# 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): May 11, 2026**

# 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**<br>**New York, New York**<br>**(Address of Principal Executive Offices)** | **10010**<br>**(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 2.02 Results of Operations and Financial Condition.**

On May 11, 2026, Lexeo Therapeutics, Inc. (the "**Company**") issued a press release announcing business highlights and its financial results for the three months ended March 31, 2026. A copy of this press release is furnished herewith as Exhibit 99.1 to this Current Report and is incorporated herein by reference.

The information in this Item 2.02 and Exhibit 99.1 hereto shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any of the Company's filings under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, except as expressly set forth by specific reference in such a filing.

**Item 8.01 Other Events.**

On May 11, 2026, the Company posted on its website an updated corporate presentation (the "**Corporate Presentation**"). 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 99.2 and is incorporated by reference herein.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

| Exhibit Number | Exhibit Description | Incorporated by Reference | | | | Filed or Furnished Herewith |
|---|---|---|---|---|---|---|
| | | Form | File No. | Exhibit | Filing Date | |
| 99.1 | Press Release | | | | | X |
| 99.2 | Corporate Presentation, dated May 2026 | | | | | X |
| 104 | Cover Page Interactive Data File (embedded within the Inline XBRL document) | | | | | X |

**SIGNATURES**

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

Lexeo Therapeutics, Inc.

Date: May 11, 2026

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

**Exhibit 99.1**

**Lexeo Therapeutics Reports First Quarter 2026 Financial Results and Operational Highlights**

*SUNRISE-FA2 open-label, pivotal trial protocol and SAP for LX2006 submitted to FDA in Q1 2026; Awaiting final FDA feedback*

*Multiple presentations highlighting progress across cardiac genetic medicine pipeline and optimized, Sf9-baculovirus AAV manufacturing platform to be presented at ASGCT 2026*

*Appointed Laura Sepp-Lorenzino, Ph.D. to Board of Directors*

*Cash, cash equivalents and investments of $227.6 million expected to provide operational runway into 2028*

**NEW YORK** – May 11, 2026 (GLOBE NEWSWIRE) – Lexeo Therapeutics, Inc. (Nasdaq: LXEO), a clinical stage genetic medicine company dedicated to pioneering novel treatments for cardiovascular diseases, today provided business updates across its portfolio and reported financial results for the first quarter 2026.

"We continued to make steady progress across our key priorities in the first quarter of 2026. As we work with the FDA to finalize the SUNRISE-FA 2 pivotal study protocol, we are advancing site readiness and patient identification activities to ensure we are prepared to initiate the study promptly once the protocol is complete," said R. Nolan Townsend, Chief Executive Officer of Lexeo Therapeutics. "We will also have a meaningful scientific presence at ASGCT this week, where we will share updates from our LX2006 program as well as new preclinical data for LX2022. We remain committed to advancing our pipeline toward meaningful therapies for patients and look forward to providing further updates as our programs continue to progress."

**Program Updates and Recent Progress**

***LX2006 in Friedreich Ataxia (FA)***

- In May 2026, Lexeo will share multiple presentations on LX2006 at the 29th American Society of Gene and Cell Therapies (ASGCT) Annual Meeting:
  - **Phase I/II interim clinical data of LX2006** continue to show sustained or deepening improvements across both cardiac and neurologic measures of FA, including statistically significant improvement in mean mFARS scores for LX2006-treated participants compared to a propensity-matched control cohort from the UNIFAI natural history study (n=17; p=0.003). LX2006 remains generally well tolerated with no Grade 3+ SAEs to date.
  - **Nonhuman primate research with LX2006** conducted by researchers at Weill Cornell Medicine demonstrates the potential of sequential dosing strategies to treat FA. Eight weeks following systemic intravenous administration of LX2006, nonhuman primates were administered LX2006 directly to the cerebellum or cerebral spinal fluid (CSF), and potentially therapeutic levels of cerebellar vector genome copies were detected via both routes of administration despite pre-existing immunity to the therapeutic vector.
  - **CMC comparability data for LX2006** between adherent HEK293 and Sf9 baculovirus suspension processes was shared, highlighting Lexeo's optimized manufacturing platform that can maintain purity and potency while significantly improving scalability of production and reducing cost.
- In February 2026, Lexeo submitted the final registrational trial design and statistical analysis plan (SAP) for the SUNRISE-FA 2 pivotal study to the FDA following a Type B meeting. The company is in contact with the FDA and is awaiting final feedback on the study protocol. Lexeo plans to provide an update when the protocol and SAP are finalized.
- Anticipated milestones for the remainder of 2026 include:
  - FDA feedback on protocol submission expected in Q2 2026
  - Initiation of SUNRISE-FA 2 pivotal trial in Q2 2026

