2)

Distribution to the heart ~2x higher with AAVrh10 than AAV9



Greater Trends of Functional Improvement Versus AAV9 in PKP2-ACM Model(1)

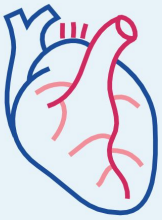


Note: PKP2 homozygous mouse model administered with human PKP2 (N = 5 mice / group).

(1) Data presented at ASGCT 2023.
(2) Ballon DJ et al, Human Gene Therapy, 2020.

LEXEO therapeutics

LX2006 (FA Cardiomyopathy)



Friedreich Ataxia (FA) is a Devastating Rare Disease Impacting Both the Nervous System and the Heart

FA is a **rare, devastating and progressive disorder** caused by loss of function mutations in the *FXN* gene (GAA repeat expansion)

With a typical age of onset between 10 and 15 years, people with FA experience a **combination of neurological and cardiac manifestations**, with ~80% developing cardiomyopathy(1)

Complications from **cardiac dysfunction** are the **leading cause of death in FA**

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

~5,000 individuals affected by FA in the U.S.(2)

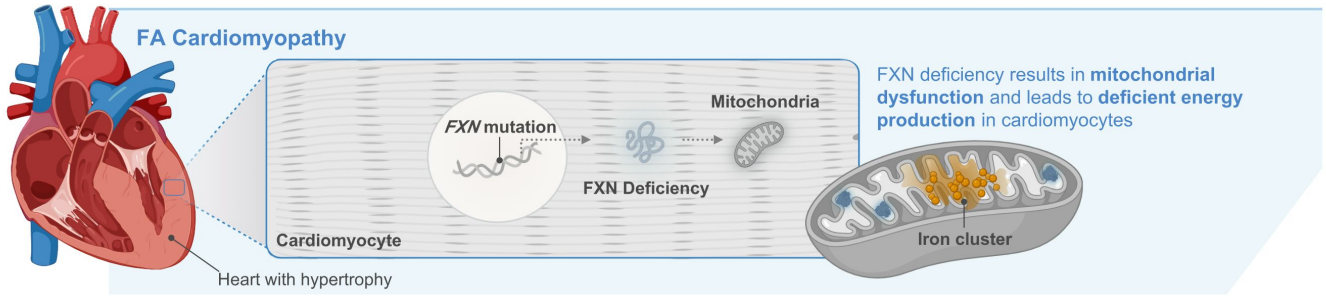
~15,000 individuals affected by FA worldwide(2)

Cardiac dysfunction is the cause of death in **60-80%** of those with FA(3)(4)

FXN, Frataxin.

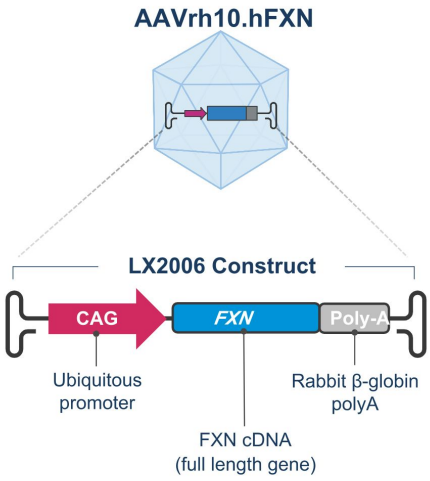
(1) Regner S, et al. *American Journal of Cardiology*, 2012. (2) Friedreich's Ataxia Research Alliance, 2024. (3) Subramoney S, et al. *MDA Clinical and Scientific Conference*, 2023. (4) Pousset, F. et al. *JAMA Neurol*, 2015;72(11):1334-1341.

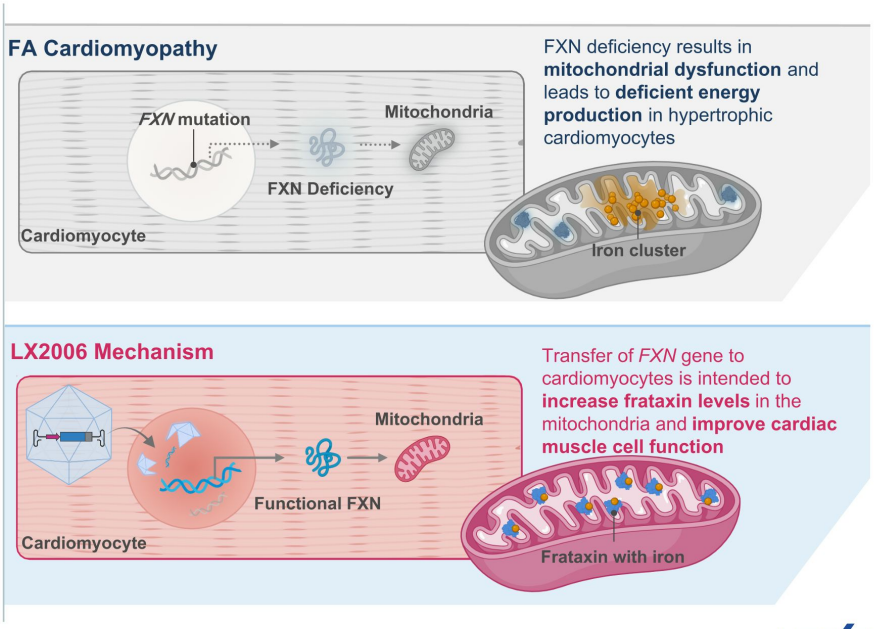
Friedreich Ataxia is a Result of Mutations in the Frataxin Gene, Leading to Impaired Mitochondrial Function in the Heart



- FA is caused by mutations in the gene Frataxin (*FXN*), resulting in reduced FXN protein expression
- Reduced FXN protein expression decreases mitochondrial iron-sulfur cluster formation, causing mitochondrial dysfunction across multiple cells including cardiomyocytes
- Mitochondrial dysfunction leads to impaired cellular energy production and mitochondrial proliferation
- Impaired energetics and mitochondrial proliferation speculated to lead to cardiac hypertrophy and cell death

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





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

Small Increases in Frataxin Following Treatment May Produce Clinical Benefits

Modest FXN Levels Resulted in Near Normal Cardiac Function in FA Murine

YG8-800 FA Murine Model

- YG8-800 mice have **5% of normal frataxin levels** in the heart, with approximately 800 GAA repeats, but display **near normal** cardiac output and stroke volume(1)
- Suggests **potential to improve cardiac phenotype with restoration to modest frataxin levels**

Moderate Restoration of Protein Function Correlates with Better Disease Prognosis and Physiological Improvement in Other Diseases

