

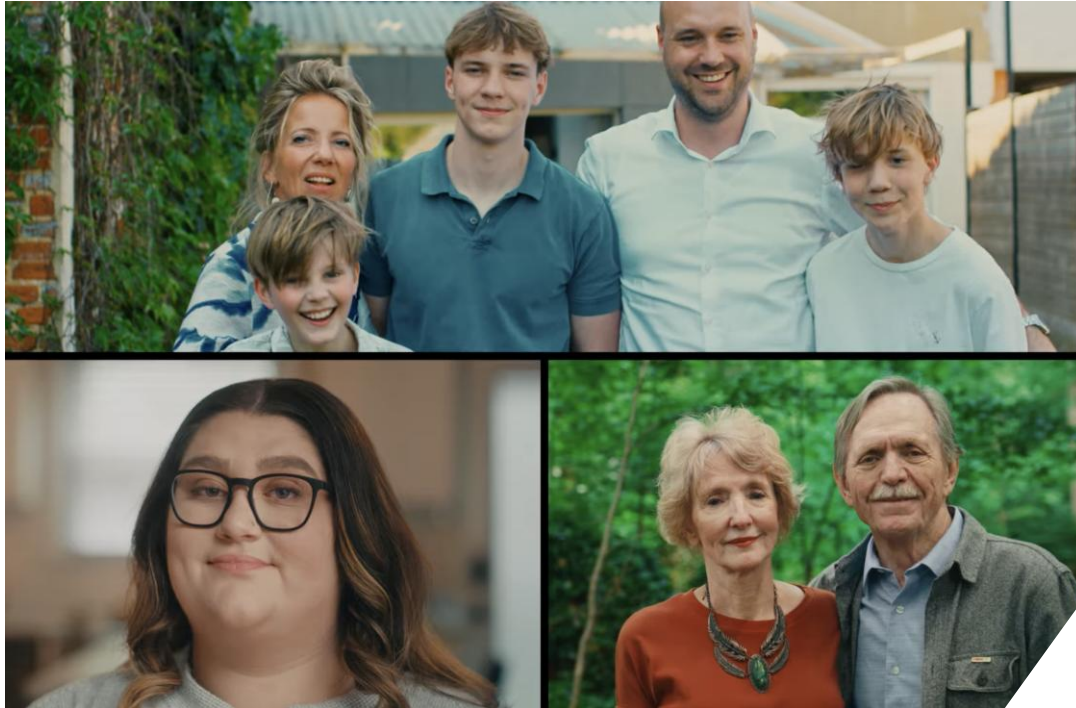
Lexeo Therapeutics Corporate Overview

May 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 Annual Report on Form 10-K for the annual period ended December 31, 2025, filed with the SEC on March 30, 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.



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

— Individuals and families impacted by Friedreich ataxia



Genetic medicine leader with rare cardiac disease focus



Proven experience in the clinic



Platform designed for safety and scalability



Lexeo: Advancing cardiac genetic medicines in diseases with high unmet need



Focus:

Leveraging gene therapy to address devastating cardiac diseases with no existing disease-modifying treatments

LX2006

Friedreich Ataxia Cardiomyopathy

- Only program with clinical-stage data in FA cardiomyopathy, which accounts for death in up to 80% of people with FA
- Interim clinical data demonstrate encouraging safety profile and evidence of meaningful cardiac and functional benefit, including improvements in cardiac structure, biomarkers, and functional outcomes as well as improvements in neurologic measures of FA such as mFARS
- Submitted the final registrational trial design and SAP in February 2026, awaiting final feedback from FDA; pivotal study initiation expected in the second quarter of 2026

LX2020

PKP2 Arrhythmogenic Cardiomyopathy

- Potential best-in-class treatment for PKP2-ACM; ~60K people in US with no disease-modifying treatment available
- Interim clinical data show encouraging early signals on efficacy and safety measures across patients dosed in the low and high dose cohorts
- 12-month data update for all high dose participants expected in Q4 2026; regulatory engagement expected in 2026.

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 gene¹.



With a typical age of onset between 5 and 15 years², 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 disease³



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 worldwide²

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.
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4 - Reetz, K., et al. Lancet Neurol, 2025;24(7):614-624.

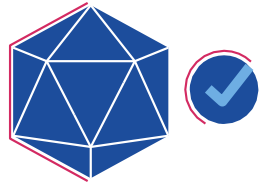
5 - Indelicato, E., et al. Mov Disord, 2024;39(3), 510–518.
6 - Clinical Management Guidelines for Friedreich Ataxia. Chapter 4. The heart and cardiovascular system in Friedreich ataxia. 2022.
7 - Lexeo Therapeutics, Data on File, 2025.

Building a leading cardiac gene therapy platform



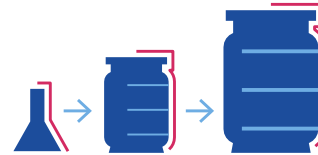
Genetic cardiac disease expertise

Leader in genetic medicine for inherited cardiac diseases



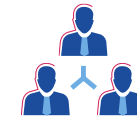
Differentiated AAVrh10 capsid

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

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's AAVrh10 is a highly differentiated capsid

Cardiac tropism of AAVrh10 may allow lower doses for cardiac gene therapy



AAVrh10 cardiac tropism may allow for lower doses compared to other vector serotypes while achieving targeted transgene biodistribution



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

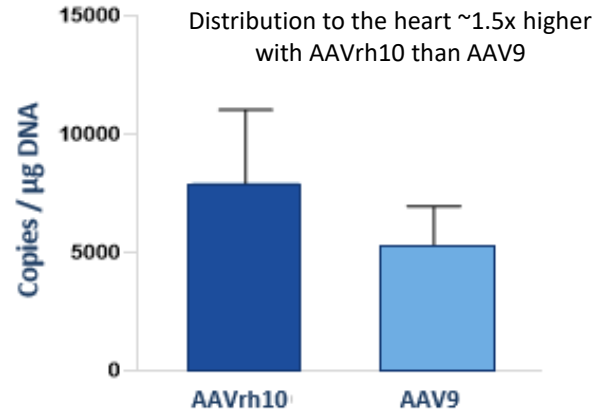


AAVrh10 has been utilized systemically across multiple Lexeo clinical programs with **no clinically significant complement activation**; both LX2006 and LX2020 have been generally well-tolerated to date

