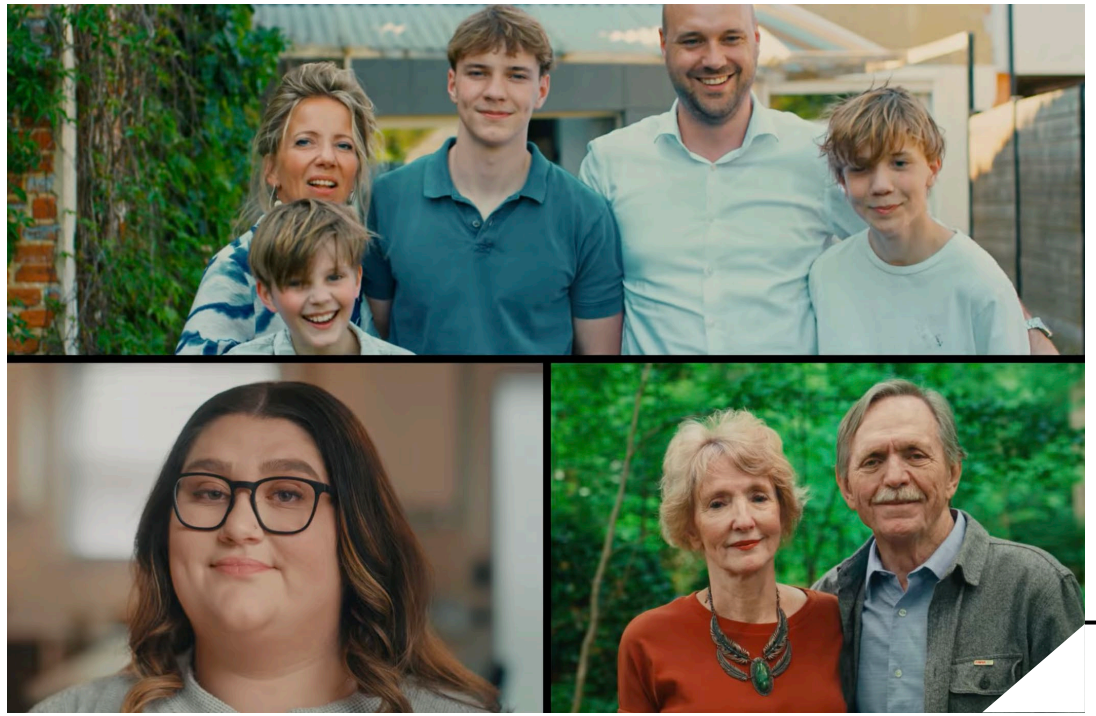
Lexeo Therapeutics
Corporate Overview

January 2026

Forward-looking statements

This presentation contains “forward-looking statements” within the meaning of the federal securities laws, including, but not limited to, Lexeo’s expectations and plans regarding its current product candidates and programs and the timing for receipt and announcement of data from its clinical trials, the timing and likelihood of potential regulatory approval, and expectations regarding the time period over which Lexeo’s capital resources will be sufficient to fund its anticipated operations and estimates regarding Lexeo’s financial condition. 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 global macroeconomic conditions and related volatility; 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 Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2025, filed with the SEC on November 5, 2025, 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

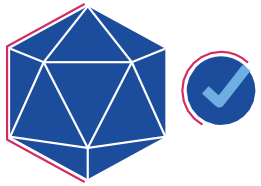
- **Genetic medicine leader with rare cardiac disease focus**
- **Proven experience in the clinic**
- **Platform designed for safety and scalability**

LEXEO therapeutics

Building a leading cardiac gene therapy platform

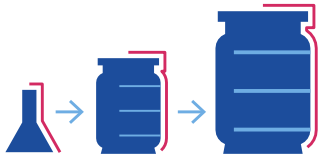
Genetic cardiac disease expertise

Leader in genetic medicine for inherited cardiac diseases



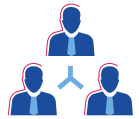
Differentiated AAVrh10 capsid

Proven cardiac tropism allows for lower doses and improved therapeutic index



Innovative AAV manufacturing

Optimized Sf9 baculovirus manufacturing platform designed to support future commercial scale-up



Operating experience

Deep cardiac genetic medicine know-how, anchored by two clinical and two preclinical programs

Strong financial position

Cash runway into 2028, supporting multiple value creating milestones

LEXEO therapeutics

Advancing cardiac genetic medicines in diseases with high unmet need

Market opportunity:

High unmet need
Cardiomyopathies have few disease-modifying therapies and high morbidity/mortality

White space
Cardiac gene therapy is less competitive, offering opportunity to establish leadership