Hemophilia B

- In humans, factor IX clotting activity is typically 50 – 150%(2)
- Individuals with > 40% usually have normal coagulation *in vivo*(2)
- Clinical data indicates even a **small increase to 5% of normal factor IX levels significantly reduces bleeding**(3)

Muscular Dystrophies

- In DMD **dystrophin is virtually absent**; whereas individuals with BMD have **10 – 40% of normal**, resulting in a milder disease with later onset and slower progression than DMD(4)
- Suggests **incremental dystrophin levels could result in improved clinical phenotype**(4)

Existing literature suggests small increases in frataxin may be sufficient to produce physiological improvement

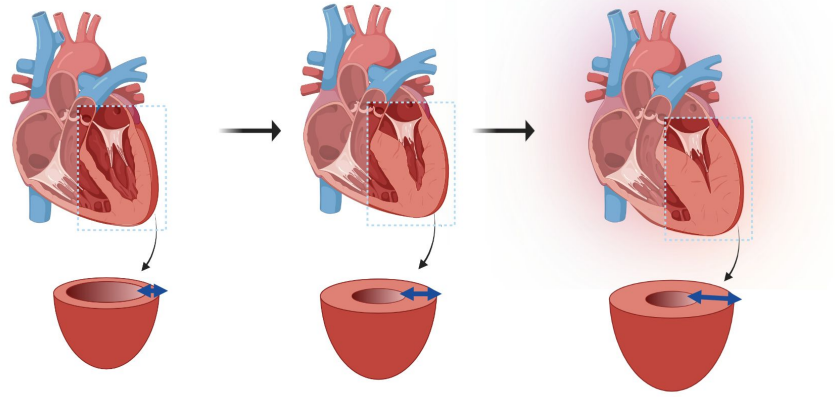
BMD, Becker Muscular Dystrophy; DMD, Duchenne Muscular Dystrophy; FXN, Frataxin; GAA, Guanine-adenine-adenine.
(1) Gérard C, et al. *Behav Brain Res*, 2023. (2) Konkle BA, Fletcher SN. *Gene Reviews*, 2000 [Updated 2023]. (3) Nathwani AC. *Hematology Am Soc Hematol Educ Program*, 2022. (4) Bellayou et al. *Journal Biomedicine Biotechnology*, 2009.

LEXEO therapeutics

Dysfunction in Heart Muscle Cells Can Lead to Concentric Hypertrophy and Poorer Outcomes in Multiple Cardiomyopathies

Disease Progression

Normal Heart → **Concentric Hypertrophy**



Normal LVMI Normal LV Wall Thickness Normal hs-Troponin I	High Normal LVMI ↑LV Wall Thickness ↑ Hs-Troponin I	↑LVMI ↑ LV Wall Thickness ↑ Hs-Troponin I

Measurements of Hypertrophy

✓Left Ventricular Mass Index (LVMI)

- Indicator of left ventricular hypertrophy
- Closely correlated with outcomes such as death or hospitalization in multiple conditions:
  - Heart failure with preserved ejection fraction[1]
  - Hypertensive cardiomyopathy[2]
  - Fabry disease[3,4]
  - Obstructive hypertrophic cardiomyopathy (HCM)[5]

✓Left Ventricular (LV) Wall Thickness

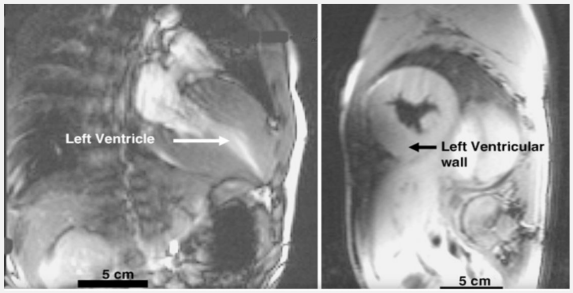
- Early indicator of left ventricular hypertrophy
- Associated with increase in cardiovascular events;[2] magnitude of LV wall thickness is directly related to risk of sudden cardiac death in HCM[6]

(1) Shah et al, *Journal of American College of Cardiology,* 2019. (2) Muiesan et al, *Hypertension,* 2004. (3) Orsborne et al, *Journal of American College of Cardiology,* 2022. (4) Hanneman et al, *Radiology,* 2020. (5) Hegde et al, *Journal of American College of Cardiology,* 2021. (6) Spirito et al, *NEJM,* 2000.

Individuals with FA Demonstrate Concentric Hypertrophy Including Increased Wall Thickness and Elevated LVMI, Which Predicts Mortality

Increases in LVMI Independently Predict Mortality in Friedreich Ataxia (FA)

Natural history study showed a 19% higher risk of death per 10g/m^2 (HR 1.19; 95% CI)(1)



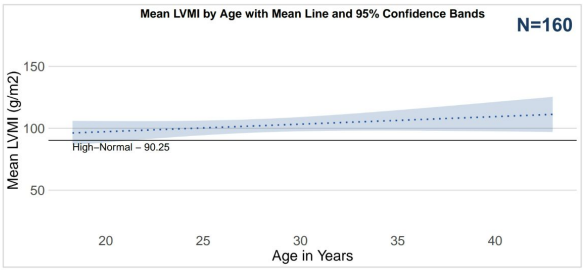
MRI of Individual With FA Cardiomyopathy Demonstrating Significant Hypertrophy

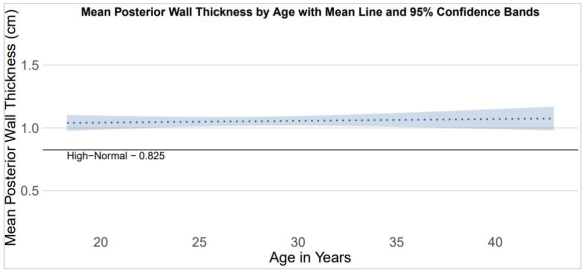
- Concentric hypertrophy is a hallmark of FA cardiomyopathy, including increased LVMI and abnormal left ventricular wall thickness(1)(2)
- Natural history suggests a 19% incremental risk of all cause mortality per ~10% increase in LVMI in individuals with FA; increased wall thickness was also associated with mortality(1)
- **Improvement in LVMI and left ventricular wall thickness may improve cardiac outcomes in those with FA**

HR, Hazard Ratio; CI, Confidence Internal; LVMI, Left Ventricular Mass Index.
Note: 10g/m^2 represents approximately 10% change in LVMI based on echocardiography measurements of upper bound of normal (105 g/m^2).
(1) Pousset, F. et al. *JAMA Neurol,* 2015;72(11):1334-1341. (2) Peverill et al, *PLOS ONE,* 2019.