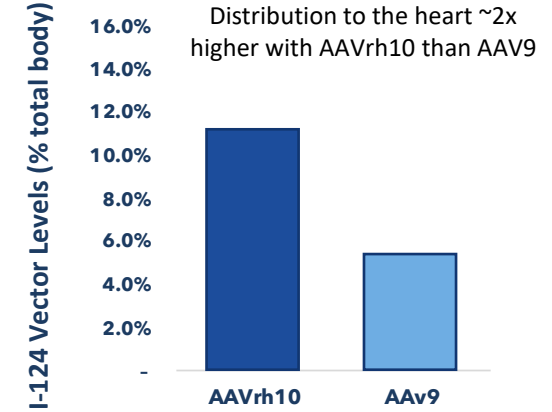
Compelling Cardiac Tropism



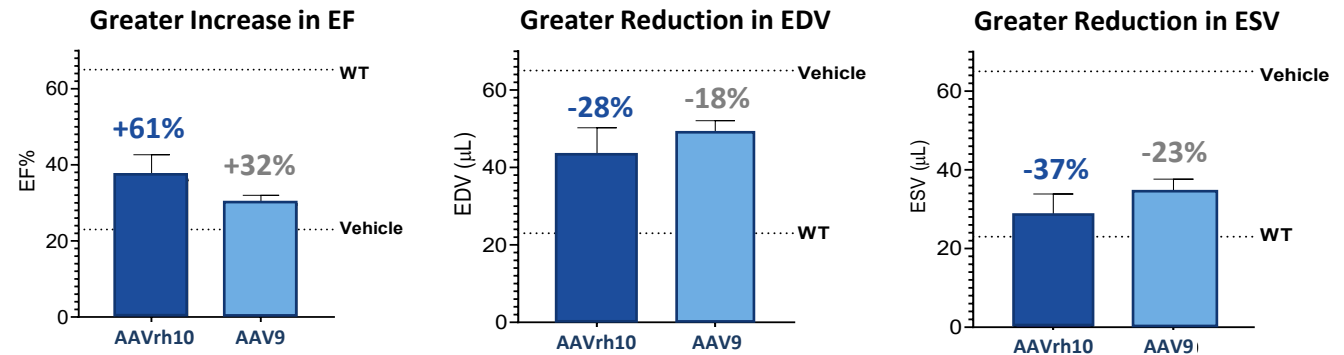
Yucatan Minipig Biodistribution⁽¹⁾



NHP Biodistribution⁽²⁾



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.

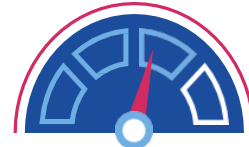
Lexeo manufactures AAVrh10 utilizing an optimized Sf9 baculovirus process

Innovative approach

- High yield, high quality Sf9 baculovirus manufacturing platform compared to conventional manufacturing (e.g. HEK based)

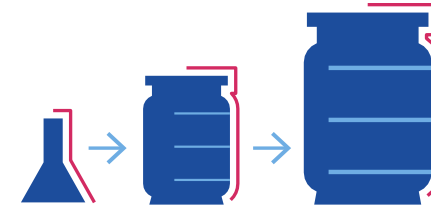


- LX2006 selected for **FDA CDRP program**, created to facilitate CMC registrational readiness and support faster patient access



Optimal potency

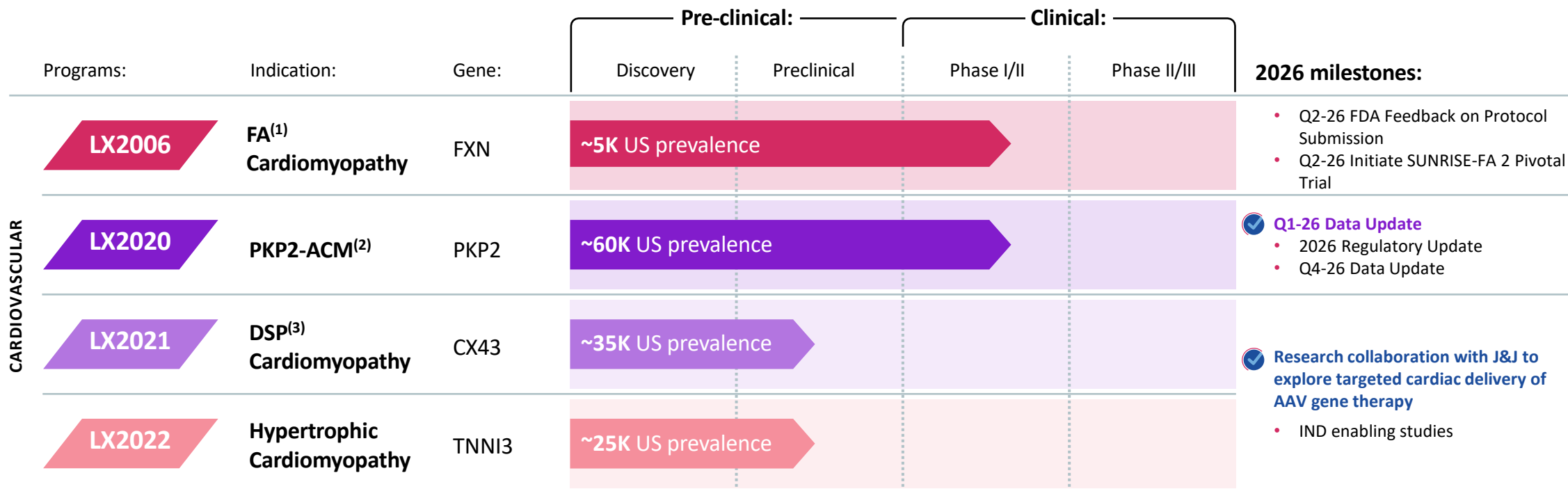
- Higher yields (1.0E15 vg/L)
- Greater downstream recovery (>55%)
- Fewer empty AAV capsids (<25%)
- Improved genomic purity owing to lack of plasmid transfections



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

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



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 gene¹.



With a typical age of onset between 5 and 15 years², 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 disease³



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 worldwide²

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 LVMI⁶

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

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5 - Indelicato, E., et al. Mov Disord, 2024;39(3), 510–518.
6 - Lexeo Therapeutics, Data on File, 2025.

Timely, multidisciplinary care is critical to diagnose and manage FA-CM

Individuals with FA typically present with cardiac symptoms in adolescence, and face an average life expectancy of 35-40 years



Symptom onset

Early signs often associated with the onset of ataxia

~5% of young children present with cardiac symptoms years before ataxia²



Journey to diagnosis

Journey to diagnosis with genetic test can take years

Guidelines recommend an EKG and ECHO at diagnosis and annually⁵



Cardiac dysfunction

Almost all individuals with FA will develop cardiomyopathy or cardiac dysfunction during their lifetime¹



Life expectancy

Cardiac dysfunction is the cause of death in 60-80% of those with FA, often occurring by mid-30s^{3,4}

Ron Bartek 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 | Friedrich's Ataxia Research Alliance

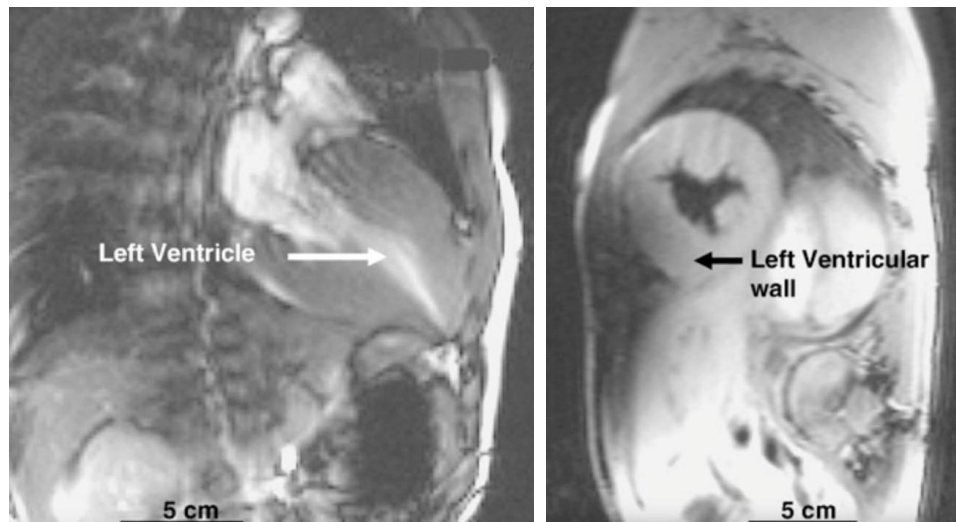
1 - Regner S, et al. American Journal of Cardiology, 2012.
2 - Norrish G., et al. Friedrich's ataxia-associated childhood hypertrophic cardiomyopathy: a national cohort study. Archives of disease in childhood, 107(5), 450-455, 2022.