Transformative potential
Lexeo's vision is to fundamentally change the course of inherited cardiac disease with a single infusion

Lexeo cardiac programs and expertise:

Clinical:

LX2006
Friedreich Ataxia Cardiomyopathy

LX2020
PKP2 Arrhythmogenic Cardiomyopathy

Proven clinical experience with 27 patients treated using AAVrh10

Pre-Clinical:

LX2021
Desmoplakin Cardiomyopathy

LX2022
Hypertrophic Cardiomyopathy

Deep expertise in genetic cardiac disease models and IND enabling studies

LEXEO therapeutics

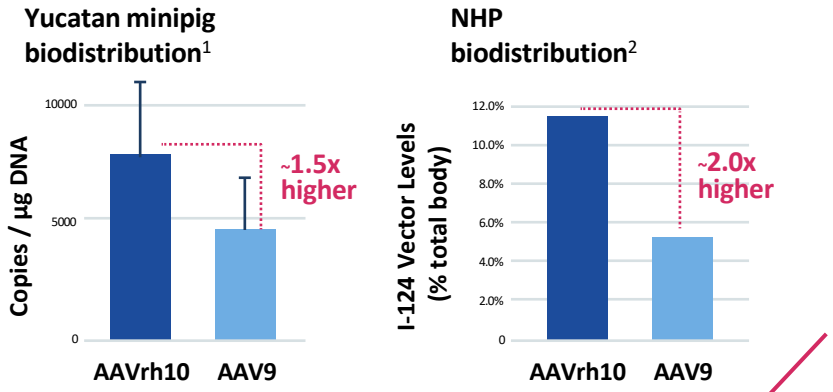
Lexeo's AAVrh10 is a highly differentiated capsid

AAVrh10 cardiac tropism → **Strong expression in the heart**

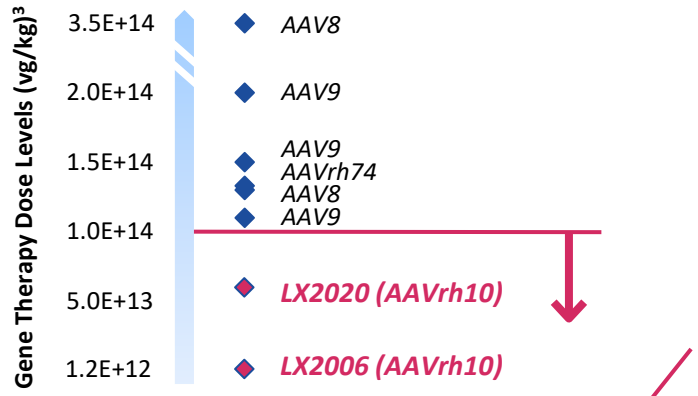
No history of clinically significant complement activation → **Reduced pre-dose immunosuppression**

Cardiac tropism can reduce systemic dose levels → **Potentially improved safety profile**

Distribution to the heart ~1.5x to 2.0x higher with AAVrh10 than AAV9

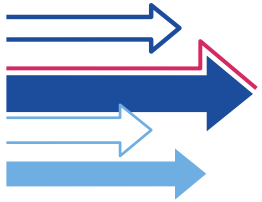


Majority of mortality and severe complement activation in gene therapy at doses ≥1.0E14 vg/kg



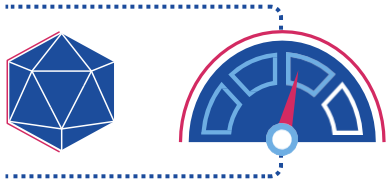
(1) Data presented at ASGCT 2023. (2) Ballon DJ et al, Human Gene Therapy, 2020. (3) Dose Levels (vg/kg): Lexeo LX2006 (1.2E+12), Lexeo LX2020 (6.0E+13), Zolgensma (1.1E+14), Astellas AT132 low dose (1.3E+14) and high dose (3.5+E14), Elevidys (1.3E+14), Neurogene NGN-401 high dose (3.0+E15 vg fixed, assumes patient weight of 20kg), Pfizer PF-06939926 (low dose 1.0E+14, high dose 3.0E+14, average shown).