LVMI is Elevated in Individuals with FA Cardiomyopathy, and Not Expected to Decrease Without Intervention

Natural History Data of Adults with FA Cardiomyopathy Show Elevated LVMI and Posterior Wall Thickness (PWT)[1]





Across Multiple Randomized Controlled Trials, No Significant Change Observed in LVMI or LV Mass (LVM) in Control Arms

Disease	Measure	LVMI / LVM Percent Change from Baseline in Placebo/Control Arm
Fabry Disease	LVMI at 18 months on ERT[2]	-2 g/m² (-2.2%)
Amyloidosis (ATTR)	LVM at 18 Months[3]	+0.6g (0.3%)
HCM	LVMI at 30 Weeks[4]	-1.6 g/m² (-1.7%)

-10% 0% 10%

Note: Percent change in LVM / LVMI calculated based on change applied to baseline levels.

In other cardiac diseases, LVMI does not significantly decrease without intervention

(1) Subset analysis performed by Lexeo Therapeutics including adults 18-50 years old with abnormal relative wall thickness, LV mass or LVMI (n=160; 830 echocardiographs) from a natural history cohort followed primarily at Children's Hospital of Philadelphia of FA patients including children and adults. (2) Hughes DA, et al. *J Med Genet,* 2017;54:288–296. Migalastat. (3) Solomon S, et al. *Circulation,* 2018. Patisiran.
(4) Saberi S, et al. *Circulation.* 2021;143:606–608. Mavacamten.

Recent LX2006 Program Updates

- In April 2024, Lexeo announced a license agreement with Cornell University for intellectual property rights including current and future clinical data from the ongoing Weill Cornell Medicine investigator-initiated trial of AAVrh10.hFXN (LX2006)
- Lexeo-sponsored SUNRISE-FA trial and Weill Cornell Medicine investigator-initiated trial utilize identical drug product manufactured at Weill Cornell for these ongoing studies
- Both studies share similar inclusion and exclusion criteria, however the Weill Cornell trial does not conduct cardiac biopsies

Interim Data Update Supports LX2006 as Potential Treatment for FA Cardiomyopathy

Data from Lexeo Sponsored SUNRISE-FA and Weil Cornell Medicine Investigator-Initiated Phase 1/2 Trials

Safety and Tolerability

- LX2006 well tolerated with no treatment-related serious adverse events to date
- No signs of complement activation or other immunogenicity
- No cardiac or hepatic safety signals observed
- All adverse events were transient and resolved
- No participants discontinued from either study

Cardiac Biomarkers

LVMI:

- Among participants with elevated LVMI at baseline, 75% achieved >10% improvement at 12 months with mean reduction of 11% at 12 months (n=4) and 18% at 18 months (n=2)
- Natural history analysis shows elevated LVMI in adults with FA cardiomyopathy, stable to increasing with age

LV Lateral Wall Thickness:

- Early indicator of LV hypertrophy
- 14% mean improvement at 12-months (n=6)

Hs-Troponin I:

- Biomarker of myocardial injury
- 53% mean improvement at 12-months (n=5)

Cardiac Biopsy Analyses

- **LCMS:** increase in post-treatment FXN levels observed in 3 of 3 participants
- **IHC:** increase in post-treatment FXN levels observed in 2 of 2 participants

Program Status

- As of July 15, 2024, 13 participants dosed, including 1 participant in Cohort 3
- SUNRISE-FA currently enrolling Cohort 3 ($1.2x10^{12}$vg/kg) and will include at least 3 participants
- The Weill Cornell investigator-initiated trial is currently enrolling in Cohort 2
- Previously disclosed data, and one additional cardiac biopsy from Cohort 2 will be shared at a scientific conference in Fall 2024

Note: Data as of interim clinical update shared July 15, 2024.

The SUNRISE-FA and Weill Cornell Trials Are Similarly Designed to Assess the Effect of LX2006 in Adults with FA Cardiomyopathy

1 Study Design & Objective

Design:
52-week open-label study with a **4-year** long term follow up

Objective:
To assess the **safety** and **efficacy** of LX2006 in individuals with cardiomyopathy associated with Friedreich Ataxia

2 Key Inclusion Criteria

Adults (18-50 years)

Evidence of FA cardiomyopathy

Neutralizing anti-AAVrh.10 titer cutoff

3 Key Measurements

Cardiac Structure & Function (LVMI, hsTnI, other measures)

Functional Capacity (CPET)

FXN Protein Expression (LCMS and IHC)[1]

SUNRISE-FA and Weill Cornell trials share a similar study design, enabling data from the two studies to be evaluated together

CPET, Cardiopulmonary Exercise Testing; hsTnI, High Sensitivity Troponin I; IHC, Immunohistochemistry; LCMS, Liquid Chromatography Mass Spectrometry; LVMI, Left Ventricular Mass Index.
(1) Cardiac biopsies are evaluated in SUNRISE-FA only.
Note: LX2006 is administered systemically; participants receive immune suppression with prednisone beginning on the day prior to treatment through 14 weeks following LX2006 administration.

Both Studies Utilize Similar Metrics to Evaluate Safety and Efficacy

SUNRISE-FA
Lexeo Sponsored

- Cohort 1: $1.8x10^{11}$ vg/kg
- Cohort 2: $5.6x10^{11}$ vg/kg
- Cohort 3: $1.2x10^{12}$ vg/kg
  Currently Enrolling

Weill Cornell
Investigator Initiated

- Cohort 1: $1.8x10^{11}$ vg/kg
- Cohort 2 : $5.6x10^{11}$ vg/kg
  Currently Enrolling

	Open Label Study Period				Long Term Follow Up
	Baseline	Month 3	Month 6	1 Year	
Cardiac Biopsy	●	●	--	--	--
Cardiac Imaging	●	●	●	●	●
Biomarkers and Labs	●	●	●	●	●
CPET	●	--	●	●	●

● *Applicable to Both Studies* ● *Specific to SUNRISE-FA*

Note: Participants receive immune suppression with prednisone beginning on the day prior to treatment through 14 weeks following LX2006 administration, as such cardiac imaging and biomarkers post-treatment are shown beginning with the 6-month timepoint.