3 - Subramoney S, et al. MDA Clinical and Scientific Conference, 2023.
4 - Pousset, F. et al. JAMA Neurol, 2015;72(11):1334-1341.
5 - Clinical Management Guidelines for Friedreich Ataxia. Chapter 4. The heart and cardiovascular system in Friedreich ataxia. 2022.

Elevated LVMI predicts mortality in FA and is not expected to decrease significantly without intervention

Increases in LVMI independently predict mortality in Friedreich Ataxia (FA)

Natural history study showed a **19%** higher risk of death per 10g/m² (HR 1.19; 95% CI)¹



MRI of individual with FA cardiomyopathy demonstrating significant hypertrophy.

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

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

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

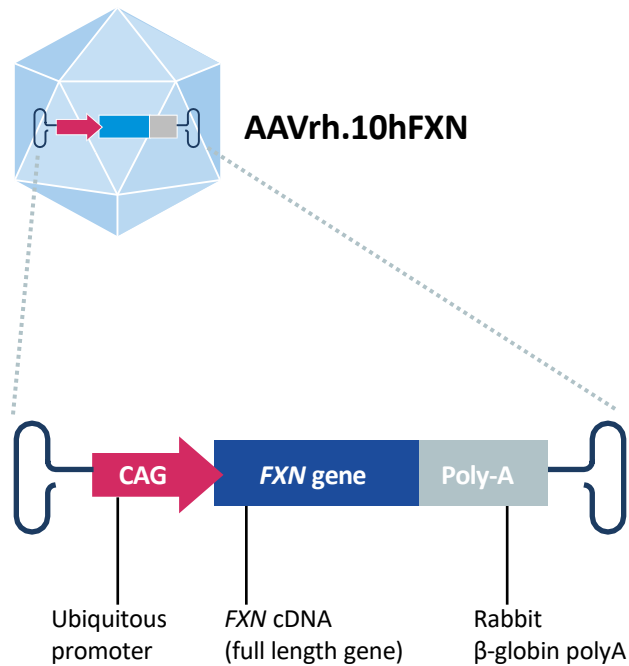
- Concentric hypertrophy, with increased left ventricular mass and wall thickness, is a hallmark of FA cardiomyopathy¹
- In FA and many other cardiac diseases, elevated LVMI is not expected to significantly decrease without intervention^{1,3} – and abnormal LVMI is closely correlated with poor outcomes²
- Reduction in LVMI may improve cardiac outcomes; FDA alignment on endpoint for pivotal trial in FA cardiomyopathy

HR - Hazard Ratio; CI - Confidence Interval; LVMI - Left Ventricular Mass Index.
 Note: 10g/m² represents approximately 10% change in LVMI based on echocardiography measurements of upper bound of normal (105 g/m²).

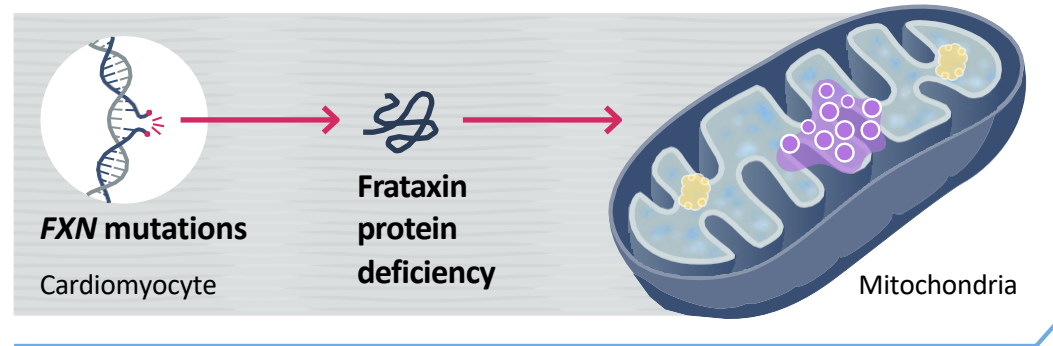
1 - Pousset, F. et al. *JAMA Neurol*, 2015;72(11):1334-1341.
 2 - Includes heart failure with preserved ejection fraction, Shah et al, *Journal of American College of Cardiology*, 2019; hypertensive cardiomyopathy, Muiesan et al, *Hypertension*, 2004; Fabry disease, Orsborne et al, *Journal of American College of Cardiology*, 2022; and obstructive hypertrophic cardiomyopathy, Hegde et al, *Journal of American College of Cardiology*, 2021.
 3 - Hughes DA, et al. *J Med Genet*, 2017;54:288-296; Migalastat; Solomon S, et al. *Circulation*, 2018. Patisiran; Saberi S, et al. *Circulation*, 2021;143:606-608. Mavacamten; Data on file.

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

LX2006 construct:

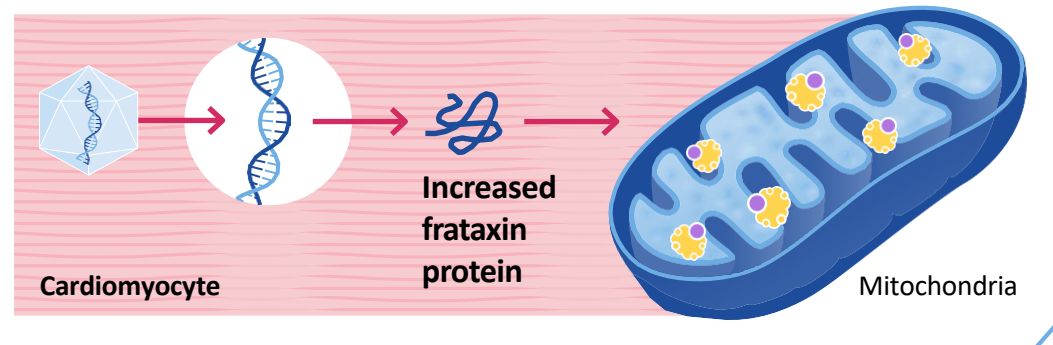


FA cardiomyopathy:



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**

LX2006 is being evaluated in parallel Lexeo-sponsored SUNRISE-FA and Weill Cornell investigator-initiated trials