Lexeo manufactures AAVrh10 utilizing an optimized Sf9 baculovirus process



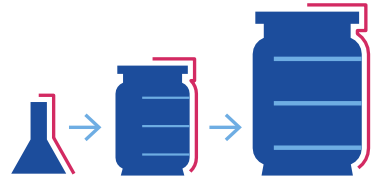
Innovative approach

- High yield, high quality Sf9 baculovirus manufacturing platform compared to conventional manufacturing (e.g. HEK based)
- LX2006 selected for **FDA CDRP program**, created to facilitate CMC registrational readiness and support faster patient access



Optimal potency

- Higher yields (1.0E15 vg/L)
- Greater downstream recovery (>55%)
- Fewer empty AAV capsids (<25%)
- Improved genomic purity owing to lack of plasmid transfections



Scalable manufacturing

- Sustainable and defined starting materials, similar to therapeutic protein process (e.g. cell banks, virus banks)
- Low overall complexity
- Enables robust commercialization
- Poised to deliver an industry-leading and potentially transformational COGS profile

LEXEO therapeutics

2025 year in review

LX2006

Friedreich Ataxia Cardiomyopathy

- **Announced positive data from Phase I/II studies**
- **Received FDA Breakthrough Designation**
- **Initiated CLARITY-FA natural history study**

LX2020

PKP2 Arrhythmogenic Cardiomyopathy

- **Completed enrollment in HEROIC Phase I/II study**
- **Shared interim Phase I/II safety and efficacy data from low dose cohort**

LEXEO therapeutics

- **Completed two financings totaling $234M of capital; secured runway into 2028**
- **Appointment of new CFO with commercial finance experience**
- **Partnership to advance novel cardiac RNA therapeutics**

Our pipeline: focused on diseases with significant unmet need and clear mechanisms

CARDIOVASCULAR

Programs:	Indication:	Gene:	Pre-clinical: Discovery	Pre-clinical: Preclinical	Clinical: Phase I/II	Clinical: Phase II/III	2026 milestones:
LX2006	FA[1] Cardiomyopathy	FXN	~5K US prevalence				• Early 2026 Regulatory Update • 1H-26 Initiate SUNRISE-FA 2 Pivotal Trial
LX2020	PKP2-ACM[2]	PKP2	~60K US prevalence				✓ Q1-26 Data Update • 2026 Regulatory Update • Q4-26 Data Update
LX2021	DSP[3] Cardiomyopathy	CX43	~35K US prevalence				✓ Research collaboration with J&J to explore targeted cardiac delivery of AAV gene therapy
LX2022	Hypertrophic Cardiomyopathy	TNNI3	~25K US prevalence				• IND enabling studies

Lexeo retains global rights across all programs.

(1) Friedreich ataxia. (2) Plakophilin 2 Arrhythmogenic Cardiomyopathy. (3) Desmoplakin.

LX2006

Friedreich Ataxia Cardiomyopathy (FA-CM)

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 cardiac and neurological manifestations

Cardiac dysfunction in FA presents as cardiac hypertrophy and subsequent heart failure(1); with up to **40% of adults with FA having left ventricular hypertrophy as defined by abnormal LVMI**(5)(6)

The only approved disease-specific treatment for FA was not evaluated for the treatment of cardiac dysfunction in clinical trials, **leaving significant unmet need within FA cardiomyopathy**(3)

Prevalence:

US: **~5,000**(2)

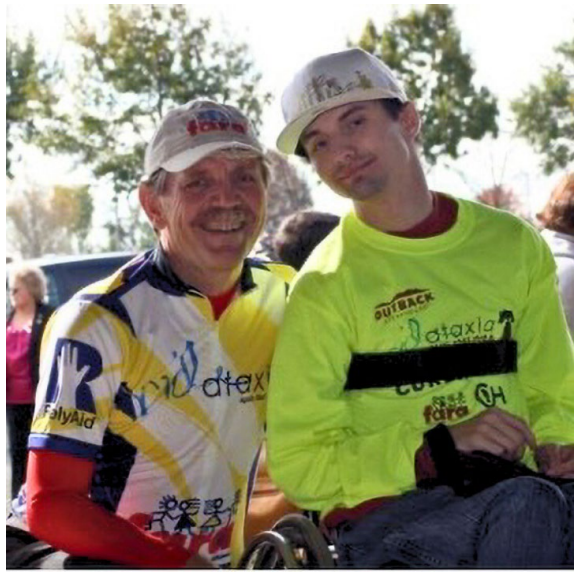
Global: **~15,000**(2)

Mortality:

Cardiac complications account for **up to 80%** of deaths in those with FA, with an average life expectancy of 35-40 years(1)(4)

Standard of care:

Omaveloxolone (SKYCLARYS®) is FDA-approved for FA based on neurologic endpoints; **cardiac efficacy was not established**(3)



Ron and his son, Keith, who passed from FA cardiomyopathy at age 24.