Baseline Characteristics Consistent with Cardiac Phenotype of FA

Characteristic	Cohort 1 ($1.8x10^{11}$ vg/kg)						Cohort 2 ($5.6x10^{11}$ vg/kg)				
	Participant 1	Participant 2	Participant 3	Participant 4	Participant 5	Participant 6	Participant 7	Participant 8	Participant 9	Participant 10	Participant 11
Gender	F	M	F	F	M	M	F	M	F	F	F
LVMI, g/m²	81.0	109.0	53.0	65.0	60.0	86.1	63.0	74.0	57.4	65.0	99.5
LWT, cm	1.2	1.1	0.8	1.1	0.9	0.9	0.9	1.0	0.7	1.0	1.0
Hs Troponin I, pg/ml	224	148	147	2023	5	22	53	376	820	650	115
Follow-up, months	18	18	12	12	6	12	<6	<6	12	9	<6

Abnormal(1) High-normal(1) Normal(1)

- 8 of 11 participants have high-normal or abnormal LVMI
- 10 of 11 participants have high-normal or abnormal lateral wall thickness and high-sensitivity Troponin I
- Safety data summarized for all 11 participants; efficacy data inclusive of 8 participants with ≥ 6 months of follow-up

(1) For cardiac imaging, abnormal defined as values 2 standard deviations (SD) above mean and high-normal defined as values 1SD above mean for respective gender (from healthy volunteers) as referenced in Kawel-Boehm et al. *J Cardiovasc Magn Reson* (2020) 22:87 and for hs-troponin I abnormal defined as 99th percentile and high-normal defined as level above the threshold to detect individuals at risk of future CV events as referenced in Zeller at al. *European Heart Journal* (2014) 35, 271–281.

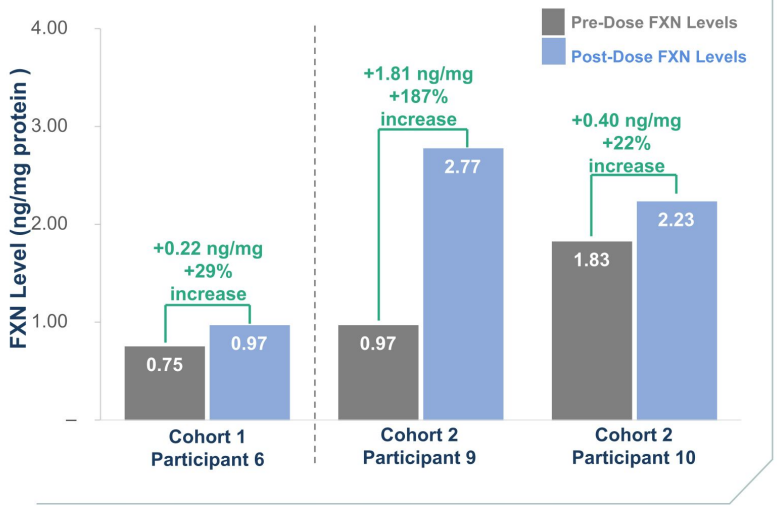
Treatment with LX2006 Has Been Well Tolerated to Date

- LX2006 has been well tolerated with no treatment-related serious adverse events
- No signs of complement activation or other immunogenicity
- No cardiac or hepatic safety signals
- All AEs were transient and resolved
- No participants discontinued from either study
- SUNRISE-FA independent Data and Safety Monitoring Board endorsed proceeding to Cohort 3 dose level ($1.2x10^{12}$vg/kg)

Note: Data as of interim clinical update shared July 15, 2024.

Cardiac Biopsies Have Demonstrated Increased Frataxin Expression in Heart in All Participants Evaluated to Date Utilizing Two Measurement Techniques

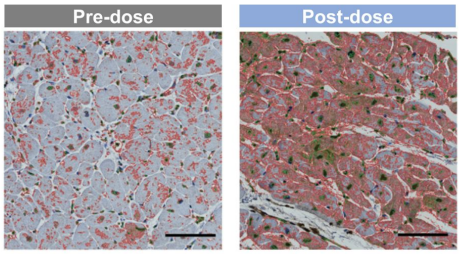
Pre- and Post-Treatment FXN Levels (LCMS)



Quantified IHC (FXN % Positive Area(1))

	Pre-Dose	Post-Dose
Participant 6	31%	51%
Participant 10	18%	54%

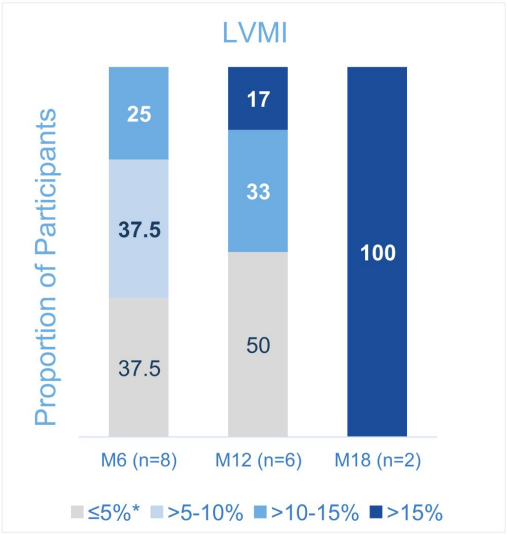
IHC images from Participant 10



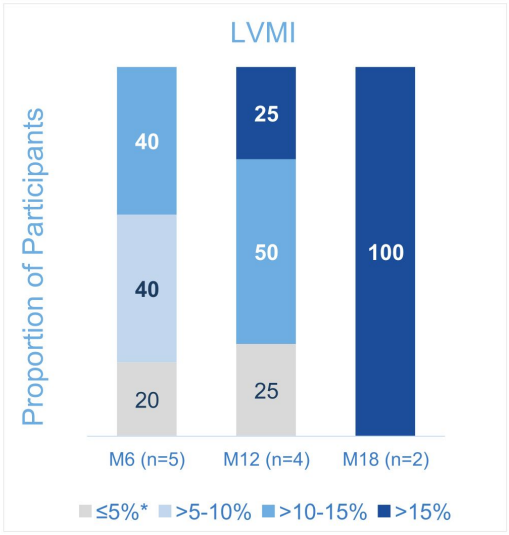
LCMS, Liquid chromatography mass spectrometry; FXN, Frataxin; IHC, Immunohistochemistry.
Note: Frataxin levels measured by ultrahigh performance liquid chromatography-multiple reaction monitoring/mass spectrometry (UHPLC-MRM/MS).
Note: Cohort 1 dose of $1.8x10^{11}$ vg/kg and Cohort 2 dose of $5.6x10^{11}$ vg/kg.
Note: Lexeo data on file from healthy cadaver samples (n=29 tissue samples from 16 patients) with mean and median FXN levels of 56.97 ng/mg and 50.84 ng/mg, respectively.
Note: Participant 9 IHC data could not be interpreted reliably due to technical issues due to sample quality.
(1) Area measurement in square microns, FXN area as a percentage of total tissue showing FXN expression.