***LX2020 in PKP2 Arrhythmogenic Cardiomyopathy (PKP2-ACM)***

- In January 2026, Lexeo reported positive interim clinical data from the HEROIC PKP2 Phase I/II clinical trial evaluating LX2020. LX2020 remains generally well tolerated across ten participants dosed with no clinically significant complement activation to date.
- Anticipated milestones for the remainder of 2026 include:
  - 12-month data update for all high dose participants in Q4 2026
  - Regulatory engagement with the FDA expected in 2026

***Pre-Clinical Assets***

- In May 2026, Lexeo will present preclinical data for LX2022 at the ASGCT Annual Meeting, demonstrating proof-of-concept efficacy for TNNI3 replacement in a newly developed porcine model of hypertrophic cardiomyopathy. This novel model closely recapitulates severe disease physiology and mortality and was specifically developed by Lexeo to evaluate TNNI3-targeted therapies. TNNI3-related disease is estimated to account for approximately 1-3% of genetic cardiomyopathies.

***Corporate Updates***

- Appointed Laura Sepp Lorenzino, Ph.D., as an independent, non-executive director to the Board of Directors. Laura was the former Chief Scientific Officer at Intellia Therapeutics and previously held senior research leadership roles at Alnylam Pharmaceuticals and Vertex Pharmaceuticals. She currently serves on the boards of AskBio, Taysha Gene Therapies, Ursa Medicines, the American Society of Gene & Cell Therapy (ASGCT) and the Oligonucleotide Therapeutics Society, and contributes to multiple scientific advisory boards including Inverna Therapeutics, Thermo Fisher Scientific, Arsenal Capital Partners and the UK Nucleic Acid Therapy Accelerator.

***First Quarter 2026 Financial Results***

- **Cash Position:** As of March 31, 2026, cash, cash equivalents, and investments in marketable securities were $227.6 million, which Lexeo believes will be sufficient to fund operations into 2028.
- **Research & Development Expenses:** Research and Development expenses were $15.7 million for the three months ended March 31, 2026, compared to $17.2 million for the three months ended March 31, 2025.
- **General & Administrative Expenses:** General and Administrative expenses were $6.6 million for the three months ended March 31, 2026, compared to $16.6 million for the three months ended March 31, 2025.
- **Net Loss:** Net loss was $20.2 million or $0.25 per share (basic and diluted) for the three months ended March 31, 2026, compared to $32.7 million or $0.99 per share (basic and diluted) for the three months ended March 31, 2025.

**About Lexeo Therapeutics**

Lexeo Therapeutics is a New York City-based, clinical stage genetic medicine company dedicated to reshaping heart health by applying pioneering science to fundamentally change how cardiovascular diseases are treated. The Company is advancing a portfolio of therapeutic candidates that take aim at the underlying genetic causes of conditions, including LX2006 in Friedreich ataxia (FA), LX2020 in plakophilin-2 (PKP2) arrhythmogenic cardiomyopathy, and others in devastating diseases with high unmet need.

**Cautionary Note Regarding Forward-Looking Statements**

Certain statements in this press release may constitute “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 developments and approval, 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.

**Media Response:**

Media@lexeotx.com

**Investor Response:**
Ashley Kaplowitz
akaplowitz@lexeotx.com

**Lexeo Therapeutics, Inc.**
**Selected Financial Information**
*(Unaudited, in thousands, except share and per share amounts)*

**Statements of Operations**

| | Three Months Ended March 31, | |
|---|---|---|
| | 2026 | 2025 |
| Operating expenses | | |
| Research and development | $ 15,703 | $ 17,171 |
| General and administrative | 6,630 | 16,634 |
| Total operating expenses | 22,333 | 33,805 |
| Operating loss | (22,333) | (33,805) |
| Other income and expense | | |
| Other expense, net | (1) | (4) |
| Interest expense | (17) | (28) |
| Interest income | 2,113 | 1,193 |
| (Amortization of premium) accretion of discount on investments in U.S. Treasury securities, net | 42 | (12) |
| Total other income and expense | 2,137 | 1,149 |
| Loss from operations before income taxes | (20,196) | (32,656) |
| Income taxes | - | - |
| Net loss | $ (20,196) | $ (32,656) |
| Net loss per common share, basic and diluted | $ (0.25) | $ (0.99) |
| Weighted average number of shares outstanding used in computation of net loss per common share, basic and diluted | 81,183,812 | 33,113,991 |