"There are no approved treatments for the cardiomyopathy of FA. **Time is of the essence.**"

- Ron Bartek, Co-founder of FARA

FARA Friedreich's Ataxia Research Alliance

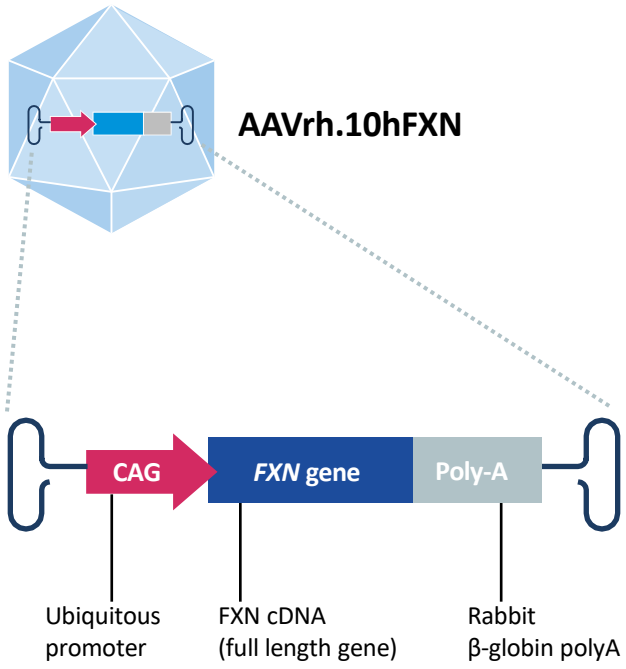
FA, Friedreich Ataxia; FXN, Frataxin; LVMI, Left Ventricular Mass Index.

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

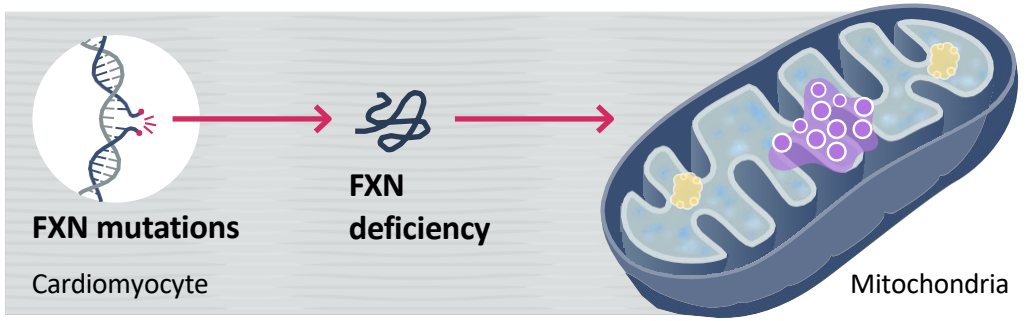
LEXEO therapeutics

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

LX2006 construct:

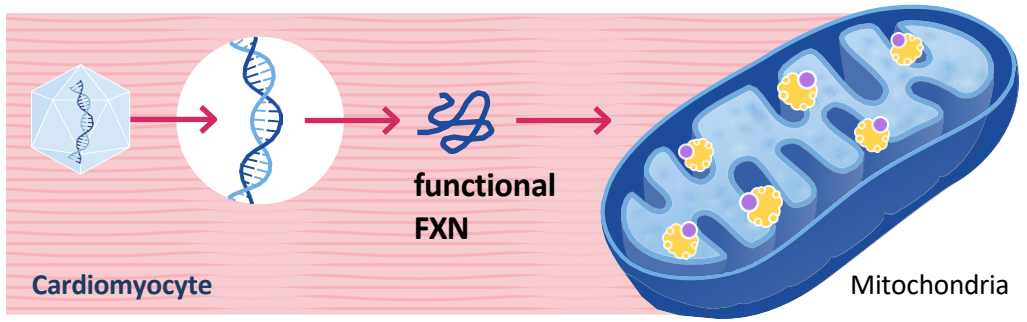


FA cardiomyopathy:



FXN 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.

Lexeo's role in advancing FA cardiomyopathy research

SUNRISE FA

Phase I/II Trial

Objective: Assess the safety and efficacy of LX2006 in individuals with cardiomyopathy associated with FA

Dose: 1.8E11 vg/kg (Cohort 1), 5.6E11 vg/kg (Cohort 2), 1.2E12 vg/kg (Cohort 3)

Key Endpoints: frataxin expression, LVMI, lateral wall thickness, troponin, mFARS

Status: Ongoing (fully enrolled)

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

CLARITY FA

Observational Natural History Study

Objective: Learn about how heart disease develops and worsens in individuals with FA

Dose: N/A

Key Assessments: LVMI, lateral wall thickness, troponin, mFARS, other biomarkers, cMRI and functional measures

Status: Ongoing (actively recruiting)

SUNRISE FA2

Phase III Pivotal Trial

Objective: Assess the safety and efficacy of LX2006 in individuals with cardiomyopathy associated with FA