Across Participants With ≥ 6 Months of Follow-Up, Percentage of Participants with LVMI Reduction >10% Increased Over Time

All Participants: Responder Rate by LVMI Reduction



Elevated LVMI at Baseline: Responder Rate by LVMI Reduction

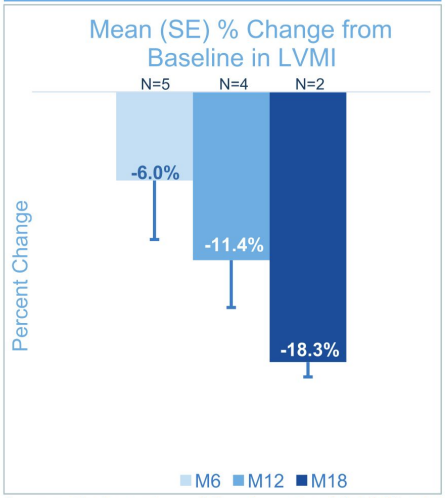


- Overall by month 12 (M12), 50% experienced a reduction in LVMI greater than 10%
- In participants with elevated LVMI at baseline, 75% experienced a reduction in LVMI greater than 10% by month 12

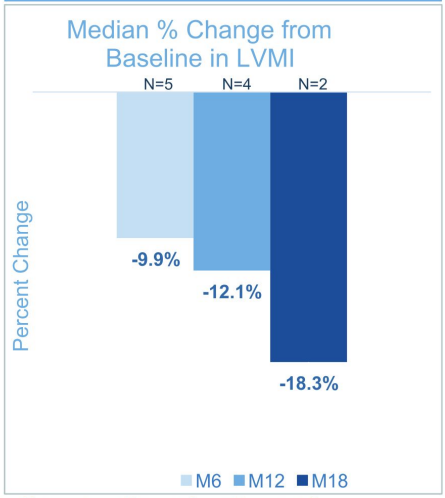
*Inclusive of participants with observed increases. LVMI, Left Ventricular Mass Index.
Note: Elevated defined as 1 or 2 standard deviations above mean for respective gender (from healthy volunteers) as referenced in Kawel-Boehm et al. *J Cardiovasc Magn Reson* (2020) 22:87.

Meaningful LVMI Change from Baseline With Pattern of Increased Improvement Over Time in Participants with Elevated LVMI

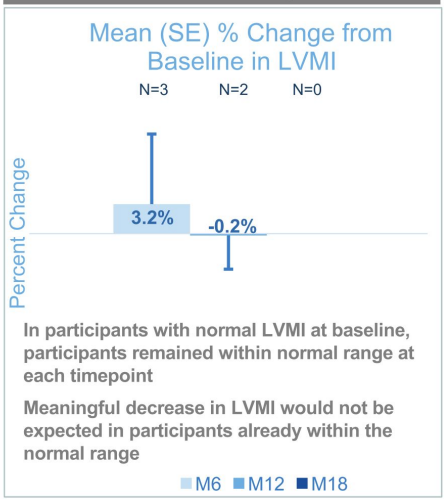
Elevated LVMI at Baseline: Mean Change



Elevated LVMI at Baseline: Median Change



Normal LVMI at Baseline: Mean Change

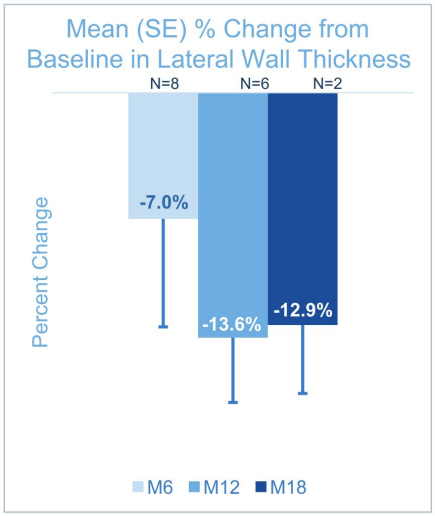


In participants with elevated LVMI at baseline, continued pattern of improvement with increased reduction over time with >10% reduction on average at 12 months

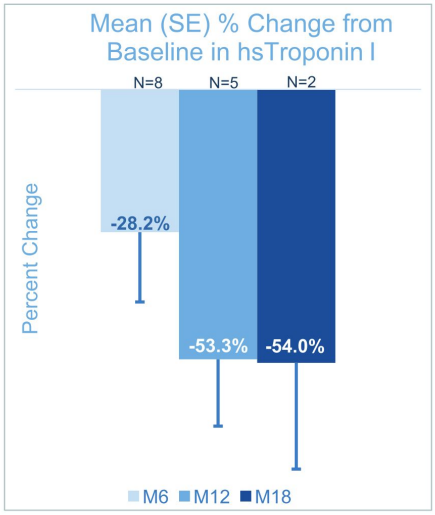
Note: Elevated defined as 1 or 2 standard deviations above mean for respective gender (from healthy volunteers) as referenced in Kawel-Boehm et al. *J Cardiovasc Magn Reson* (2020) 22:87.
Note: Standard Error of the Mean for Elevated LVMI at Baseline M6=4.0, M12=3.2, M18=1.0; For Normal LVMI at Baseline M6=7.6, M12=3.7

Average Change from Baseline in Other Key Cardiac Measures Demonstrates Pattern of Improvement with Increased Improvement Over Time

All Participants: Change in Lateral Wall Thickness



All Participants: Change in hs-Troponin I



- Continued pattern of improvement with increased reduction from 6 to 12 months
  - Reduction of >10% in lateral wall thickness from baseline in 4 of 6 participants at 12 months
  - Reduction of >25% in hs-troponin I from baseline in 4 of 5 participants at 12 months

Note: Standard Error of the Mean for Lateral Wall Thickness at Baseline M6=6.0, M12=3.6, M18=3.8; For Troponin at Baseline M6=13.7, M12=13.2, M18=21.0
Note: Troponin sample not available for one participant at 12 months.