**Balance Sheet Data**

| | March 31, 2026 | December 31, 2025 |
|---|---|---|
| Cash, cash equivalents, and investments in U.S. Treasury securities | $ 227,553 | $ 246,568 |
| Total assets | 250,356 | 268,688 |
| Total liabilities | 18,859 | 22,019 |
| Total stockholders' equity | 231,497 | 246,669 |

Exhibit 99.2

# 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.

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: 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.

FA - Friedreich Ataxia; FXN - Frataxin; LVMI - Left Ventricular Mass Index; ACM - arrhythmogenic cardiomyopathy; SAP – Statistical analysis plan.

# Cardiac complications are the leading cause of death in Friedreich Ataxia

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

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

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

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

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

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

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

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

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


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


LEXEO therapeutics

# 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

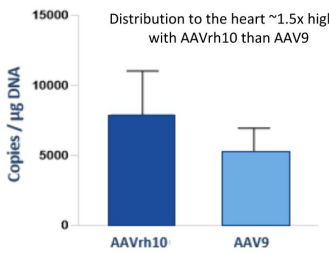
# Lexeo's AAVrh10 is a highly differentiated capsid

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

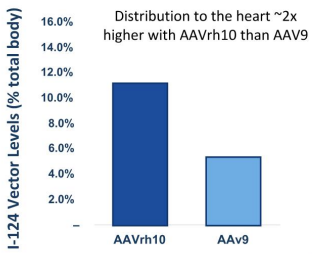
- **AAVrh10 cardiac tropism may allow for lower doses** compared to other vector serotypes while achieving targeted transgene biodistribution
- Observed ~1.5x to 2.0x greater biodistribution in the heart compared to AAV9 in multiple large animal models
- Observed greater trends of functional improvements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