Dose: 1.2E12 vg/kg

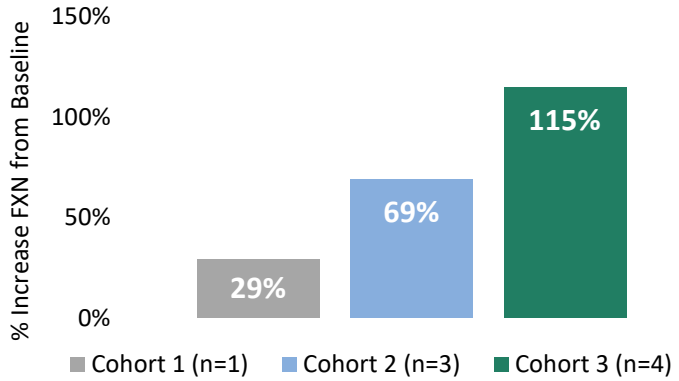
Primary Endpoints: Any increase from baseline frataxin expression and >10% LVMI reduction measured at time point earlier than 12 months

Status: To be initiated in 1H-26

LEXEO therapeutics

LX2006 clinical data show sustained or deepening improvements in the majority of participants across both cardiac and neurologic measures of FA

Mean FXN change from baseline



- Cardiac frataxin (FXN) increased by LCMS with dose-dependent response
- All subjects demonstrate an increase from baseline, **exceeding FDA-aligned threshold for pivotal study**

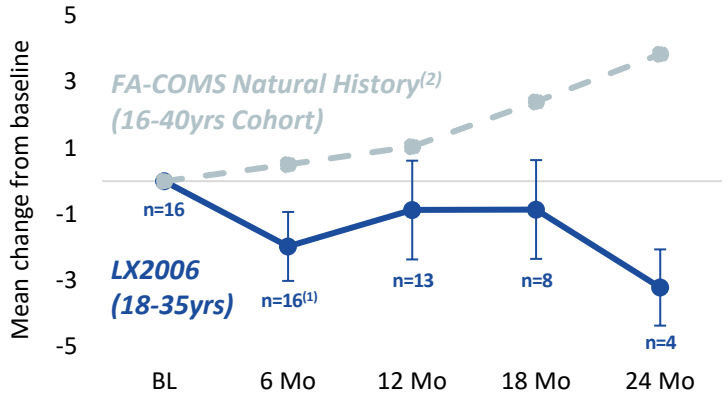
Cardiac MRI

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

- **Exceeding 10% FDA-aligned threshold for pivotal study** at 12 months and earlier

FA functional improvement: mFARS



- **11 of 16 participants improved or stabilized** relative to baseline mFARS at latest visit
- Evidence of neurological functional improvement, compared to natural history progression of disease

LX2006 generally well tolerated

- LX2006 generally well tolerated across 17 participants dosed with no Grade 3+ SAEs to date
- No clinically significant complement activation
- Minimal, transient LFT elevations; no participants above 3X upper limit of normal
- 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

FXN, Frataxin; LCMS, Liquid chromatography mass spectrometry.
FXN expression assessed with academic LCMS assay, assay validation in progress for pivotal study.
Note: Natural history for illustrative purposes only. Differences exist between trial designs and participant characteristics, and caution should be exercised when comparing data across unrelated studies.
(1) Participant 11 6-month visit not conducted due to hurricane; 3-month visit used for mean calculations. (2) Patel, M. et al. Ann Clin Transl Neurol, 2016. 3: 684-694. Progression of Friedreich ataxia: quantitative characterization over 5 years.https://doi.org/10.1002/acn3.332

LX2020

Plakophilin-2 Arrhythmogenic Cardiomyopathy (PKP2-ACM)

Arrhythmogenic cardiomyopathy caused by mutations in the *PKP2* gene: devastating genetic heart disease with clearly defined mechanism

PKP2-ACM is a **rare, genetic cardiac disease** caused by loss of function mutations in the *PKP2* gene

Progressive replacement of cardiac muscle with fatty fibrotic tissue, with an **increased risk of ventricular arrhythmias and sudden cardiac death (SCD) due to disrupted cardiac electrical signals**(1)(2)

Approximately 23% of individuals experience **SCD as the presenting symptom** and individuals often suffer from **anxiety and reduced quality of life**(3)(4)

ICDs are commonly utilized but **do not halt disease progression**. Individuals experience ongoing arrhythmias, along with both appropriate and inappropriate shocks necessitating escalating treatments, **underscoring severe unmet need**(2)(3)

Prevalence:

US **~60,000**

Mortality:

23%

of individuals experience SCD as presenting symptom

Standard of care:

Current management methods are focused on relieving symptoms and preventing SCD, **and do not address the underlying cause of ACM.**

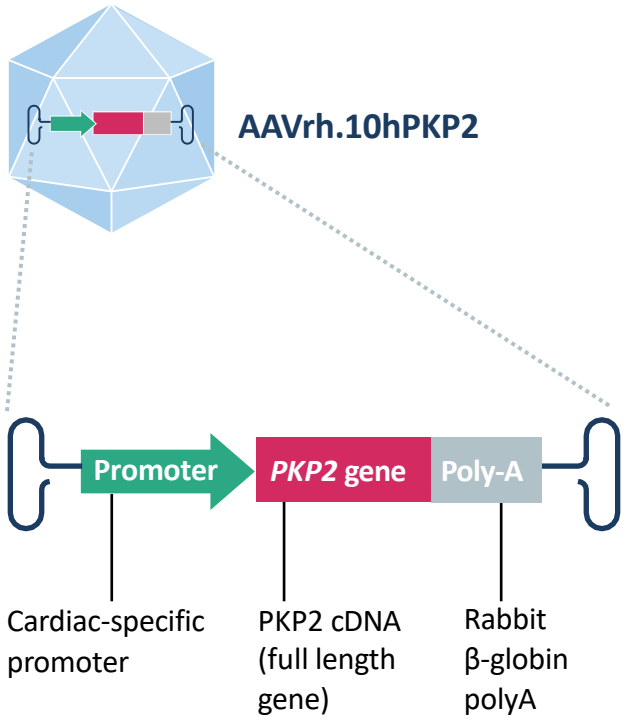
ACM, arrhythmogenic cardiomyopathy; ARVD/C, arrhythmogenic right ventricular dysplasia/cardiomyopathy; ICD implantable cardioverter defibrillator; SDC sudden cardiac death.

(1) Cedars-Sinai ARVC overview. (2023). (2) Corrado et al. (2017). (3) Dalal et al. (2005). (4) Day, Circulation: Cardiovascular Genetics (2012).

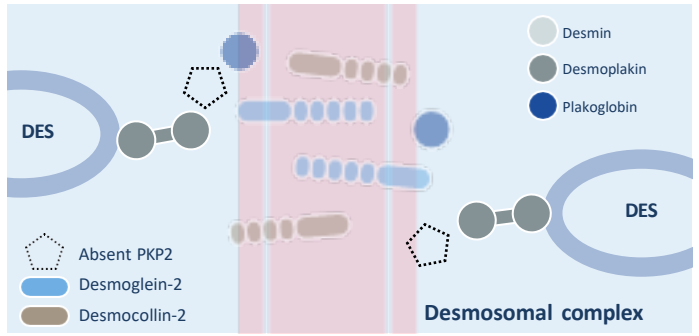
LEXEO therapeutics

Mutations in the *PKP2* gene are the most common genetic cause of ACM; LX2020 delivers a full-length *PKP2* gene to cardiomyocytes, restoring the desmosome

LX2020 construct:

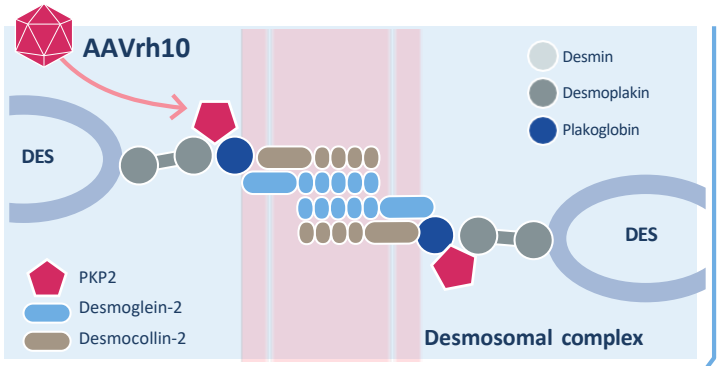


PKP2-ACM:



Absence of PKP2 results in impairment of cardiac desmosomes, leading to abnormal cardiac rhythms (arrhythmias) and onset of cardiac dysfunction

LX2020 mechanism:



PKP2 expression **is expected to restore the balance of desmosomal proteins** by scaffolding adjacent cell-cell junctional proteins

The restoration of PKP2 may lead to **improvement in cardiac electrical and mechanical function** as well as **inhibit further structural damage**

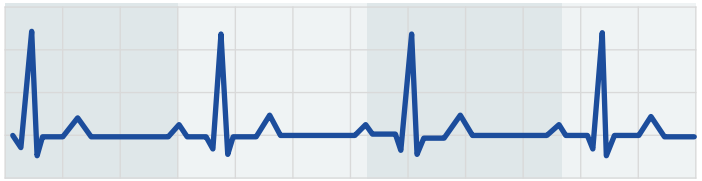
ACM, arrhythmogenic cardiomyopathy.