Multiple Cardiac Assessments in Ongoing Studies of LX2006 Have Regulatory Precedent as Potentially Approvable or Supportive Endpoints

Key Assessment	*Ability to Impact*	Assessment Method	*Timepoints*
Transgene Expression (LCMS and IHC) *Regulatory Precedent as Approvable Endpoint*	✓	Cardiac Biopsy	3 Month(1)
Left Ventricular Mass Index *Regulatory Precedent as Approvable Endpoint*	✓	Cardiac MRI	Months 6,12, Long-Term Follow Up
Lateral Wall Thickness *Clinically Meaningful Endpoint*	✓	Cardiac MRI	Months 6,12, Long-Term Follow Up
Circulating Blood Biomarkers (hs-Troponin I) *Clinically Meaningful Endpoint*	✓	Blood Sample	Months 6,12, Long-Term Follow Up

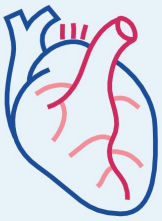
(1) Only evaluated in SUNRISE-FA.

Summary of Results and Next Steps for LX2006

- LX2006 (AAVrh10.hFXN) has been well tolerated with no treatment-related serious adverse events to date
- Improvements in key clinical parameters observed at 12-months:
  - 75% of participants with elevated LVMI at baseline experienced >10% reduction in LVMI (n=4)
  - 14% mean reduction from baseline in lateral left ventricular wall thickness (n=6)
  - 53% mean reduction from baseline in hs-troponin I (n=5)
- As of July 15, 2024, 13 participants dosed, including 1 participant in Cohort 3
  - SUNRISE-FA Data and Safety Monitoring Board endorsed proceeding to Cohort 3 dose level ($1.2x10^{12}$vg/kg); this cohort has started enrollment with 1 participant dosed, and will include at least 3 participants
  - The Weill Cornell investigator-initiated trial is currently enrolling in Cohort 2
- Previously disclosed data, and one additional cardiac biopsy from Cohort 2 will be shared at a scientific conference in Fall 2024

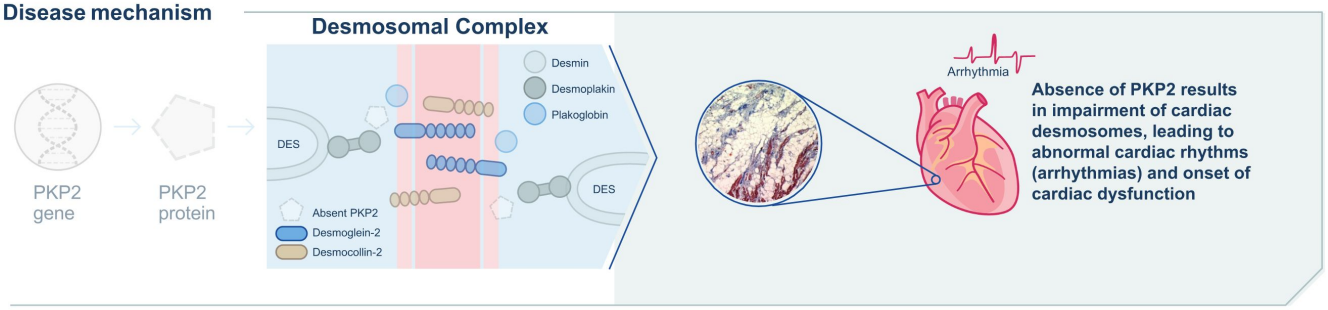
Note: Data as of interim clinical update shared July 15, 2024.

LX2020 (PKP2-ACM)

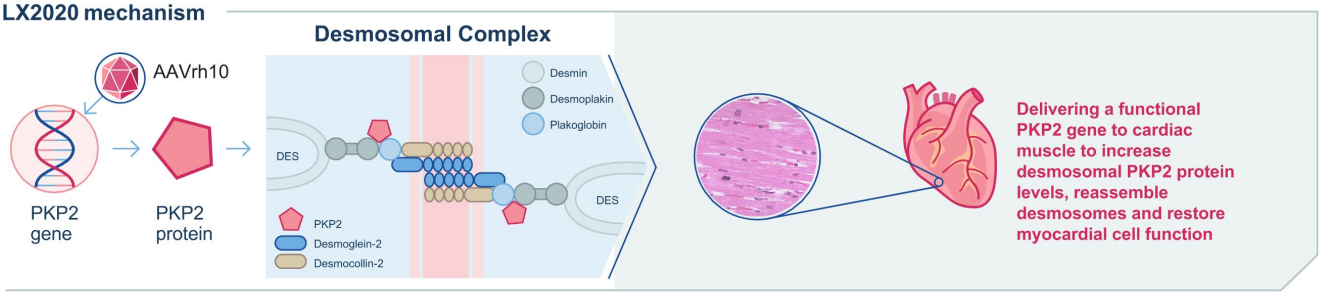


ACM Caused by Mutations in PKP2 and How LX2020 is Designed to Treat It

Disease mechanism



LX2020 mechanism



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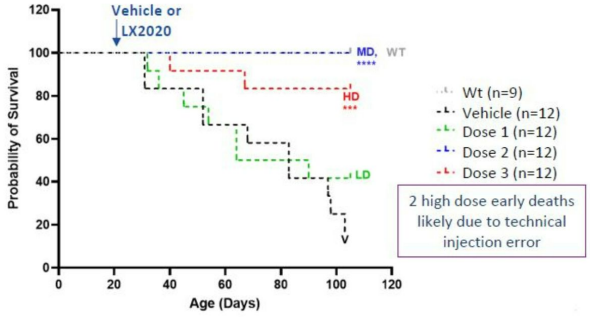
IND Clearance Supported by Robust Preclinical Package

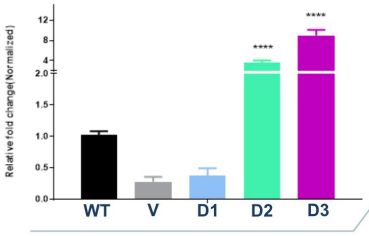
Robust Preclinical Package

- Murine studies utilizing CRISPR-Cas 9 edited model recapitulating PKP2-ACM disease features
- NHP safety study showed no toxicity at highest evaluated dose levels (low x10^{14} vg/kg)

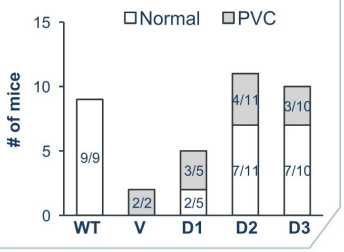
LX2020 Significantly Extended Survival in Severe Mouse Model



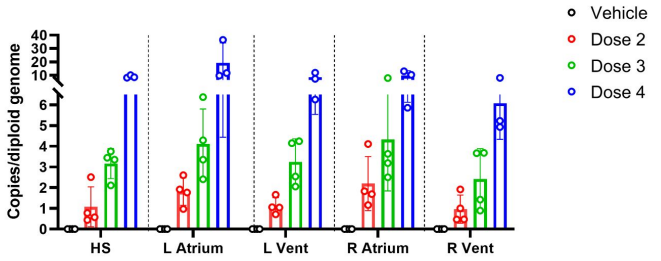
Quantification of PKP2 Expression in Severe Mouse Model



