Business Update

September 22, 2026

LEXEO therapeutics

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, the anticipated benefits of its current product candidates, the timing for receipt and announcement of data from its clinical trials, the timing and likelihood of potential regulatory developments, trial design changes 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, the expected closing of the proposed acquisition of Mantle Therapeutics Inc. and the satisfaction of the conditions thereto, the anticipated benefits of the proposed acquisition and the acquired programs, the timing and outcome of Lexeo’s evaluation of the acquired programs and research collaborations against predefined criteria, the expected timing of a program prioritization update, the expected submission of an IND for Lexeo’s next Friedreich ataxia development candidate, and the potential achievement of future clinical and regulatory milestones. Words such as “may,” “might,” “will,” “objective,” “intend,” “should,” “could,” “can,” “would,” “expect,” “believe,” “design,” “estimate,” “predict,” “potential,” “develop,” “plan” or the negative of these terms, and similar expressions, or statements regarding intent, belief, or current expectations, are forward-looking statements. While Lexeo believes these forward-looking statements are reasonable, undue reliance should not be placed on any such forward-looking statements. These forward-looking statements are based upon current information available to the company as well as certain estimates and assumptions and are subject to various risks and uncertainties (including, without limitation, those set forth in Lexeo’s filings with the U.S. Securities and Exchange Commission (SEC)), many of which are beyond the company’s control and subject to change. Actual results could be materially different from those indicated by such forward-looking statements as a result of many factors, including but not limited to: the outcome of ongoing discussions with the U.S. Food and Drug Administration (FDA) regarding the design of our pivotal trial for accelerated approval pathway and the design of our confirmatory study for obtaining full approval; expectations regarding the initiation, progress, and expected results of Lexeo’s preclinical studies, clinical trials and research and development programs; the unpredictable relationship between preclinical study results and clinical study results; topline data and final results from our pivotal trial; delays in submission of regulatory filings or failure to receive regulatory approval; risks and uncertainties related to global macroeconomic conditions and related volatility; liquidity and capital resources; and other risks and uncertainties identified in Lexeo’s Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2026, filed with the SEC on August 12, 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.

Reshaping the path of genetic disease

Our vision: To set a new standard in the treatment of genetic diseases with high unmet need, charting the path to patient outcomes once thought out of reach

- Genetic disease expertise with cardiovascular and neurological focus
- Proven experience in the clinic
- Platform designed for safety and scalability

Individuals and families impacted by Friedreich ataxia

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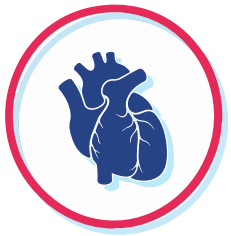
Building a best-in-class FA platform

Expanding beyond FA-CM to address full burden of FA through complementary modalities, while maintaining financial and executional discipline



Entrench Leadership in FA-CM

- LX2006 has potential to be the first disease-modifying gene therapy for FA cardiomyopathy (FA-CM)
- LX2006 to become backbone treatment for complementary FA modalities
- SUNRISE-FA 2 pivotal study remains Lexeo's highest priority

Broaden FA Opportunity

- Mantle acquisition and three new research collaborations
- Complementary modalities with potential standalone, sequential or combined use with LX2006
- Potential to address patients across full spectrum of FA, regardless of cardiomyopathy status or stage

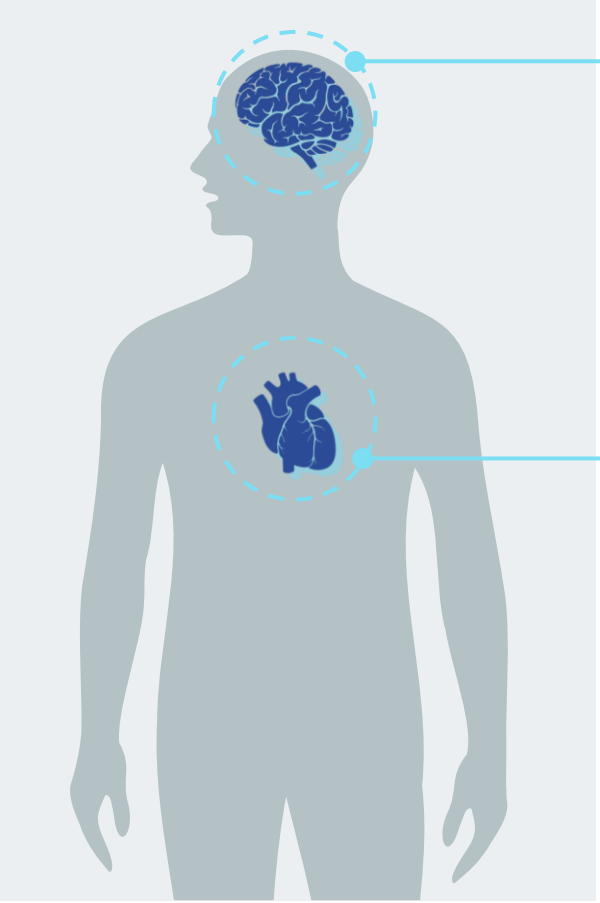
Disciplined portfolio advancement

- Programs to continue to be evaluated against predefined criteria
- Cash runway guidance into 2028 includes plans to advance one acquired program into clinical development
- Program prioritization update expected in early 2027, with an IND for the next FA development candidate planned in 2027

The combination of these approaches will advance Lexeo's objective of building a best-in-class, multimodal therapeutic platform for FA

FA = Friedreich ataxia; FA-CM = Friedreich ataxia cardiomyopathy

Friedreich Ataxia is a progressive multisystem disease with significant unmet need



Neurological Burden

Progressive ataxia, impaired coordination and peripheral nervous system involvement can materially reduce independence and quality of life

Cardiac Burden

Cardiac complications account for up to 80% of deaths in those with FA, with an average life expectancy of 35–40 years[1,2]

There is no approved treatment specifically for FA cardiomyopathy

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

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

Cardiac complications are the leading driver of mortality, while neurological decline drives substantial lifelong disability; a leading FA platform must address both.