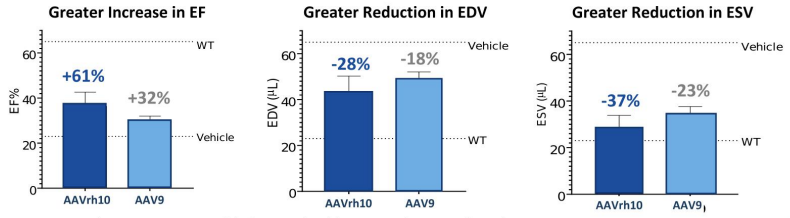
**Yucatan Minipig Biodistribution(1)**




**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

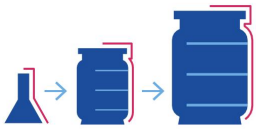
## Innovative approach

- 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

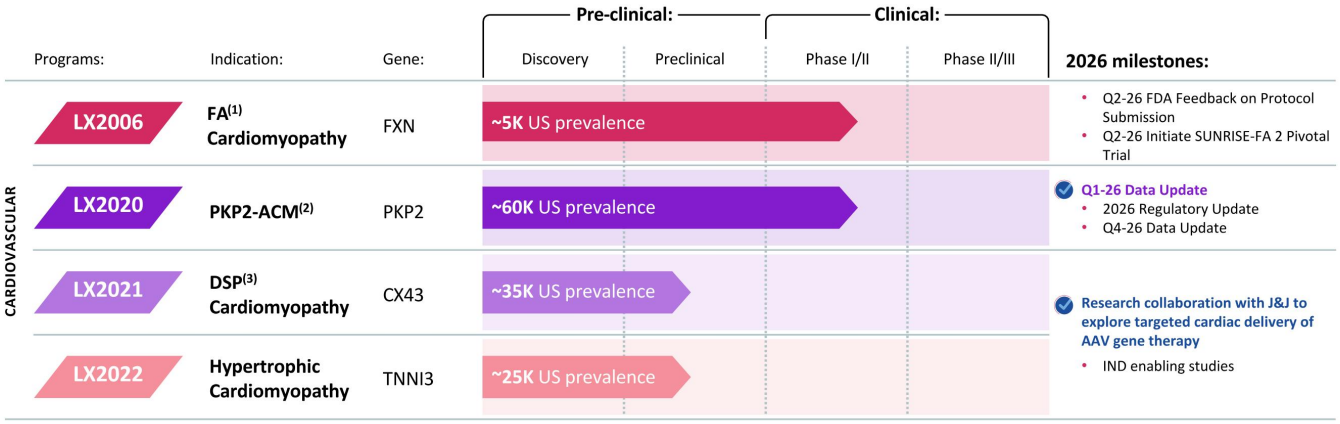


## Scalable manufacturing

- 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

LEXEO therapeutics

# 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)

LEXEO therapeutics

# Cardiac complications are the leading cause of death in Friedreich Ataxia

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

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

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

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

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

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individuals affected by FA worldwide[2]

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

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

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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 - 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 ataxia[2]

**Journey to diagnosis**

Journey to diagnosis with genetic test can take years

Guidelines recommend an EKG and ECHO at diagnosis and annually[5]

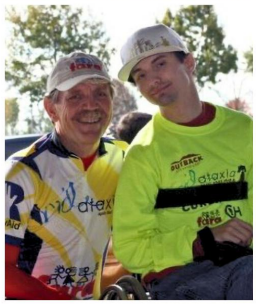
**Cardiac dysfunction**

Almost all individuals with FA will develop cardiomyopathy or cardiac dysfunction during their lifetime[1]

**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 Friedreich's Ataxia Research Alliance

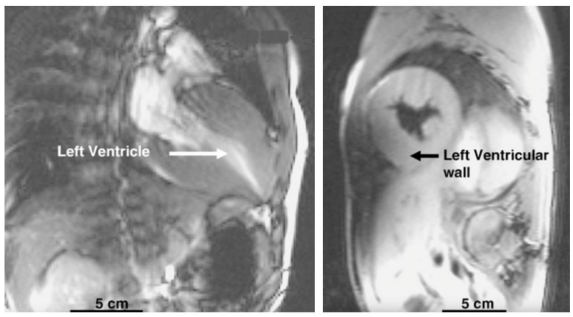
1 - Regner S, et al. American Journal of Cardiology, 2012.
2 - Norrish G., et al. Friedreich's ataxia-associated childhood hypertrophic cardiomyopathy: a national cohort study. Archives of disease in childhood, 107(5), 450–455, 2022.
3 - Subramoney S, et al. MDA Clinical and Scientific Conference, 2023.
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.

LEXEO therapeutics

# 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/m$^2$ (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.

-10% 0% 10%

- Concentric hypertrophy, with increased left ventricular mass and wall thickness, is a hallmark of FA cardiomyopathy[1]
- 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 outcomes[2]
- Reduction in LVMI may improve cardiac outcomes; FDA alignment on endpoint for pivotal trial in FA cardiomyopathy

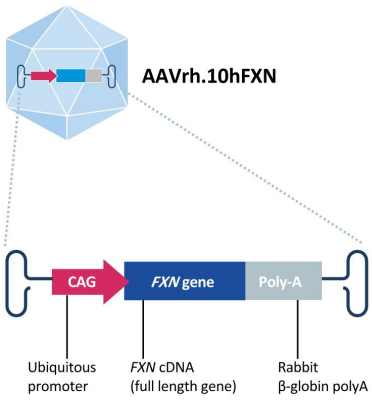
HR - Hazard Ratio; CI - Confidence Internal;
LVMI - Left Ventricular Mass Index.
Note: 10g/m$^2$ represents approximately 10% change in LVMI based on echocardiography measurements of upper bound of normal (105 g/m$^2$).

1 - Pousset, F. et al. JAMA Neurol, 2015;72(11):1334-1341.
2 - 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.

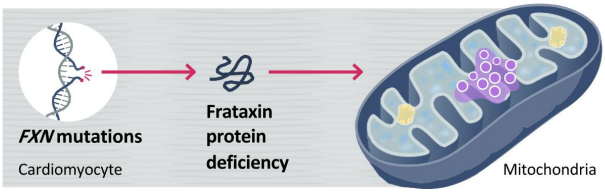
LEXEO therapeutics

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

**LX2006 construct:**

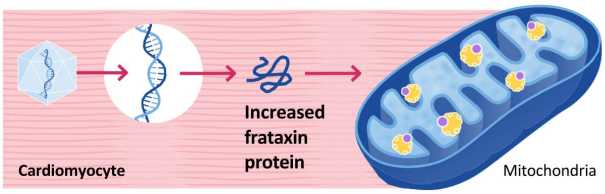



**FA cardiomyopathy:**




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

**LX2006 mechanism:**




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

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

# LX2006 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**: $1.8x10^{11}$ vg/kg
- **Cohort 2**: $5.6x10^{11}$ vg/kg
- **Cohort 3**: $1.2x10^{12}$ 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