PVC Analysis in Severe Mouse Model

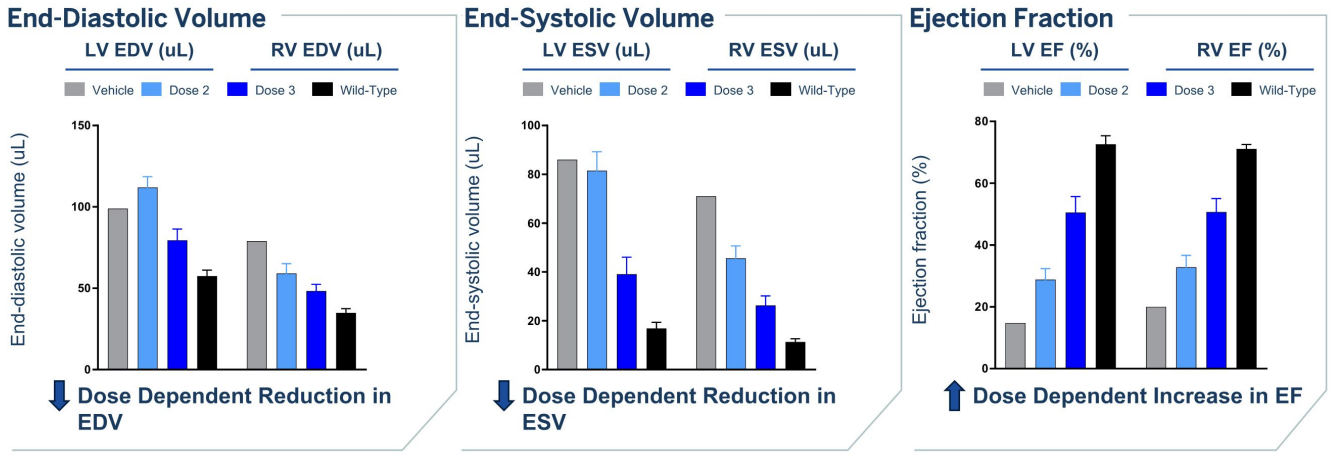


IND-Enabling NHP: VCN in Various Heart Regions



Note: PVC = premature ventricular contractions; VCN = vector copy number.

Quantitative MRI Analysis Showed Improvement in Cardiac Function in Homozygous Mouse Model



Quantitative MRI showed improved LV and RV ejection fraction and cardiac function in mid and high dose groups. RV improvements are most relevant as it is the primary ventricle impacted in PKP2-ACM

Note: LV = left ventricle; RV = right ventricle.

In Preclinical Studies LX2020 Successfully Impacted All Modifiable Elements of ACM Diagnosis and Risk Calculator

		LX2020 Preclinical Evidence
Arrhythmias	**Arrhythmia Burden** Daily Premature Ventricular Contraction (PVC) Count	⬇ **Ectopic Beats** (7/10 without PVC)
	Life-threatening Arrhythmia Events SCD, ICD Shocks, VT/VF Events	⬆ **Survival** (100%)
Repolarization & Depolarization	**Depolarization/Repolarization Abnormalities** T-wave Inversions/ QRS Complex	⬇ **QRS Interval** (18% reduction)
Cardiac Structure & Function	**Cardiac Contractility** RV Dysfunction and Enlargement	⬆ **Cardiac Fxn/EF** ⬇ **Cardiac Dilation**
	Cardiac Structure/Function Myocardial Tissue Integrity (Fibrosis, Calcifications, Fragility)	⬇ **Fibrosis, Calcifications, & Tissue Tearing**

LX2020 preclinical data demonstrated improvement across key areas for determining ACM diagnosis and risk profile

Note: PVC = premature ventricular contractions; VCN = vector copy number.

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LX2020 PKP2-ACM Phase 1/2 (HEROIC-PKP2) Overview

Key Features:

- 52-week, dose-ascending, open-label trial with long-term follow-up (5-years post dose)
- Vector: AAVrh10
- Route of Administration: systemic administration
- Immune Suppression: prednisone + rapamycin

Key Inclusion Criteria:

- Male or female 18-65 years of age
- Confirmed diagnosis of ACM with either 2010 Task Force Criteria or 2020 International Criteria for ACM as affected
- Documented PKP2 mutation
- Existing implantable cardioverter defibrillator (ICD) that is MRI compatible
- Minimum threshold of PVCs/24-hr

Trial Design

52-Week →

Cohort 1
n=3

$2.0x10^{13}$ vg/kg

Cohort 2
n=3 (potential for cohort expansion)

$6.0x10^{13}$ vg/kg

Endpoints

Primary Endpoint: Safety

Additional Endpoints:

- Change in ventricular arrhythmias and associated clinical events
- Change in 12-lead ECG
- Change in cardiac MRI and ECHO
- Change in cardiac biomarkers (including troponin and BNP)
- Change in Patient Symptoms (NYHA Functional Class and PROs)
- Change in PKP2 cardiac transduction & protein expression (cardiac biopsy)

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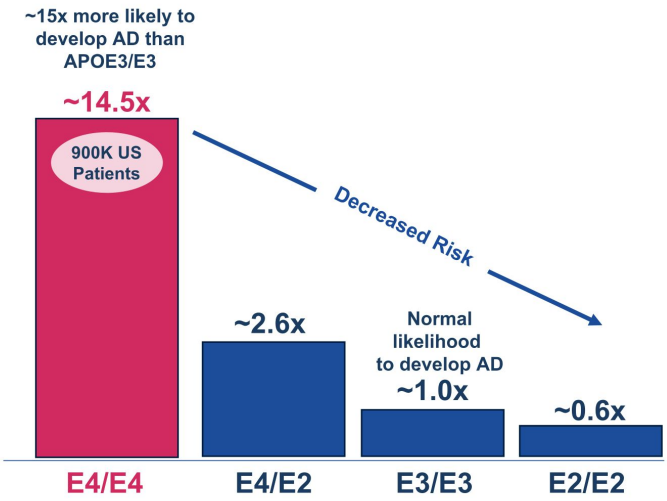
APOE4-Associated Alzheimer's Disease

APOE4 Homozygotes Represent a Patient Subgroup with Continued Unmet Need

Alzheimer's Disease Risk by APOE Genotype[1]



Unmet Need Persists Despite Recent Approvals

APOE4 homozygotes demonstrated lower efficacy results compared to heterozygotes and noncarriers and were associated with a higher incidence of ARIA-E

Reduced Efficacy[2]

CDR-SB[3]	APOE4 Noncarrier	APOE4 Heterozygote	APOE4 Homozygotes
Lecanemab	-0.75	-0.50	0.28
Donanemab	-0.76	-0.73	-0.41

Increased Incidence of Adverse Events[2]

ARIA-E	APOE4 Noncarrier	APOE4 Heterozygote	APOE4 Homozygotes
Lecanemab	5.4%	10.9%	32.6%
Donanemab	15.7%	22.8%	40.6%

Note: ARIA-E = amyloid-related imaging abnormalities characterized by edema and effusion.