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

 Cohort 1
1.8x10¹¹ vg/kg

 Cohort 2
5.6x10¹¹ vg/kg

 Cohort 3
1.2x10¹² vg/kg

2

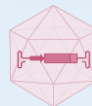
Key Inclusion Criteria



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 / Reported
Outcomes
(mFARS, KCCQ)



FXN Protein Expression
Assessed Only in SUNRISE-FA

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

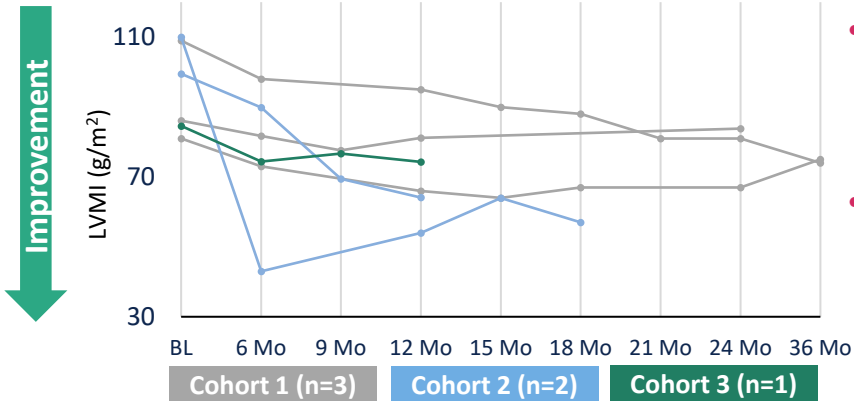
CPET, Cardiopulmonary Exercise Testing; hsTnI, High Sensitivity Troponin I; IHC, Immunohistochemistry; LCMS, Liquid Chromatography Mass Spectrometry; LVMI, Left Ventricular Mass Index.

Note: LX2006 is administered systemically; participants receive immune suppression with prednisone beginning on the day prior to treatment through 14 weeks following LX2006 administration.

Note: 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.

LX2006 clinical data show sustained or deepening improvements across both cardiac and neurologic 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

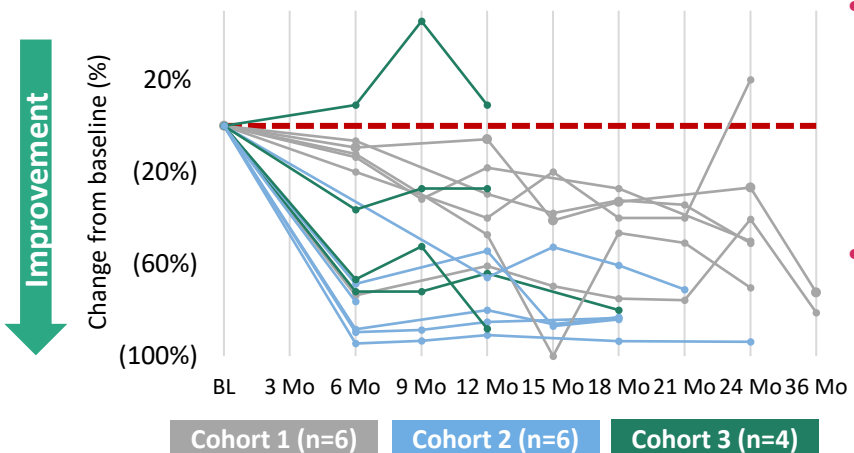
Mean LVMI Change

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):

- **Exceeding 10% FDA-aligned threshold for pivotal study at 6 months**

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



- **16 of 17 participants have significantly reduced or stable troponin I, excluding participant with myocarditis²**
- 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.

Cardiac function improvement observed in individual with later stage cardiomyopathy

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

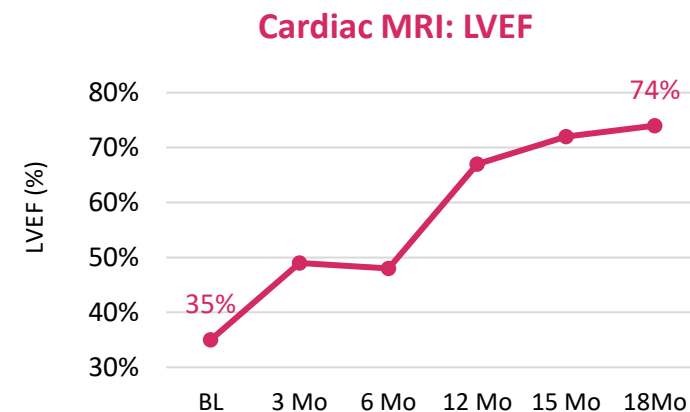
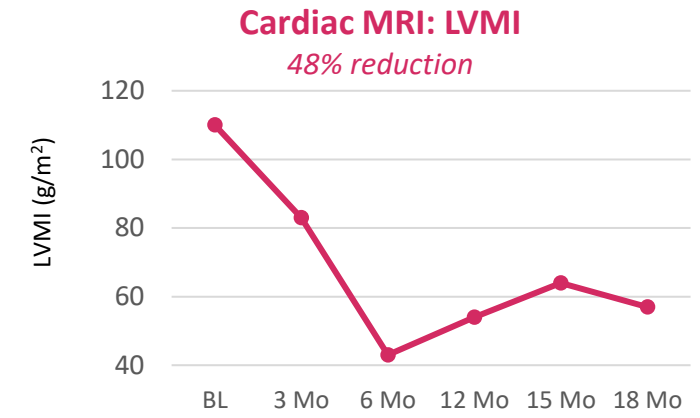
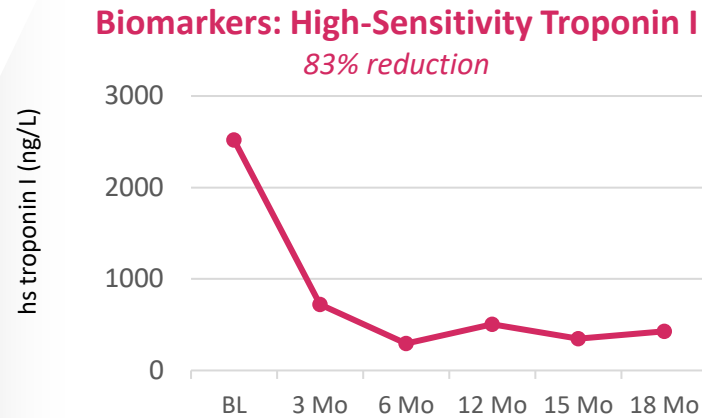
Effect of LX2006 on Cardiac Function

Majority of Participants (16/17)