Individuals with ACM experience high arrhythmia burden with a spectrum of severity

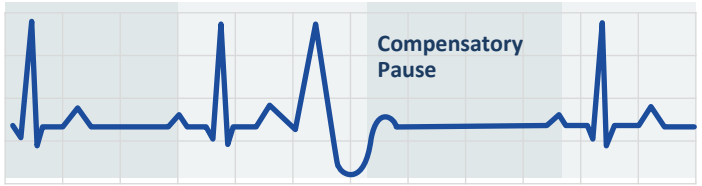
Severity of Arrhythmias

Premature Ventricular Contractions (PVCs)

Normal Sinus Rhythm

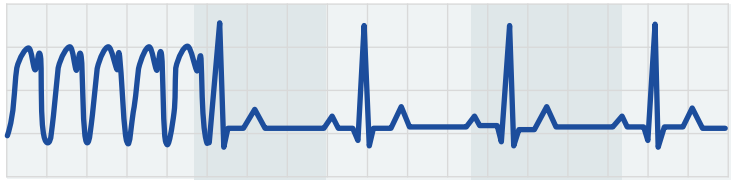


Premature Ventricular Contraction (PVC)



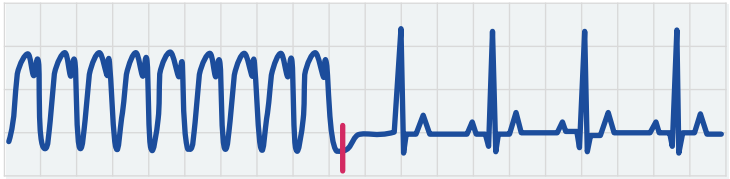
- Early indicator of electrical instability that **can trigger more severe/sustained arrhythmia**

Non-Sustained Ventricular Tachycardia (NSVT)



- **≥3 ventricular beats in a row, lasting under 30 seconds**; self-terminating
- Closely associated with **increased risk of sustained VT, ICD shock and SCD[1]**; impacts patient anxiety and quality of life

Sustained VT / ICD Shock



Ventricular Tachycardia | Cardioversion Shock | Sinus Rhythm

- ≥3 ventricular beats in a row **lasting over 30 seconds**
- **Can cause collapse, cardiac arrest or SCD**; sustained VT may be terminated by ICD shock to restore normal rhythm

SCD, sudden cardiac death; ICD, implantable cardioverter defibrillator; VT, ventricular tachycardia.

(1) Gasperetti A, et al. *JAMA Cardiology*, 2022; 7

Lexeo's role in advancing PKP2-ACM research

HEROIC PKP2

Phase I/II Trial

Objective: Assess the safety and efficacy of LX2020 in individuals with PKP2-ACM

Dose: 2.0E13 vg/kg (Cohort 1), 6.0E13 vg/kg (Cohorts 2, 3)

Key Endpoints: PKP2 expression, VT, PVC, QRS, T-wave inversion, cardiac function, PROs

Status: Ongoing (fully enrolled, n=10)

SNAPSHOT PKP2

Retrospective EMR Review and Prospective Observational Natural History Study

Objective: Evaluate the clinical burden of illness for patients with PKP2-ACM, and prospectively evaluate changes in key cardiac parameters and patient-reported outcome measures (PROs) associated with PKP2-ACM progression

Dose: N/A

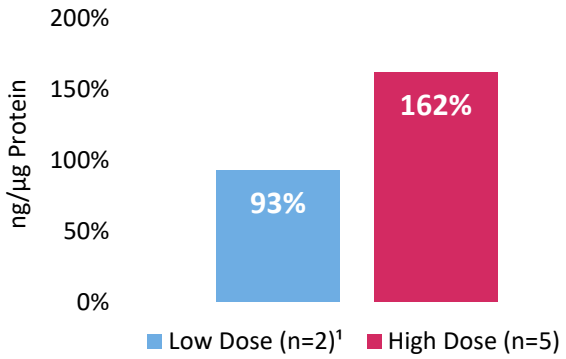
Key Assessments: VT, PVC, QRS, T-wave inversion, cardiac function, PROs

Status: Ongoing (actively recruiting)

LEXEO therapeutics

Interim results demonstrate increased PKP2 expression and potential for LX2020 to reduce severe arrhythmia burden

Mean PKP2 change from baseline (western blot, GAPDH normalized)