(1) Yamazaki Y, et al. Nature Neurology Review, 2019.
(2) Van Dyck, et al. New England Journal of Medicine, 2022. Sims, et al. JAMA, 2023.
(3) Reduction in CDR-SB is improvement.

LX1001 Phase 1/2 Trial in APOE4 Homozygotes

Key Features:

- 52-week, dose-ranging, open-label trial with long-term follow-up (5-years post dose)
- Vector: AAVrh10
- Route of Administration: C1-C2 (between cervical vertebrae 1 and 2) or intracisternal injection
- Immune Suppression: corticosteroids prior to treatment and tapering following dosing

Key Inclusion Criteria:

- ≥50 yr APOE4 homozygotes
- Mild cognitive impairment to moderate dementia with biomarkers consistent with Alzheimer's disease

Endpoints

Primary Endpoint: Safety

Secondary Endpoint: Conversion of CSF APOE4 to APOE2/APOE4

Other Secondary Endpoints:

- CSF biomarkers: Aß42, T Tau and P Tau
- Amyloid and tau PET scans
- Quantitative MRI
- Cognitive testing

Trial Design

52-Week Follow-up

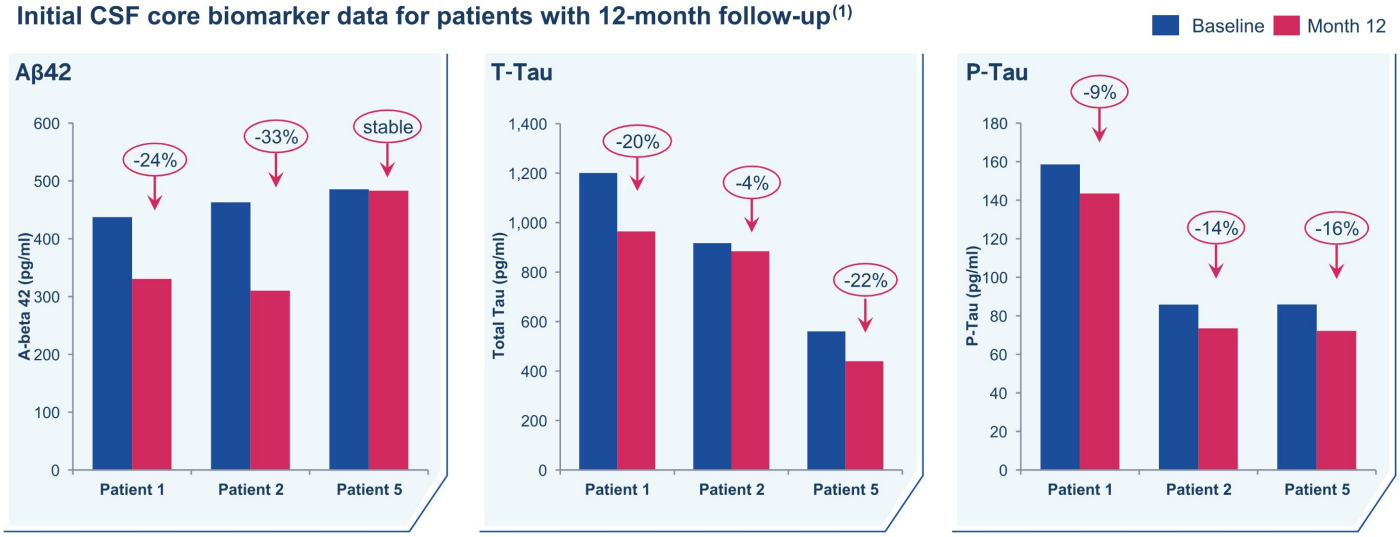
Cohort 1	Cohort 2	Cohort 3	Cohort 4
n=5	n=4	n=3	n=3
$1.4x10^{10}$ vg/ml CSF	**$4.4x10^{10}$ vg/ml CSF**	**$1.4x10^{11}$ vg/ml CSF**	
$5.7x10^{12}$ Total VGs	**$1.8x10^{13}$ Total VGs**	**$5.7x10^{13}$ Total VGs**	**$1.4x10^{14}$ Total VGs**

Study has completed enrollment of all 4 dose cohorts

Vector genomes measured using ddPCR.
Assumes average CSF in patient of 408.7 ml.

Initial LX1001 Low-Dose Cohort Data: CSF Core Biomarkers

Initial CSF core biomarker data for patients with 12-month follow-up(1)



Reduction in CSF total tau and phospho-tau were observed in all 3 patients, reduction in CSF Aβ42 was observed in 2 of the 3 patients

Note: Patient 3 transitioned to a long-term care-facility prior to Month 3 and unlikely to have follow-up efficacy data. Patient 4 was unable to travel to the study site for the month 6 and 12 visits.
(1) If a screening and baseline value was obtained the mean was used as the baseline.

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Significant Catalysts Across Lead Programs Supported by Strong Balance Sheet

Program	Upcoming Milestones	US Prevalence
LX2006 FA Cardiomyopathy	• Mid 2024: Interim Data Readout ✓ • Year End 2024: Update on ongoing regulatory engagements	~5K
LX2020 PKP2-ACM	• Late Q1/Early Q2 2025: Interim Data Readout (Cohort 1)	~60K
LX1001 Alzheimer's: APOE4	• October 2024: Interim Phase 1/2 Data Readout (CTAD Conference)	~900K
LX2021 DSP Cardiomyopathy	• 2024: Initiate IND-enabling Studies	~35K

Cash and marketable securities[1]	Projected runway into	Shares of common stock outstanding[2]
~$175M	2027	33.1M
Balance sheet as of June 30, 2024	More than 2 years of runway following key catalysts	Shares outstanding as of August 8, 2024

(1) Cash, cash equivalents and investments in marketable securities as of June 30, 2024.
(2) Shares outstanding as of August 8, 2024.

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Thank you