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

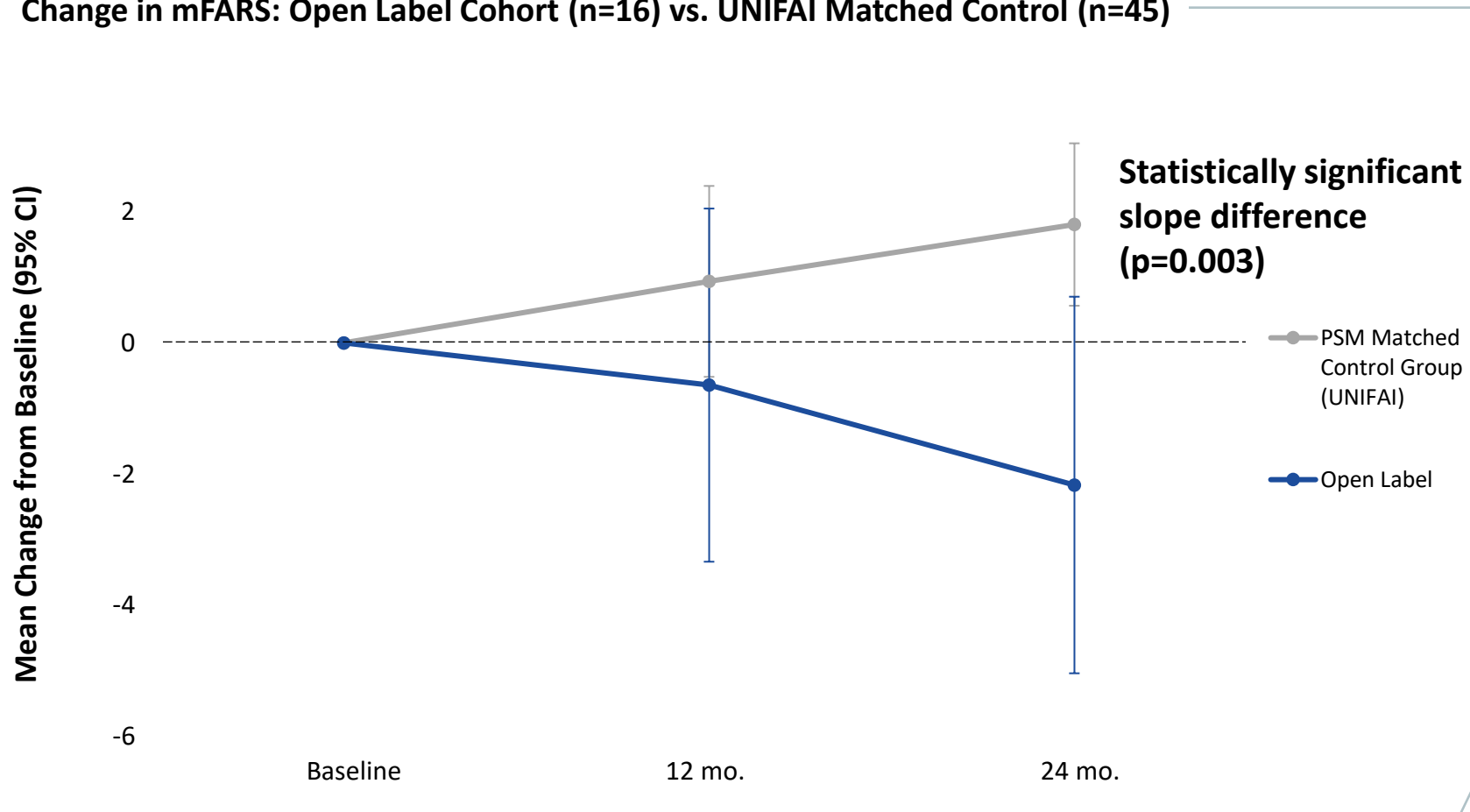
One Participant (#13) with later stage cardiomyopathy

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



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: 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.

A blue-tinted photograph of a laboratory setting. In the foreground, several glass test tubes are arranged in a row. In the background, a microscope is visible, with its objective lens and eyepiece clearly shown. The overall scene is dimly lit, with a strong blue color cast.

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%

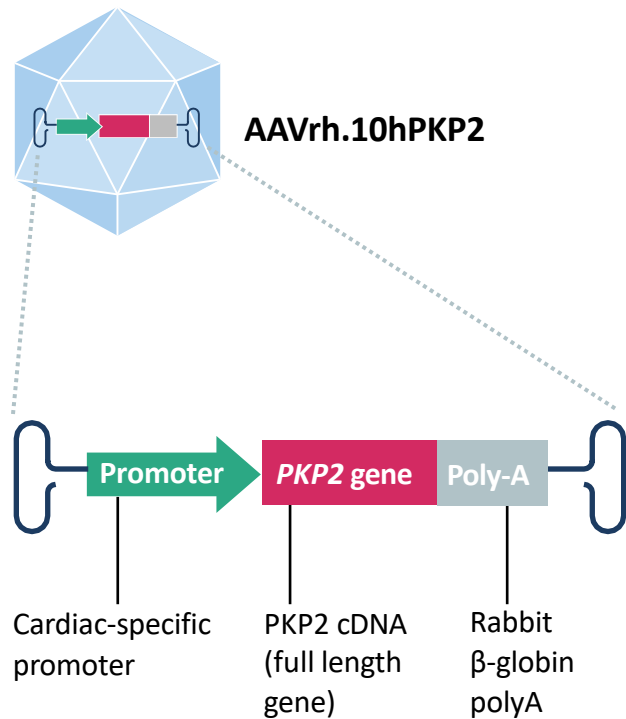
of individuals experience SCD as presenting symptom

Standard of care:

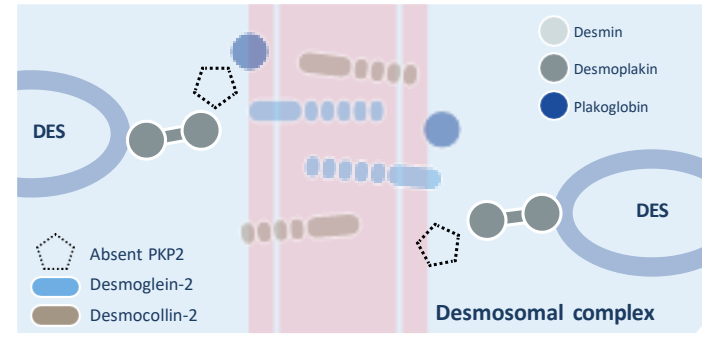
Current management methods are focused on relieving symptoms and preventing SCD, **and do not address the underlying cause of ACM.**

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:

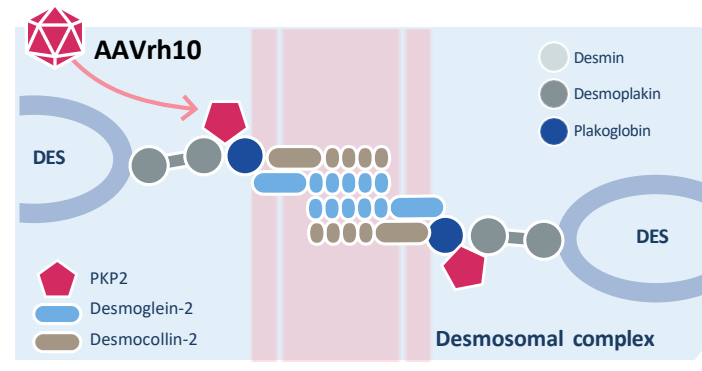


PKP2-ACM:



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

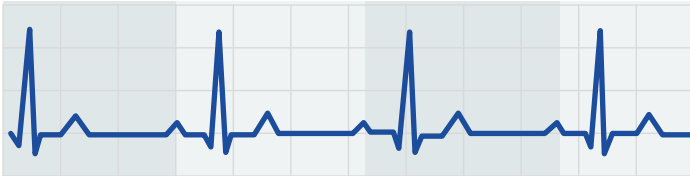
The restoration of PKP2 may lead to improvement in cardiac electrical and mechanical function as well as inhibit further structural damage

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

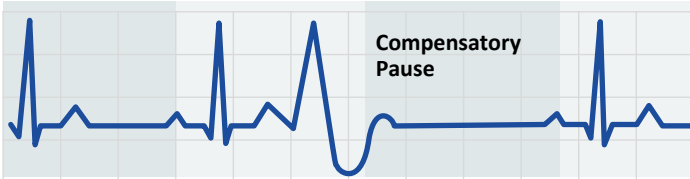
Severity of Arrhythmias

Premature Ventricular Contractions (PVCs)

Normal Sinus Rhythm



Premature Ventricular Contraction (PVC)



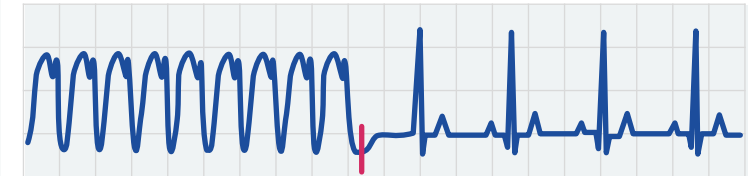
- Early indicator of electrical instability that can trigger more severe/sustained arrhythmia

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 SCD¹; 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

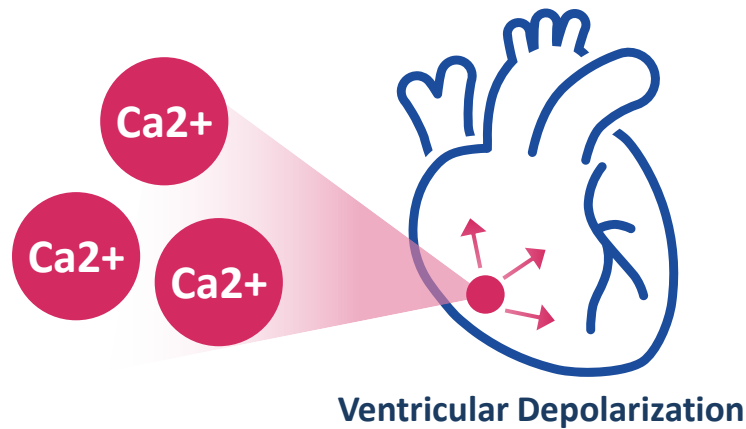
SCD, sudden cardiac death; ICD, implantable cardioverter defibrillator; VT, ventricular tachycardia.

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

Premature ventricular contractions (PVCs) may trigger ventricular tachycardia (VT); measures are related but driven by potentially different mechanisms



PVCs Are a Trigger That Can Precipitate More Severe Arrhythmias



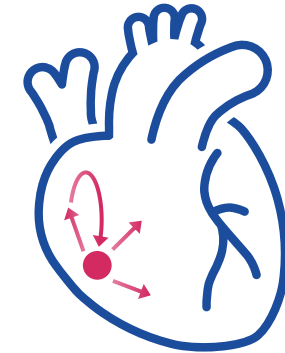
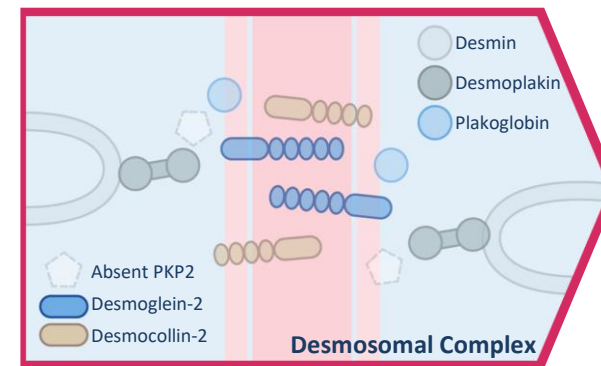
Ventricular Depolarization

- **PKP2 deficient myocytes demonstrate calcium instability;** Ca^{2+} leak can disrupt refractory period and depolarization^{1,2}
- PVCs are not reentry loops but can trigger them
- Calcium instability due to PKP2 deficiency **likely driven by downstream proteins**, which may take more time to repair versus the desmosome with direct PKP2 function



VT is Caused When a Trigger (PVC) Meets an Electrical or Structural Vulnerability

PKP2 Deficiency Reduces Cell-to-Cell Adhesion, Slowing Electrical Conduction and Causing Reentry Loops:

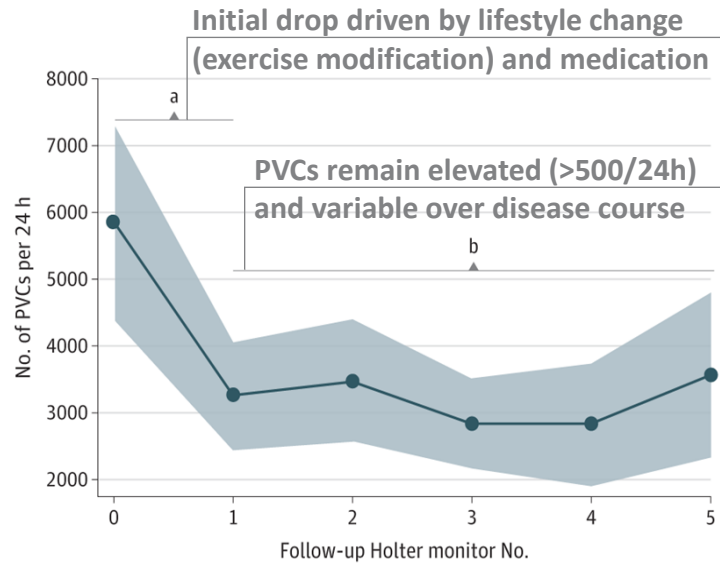


- **VT occurs when a PVC meets a vulnerability like slow electrical conduction**, enabling the premature beat to propagate as a reentry loop^{3,4}
- Reentry loops are self-sustaining electrical circuits that override normal rhythm, consistently re-exciting the heart
- PKP2 deficiency causes electrical and structural vulnerabilities like slow conduction and scarring; hypothesis that **VT could be reduced if vulnerabilities are improved even if PVCs persist**

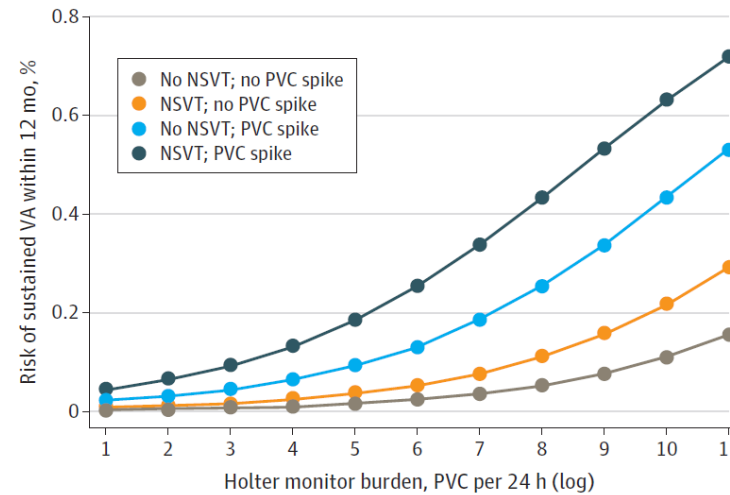
(1) Cerrone et al. *Nature Comm*, 2017. (2) Kim et al. *Circulation*, 2019. (3) Sato P. et al. *Circulation Research*, 2009. (4) Oxford E.M et al. *Circulation Research*, 2007.