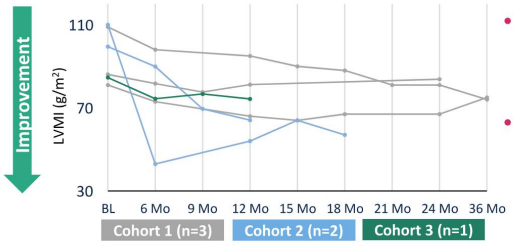
SUNRISE-FA and Weill Cornell trials share a similar study design, enabling data from the two studies to be evaluated together

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.

LEXEO therapeutics

# 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**

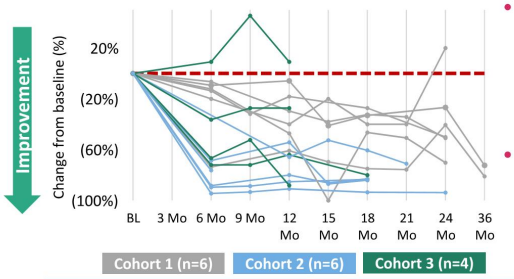
## Cardiac MRI: LVMI

| 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 myocarditis[2]
- Highly specific, blood-based marker of myocardial injury

## LX2006 generally well tolerated

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

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

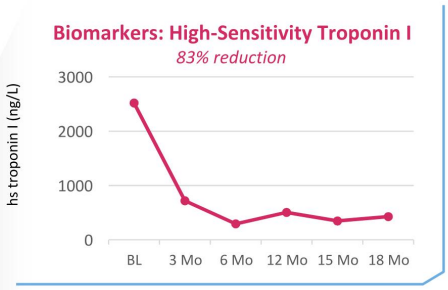
# Cardiac function improvement observed in individual with later stage cardiomyopathy

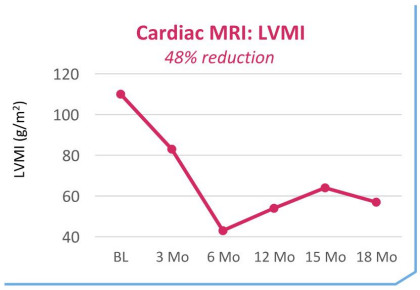
**Effect of LX2006 on Cardiac Function**

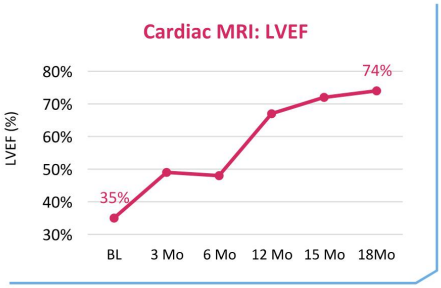
**Majority of Participants (16/17)**
- **Baseline LVEF:** Normal
- **Post therapy:** No change

**One Participant (#13) with later stage cardiomyopathy**
- **Baseline LVEF:** Low (35%)
- **Post Therapy:** Significant improvements across all cardiac biomarkers