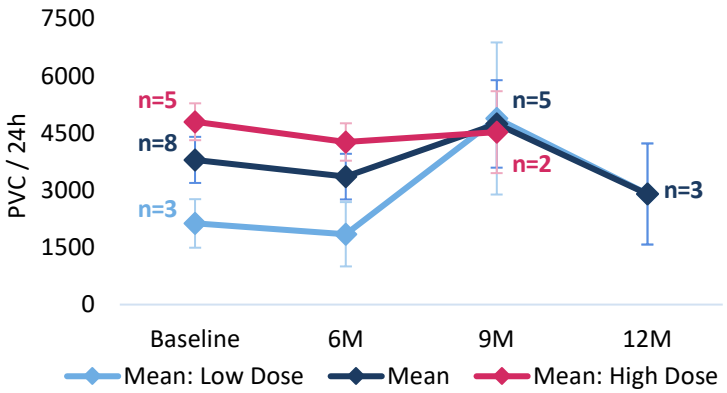


Patient reported outcomes

4 of 5

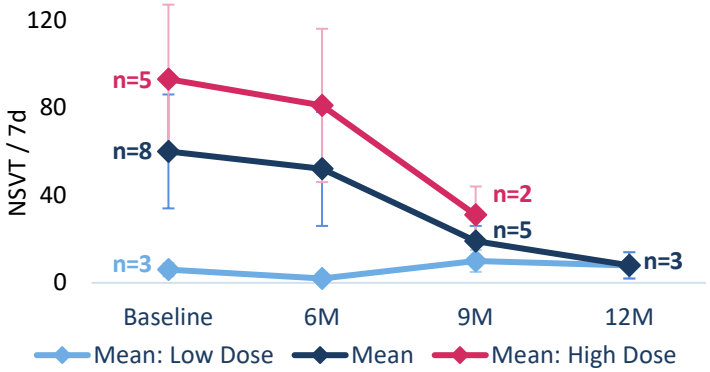
participants at high dose report improvement relative to baseline on the Patient Global Impression of Change (PGIC) scale

Mean PVC change



- **PVCs reduced or stabilized in majority of participants** with >6 months of follow up
- **-14% improvement** in mean PVCs at latest visit in high-dose cohort

Mean NSVT change



- **NSVT reduced or stabilized in majority of participants** with >6 months of follow up
- **-22% improvement** in mean NSVT at latest visit in high-dose cohort

LX2020 generally well tolerated

- LX2020 generally well tolerated across ten participants dosed
- No clinically significant complement activation
- Elevations in liver function tests (LFT) observed in five participants at the high-dose, treated successfully per the trial protocol with no complications or hospitalization[(2)]
- No participants discontinued from study
- One previously disclosed Grade 3 serious adverse event of sustained ventricular tachycardia (VT) was observed three months after dosing. This event is consistent with the natural course of PKP2-ACM and its known clinical manifestations. The participant was successfully treated with anti-arrhythmic medication and discharged with no additional intervention required.

(1) Participant 3 elected not to undergo a post-treatment biopsy (2) Three participants' elevations occurred following steroid tapering and resolved with re-introduction of low-dose prednisone; two participants' elevations occurred prior to steroid tapering and resolved with increased prednisone and sirolimus treatment; all elevations have since resolved without other complications or hospitalization, and no other medications were required for resolution

Lexeo is also advancing two preclinical cardiac gene therapy programs

LX2021

Desmoplakin Cardiomyopathy

- High unmet need characterized by extensive fibrosis, high arrhythmic risk, and high heart failure burden
- 30-50% mortality within 5 years of diagnosis for dilated phenotype
- ~35K patients in U.S.
- IND-enabling studies and regulatory engagement expected in 2026

LX2022

Hypertrophic Cardiomyopathy

- TNNI3 variants compose 3-5% of all HCM cases, causing cardiomyopathy, clinical heart failure and shortened lifespan
- Non-obstructive phenotype, often with preserved EF; myosin inhibitors not effective
- ~25K patients in U.S.

+2026 research collaboration with Johnson & Johnson exploring novel routes of administration for cardiac AAV gene therapy to maximize safety and efficacy

LEXEO therapeutics

Lexeo – a leader in cardiac gene therapy

1. Leader in cardiac genetic medicine addressing **high unmet need** and **clear market opportunity**
2. **Catalyst rich 2026** with multiple key milestones expected across **two clinical stage programs**
3. Differentiated **AAVrh10 capsid** and innovative **Sf9 baculovirus manufacturing** platform
4. **Advancing towards pivotal stage**; Phase III trial in FA-CM expected to initiate in 2026 with potential path to accelerated approval
5. Strong financial position with **cash runway into 2028**

LEXEO therapeutics

LEXEO therapeutics

Thank You