In people with ACM, sustained VT risk is predicted by increased PVC burden and by non-sustained VT events

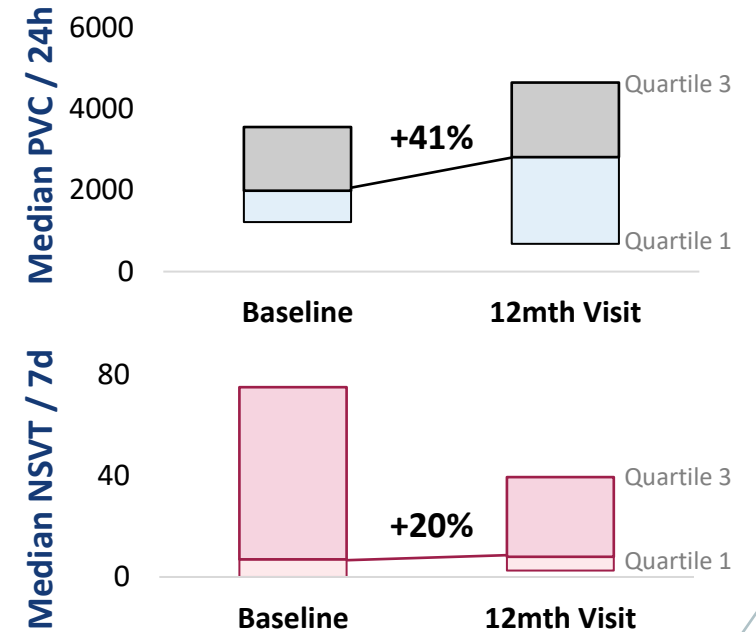
PVC burden in ACM decreases initially after diagnosis but persists long term¹



VT risk increases with PVCs and NSVT¹



Prospective natural history SNAPSHOT (n=15)



Participants mean 8 years after diagnosis

While lifestyle modification may reduce PVCs immediately following diagnosis, Lexeo-sponsored SNAPSHOT natural history data suggests that PVCs and NSVT may increase later in disease progression, both of which are associated with greater VT risk

Lexeo's role in advancing PKP2-ACM research



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)



**Retrospective EMR Review and Prospective
Observational Natural History Study**

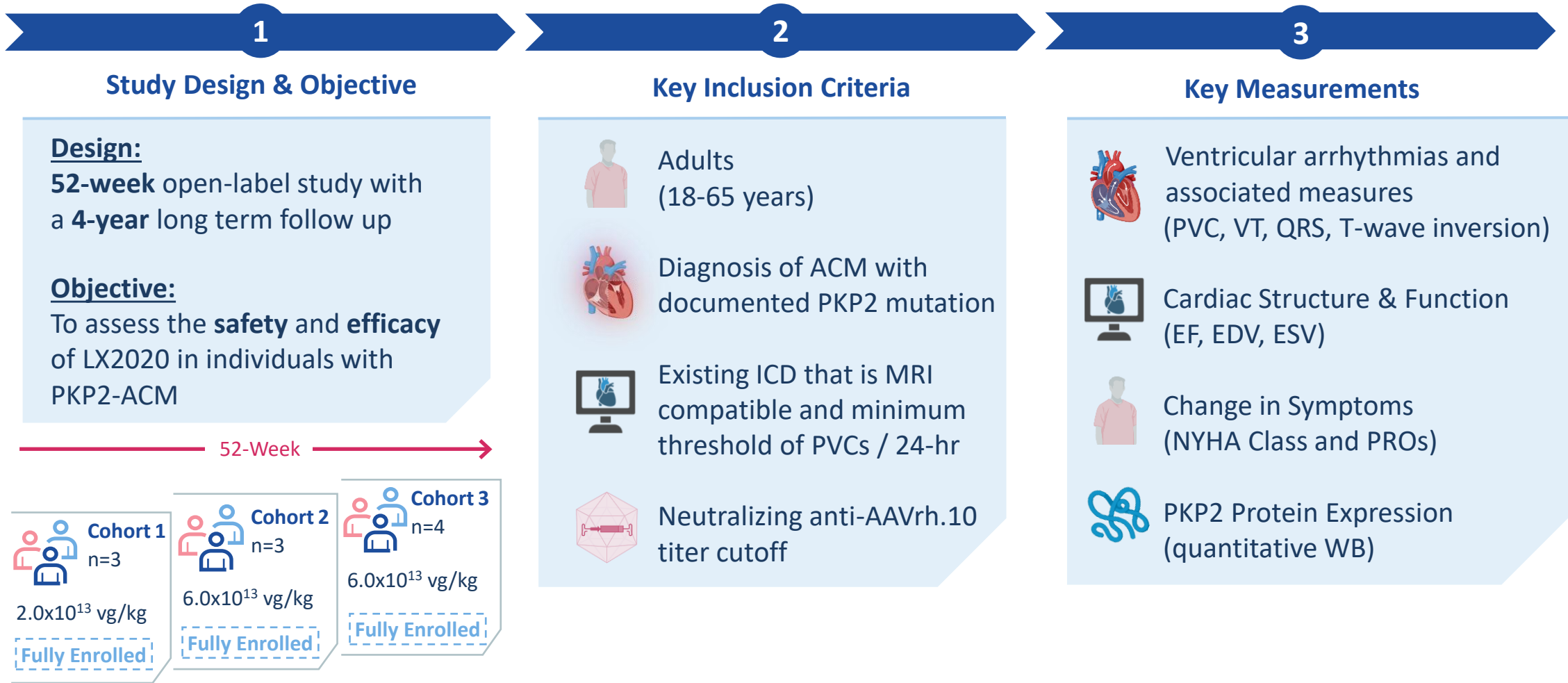
Objective: Evaluate the clinical burden of illness for patients with PKP2-ACM, and prospectively evaluate changes in key cardiac parameters and patient-reported outcome measures (PROs) associated with PKP2-ACM progression

Dose: N/A

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

Status: Ongoing (actively recruiting)

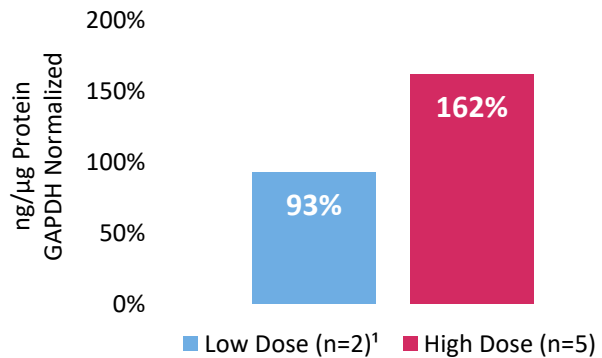
LX2020 is being evaluated in an ongoing phase 1/2 study (HEROIC- PKP2); enrollment completed in Q4 2025



PVC, Premature Ventricular Contraction; hsTnI, High Sensitivity Troponin I; WB, Western Blot; ECG, Electrocardiogram; NYHA, New York Heart Association; PROs, Patient Reported Outcomes.
Note: LX2020 is administered systemically; participants receive immune suppression with prednisone and sirolimus beginning on the day prior to treatment through 12 weeks following LX2020 administration.