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

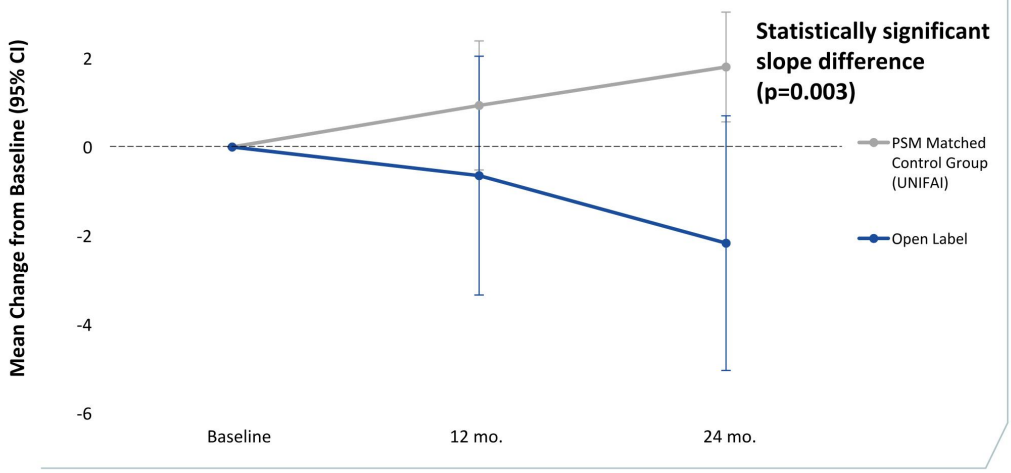


# Statistically significant improvement in mean mFARS scores for LX2006-treated participants compared to propensity-matched control cohort

**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.

LX2020

# Plakophilin 2 Arrhythmogenic Cardiomyopathy (PKP2-ACM)

LEXEO therapeutics

# 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:**

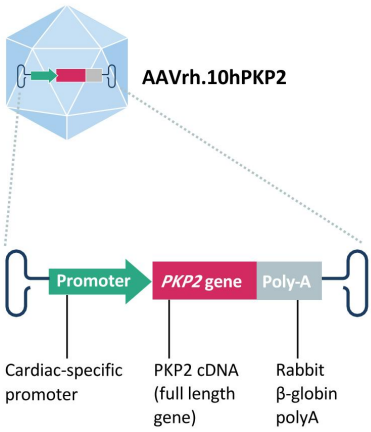
Current management methods are focused on relieving symptoms and preventing SCD, **and do not address the underlying cause of ACM.**

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).

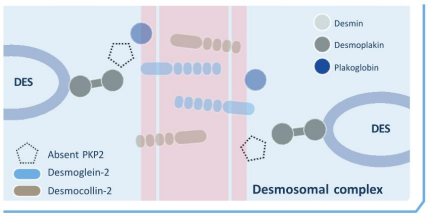
LEXEO therapeutics

# 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:**

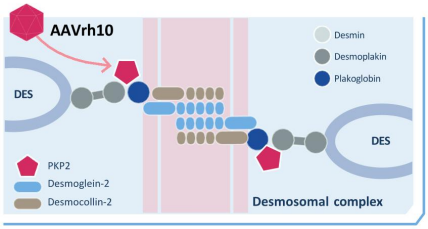



**PKP2-ACM:**




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.

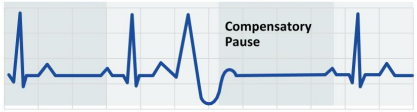
# Individuals with ACM experience high arrhythmia burden with a spectrum of severity

**Severity of Arrhythmias**

## Premature Ventricular Contractions (PVCs)

Normal Sinus Rhythm

Premature Ventricular Contraction (PVC)

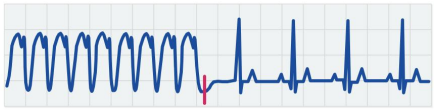



- Early indicator of electrical instability that **can trigger more severe/sustained arrhythmia**

## 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**

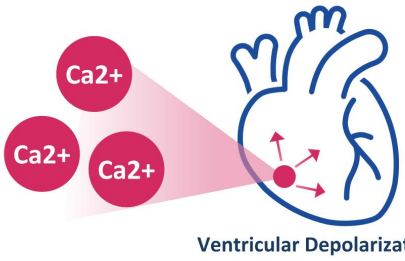
- ≥3 ventricular beats in a row **lasting over 30 seconds**
- **Can cause collapse, cardiac arrest or SCD**; sustained VT may be terminated by ICD shock to restore normal rhythm

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

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

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

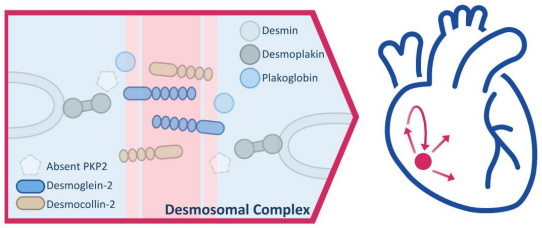
## PVCs Are a Trigger That Can Precipitate More Severe Arrhythmias