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

Mean change in PKP2 expression from baseline (western blot)

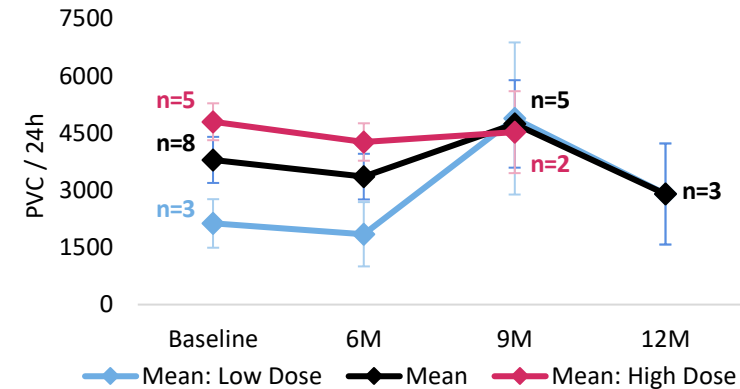


Patient reported outcomes

4 of 5

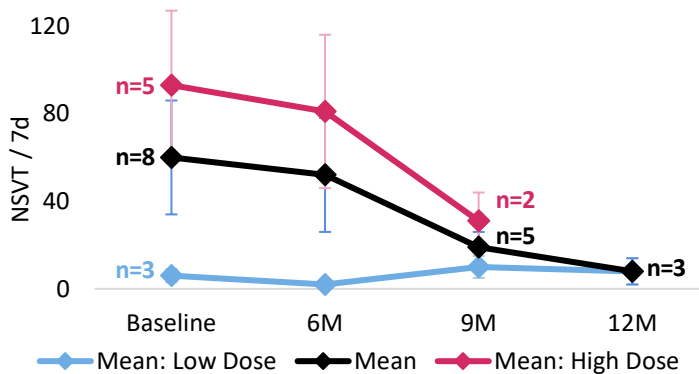
participants at high dose report improvement relative to baseline on the Patient Global Impression of Change (PGIC) scale

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



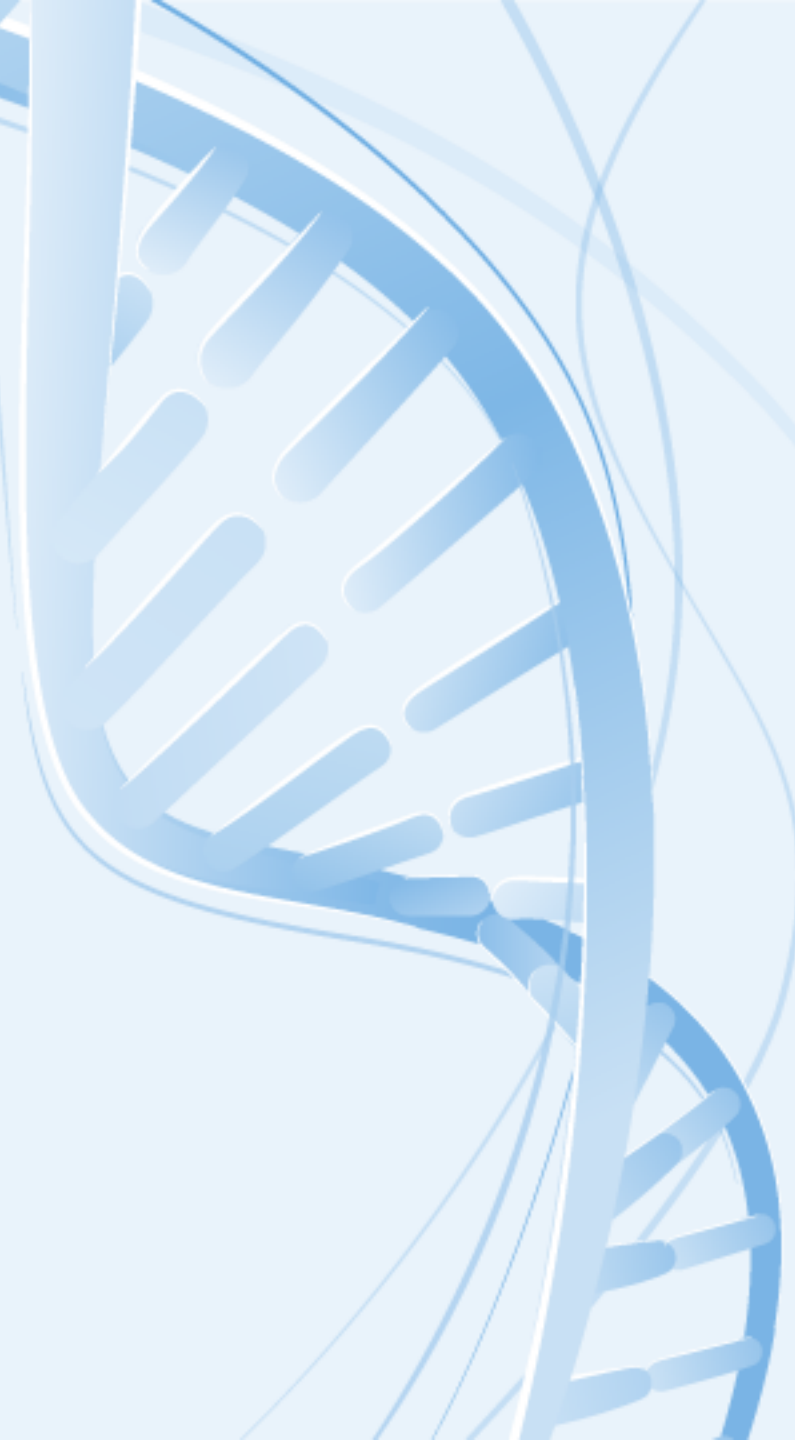
- NSVT reduced or stabilized in majority of participants with >6 months of follow up
- -22% improvement in mean NSVT at latest visit in high-dose cohort

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 seven participants at the high-dose, treated successfully per 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) Five 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

Preclinical Programs



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 potential regulatory engagement 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 – 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**; SUNRISE-FA 2 pivotal study expected to initiate in Q2 2026 with potential path to accelerated approval
- 5 Strong financial position with **cash runway into 2028**

Thank You