- **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:**



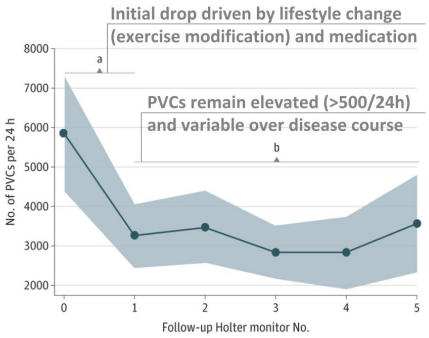

- **VT occurs when a PVC meets a vulnerability like slow electrical conduction**, enabling the premature beat to propagate as a reentry loop[3,4]
- Reentry loops are self-sustaining electrical circuits that override normal rhythm, consistently re-exciting the heart
- PKP2 deficiency causes electrical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

LEXEO therapeutics

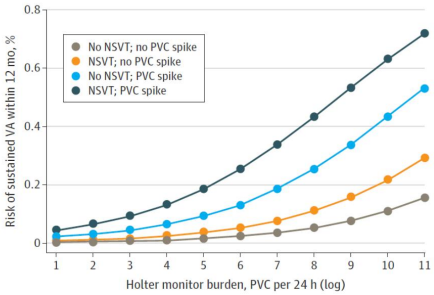
(1) Cerrone et al. *Nature Comm,* 2017. (2) Kim et al. *Circulation,* 2019. (3) Sato P. et al.*Circulation Research,* 2009. (4) Oxford E.M et al. *Circulation Research,* 2007.

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

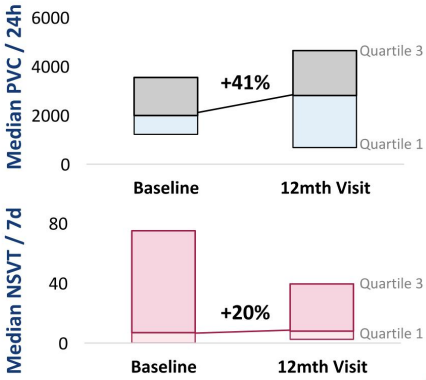
**PVC burden in ACM decreases initially after diagnosis but persists long term[1]**




**VT risk increases with PVCs and NSVT[1]**




**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**

1. Gasperetti A, et al. JAMA Cardiol. 2022;7(4):378–385

# 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)

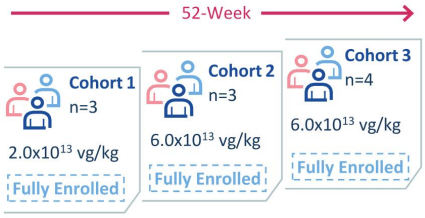
LEXEO therapeutics

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

## 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 LX2020 in individuals with PKP2-ACM




## 2 Key Inclusion Criteria

- Adults (18-65 years)
- Diagnosis of ACM with documented PKP2 mutation
- Existing ICD that is MRI compatible and minimum threshold of PVCs / 24-hr
- Neutralizing anti-AAVrh.10 titer cutoff

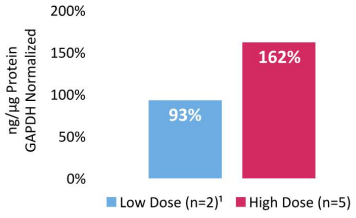
## 3 Key Measurements

- Ventricular arrhythmias and associated measures (PVC, VT, QRS, T-wave inversion)
- Cardiac Structure & Function (EF, EDV, ESV)
- Change in Symptoms (NYHA Class and PROs)
- PKP2 Protein Expression (quantitative WB)

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)

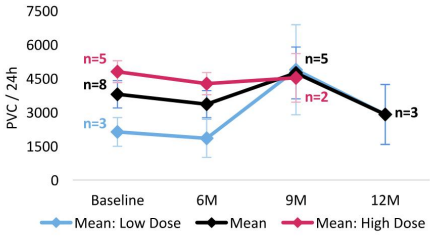



## Patient reported outcomes

**4 of 5**

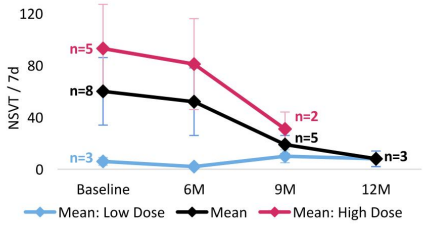
**participants at high dose report improvement** relative to baseline on the Patient Global Impression of Change (PGIC) scale

## 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

LEXEO therapeutics

# 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 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**; 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**

LEXEO therapeutics

LEXEO therapeutics

# Thank You