1 - Payne R.M. JACC Basic Transl Sci, 2022;13;7(12):1267-1283.
2 - Indelicato, E., et al. Mov Disord, 2024;39(3), 510–518.

Expanding the FA platform while maintaining strategic and financial discipline

1 Mantle Acquisition

$8.3M

Upfront consideration
(cash + equity)

up to $13M

Success-based milestones
(cash + equity)

What Lexeo will acquire:

1 Clinical-stage program
2 Preclinical fast followers
1 Discovery program

Small molecules

Protein replacement

RNA-based

2 Three CNS-Targeted Gene Therapy Research Collaborations

Cerebellar-targeted gene therapy	Strategies intended to address the neurological manifestations of FA through targeted CNS delivery.
Sequential dosing of LX2006	Evaluation of CNS-targeted gene therapy following systemic administration of LX2006.
Enabling delivery and repeat administration	Novel delivery and immune-suppression strategies intended to support CNS targeting and potential repeat gene therapy administration.

Upon closing, the acquired complementary therapies will continue to be evaluated both as standalone treatments and in concert with LX2006. Future clinical trials are expected to include a treatment arm for patients previously treated with LX2006.

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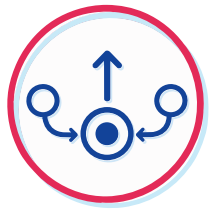
Mantle acquisition will add four differentiated approaches to increasing or replacing frataxin

Program	Therapeutic approach	Stage	Route	Role in FA platform
LX3010 (MTL-104)	Oral combination designed to increase frataxin through complementary mechanisms	Clinical	Oral	Potential complementary oral approach
LX3030 (MTL-707)	Third-generation benzamide HDAC inhibitor designed to increase production of endogenous frataxin	Preclinical	Oral	Potential differentiated oral approach
LX3050 (MTL-501)	TfR1-targeted frataxin-replacement fusion protein	Preclinical	IV	Potential tissue-directed protein replacement
LX3070 (MTL-801)	TfR1-targeted antisense oligonucleotide for FXN mRNA stabilization	Discovery	IV	Potential CNS-directed RNA approach

Plan to prioritize investment on the opportunities with the strongest potential for clinical patient impact, regulatory success and shareholder value creation

HDAC = histone deacetylase; FXN = frataxin, TfR1 = transferrin receptor 1; mFARS = modified Friedreich Ataxia Rating Scale

Program highlights: differentiated oral approaches to increase frataxin

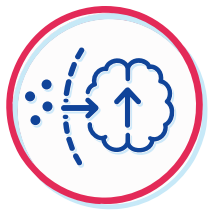


LX3010

Clinical-stage, oral combination designed to increase frataxin through complementary mechanisms

- Approximately six-point improvement in mFARS scores at 16 weeks
- Mean nine-fold increase in frataxin protein levels from baseline in muscle biopsies across 11 FA patients
- Convenient oral formulation designed with the needs of individuals with FA in mind
- Potential differentiated approach supported by both an early functional signal and evidence of increased FXN protein levels

Early functional and biological signals support the potential for a differentiated oral approach



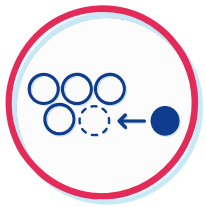
LX3030

Third-generation oral small molecule (sub-500Da) designed to increase production of endogenous frataxin in the CNS

- Builds on prior scientific validation of the HDAC target class
- Designed to enhance frataxin upregulation and central nervous system exposure
- Preclinical studies demonstrated robust increases in frataxin
- Potential differentiated oral approach to addressing the neurological manifestations of FA

Differentiated oral profile combining robust frataxin upregulation with CNS exposure

Program highlights: complementary approaches to restore frataxin

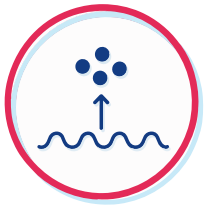


LX3050

Preclinical recombinant human frataxin fused to a proprietary anti-TfR1 Fab, designed to directly replace deficient frataxin and increase delivery to the brain

- Directly replaces deficient frataxin rather than depending on increased endogenous production
- TfR1 brain shuttle supports delivery across the blood-brain barrier and into multiple disease-relevant tissues
- In vitro studies demonstrated dose-responsive improvements in measures of mitochondrial function

Direct protein replacement diversifies the platform beyond approaches that rely on endogenous frataxin production



LX3070

Discovery-stage ASO Fab conjugate program designed to stabilize FXN mRNA and increase translation of endogenous frataxin protein

- Differentiated RNA mechanism designed to increase the body's own production of frataxin
- Combines an RNA-targeted mechanism with a proprietary anti-TfR1 Fab
- In vitro studies demonstrated dose-responsive increases in frataxin
- Potential CNS-directed RNA approach that further diversifies Lexeo's multimodal FA platform

CNS-directed RNA stabilization creates an additional path to increasing endogenous frataxin

Three new research collaborations supporting sequential dosing of CNS-targeted gene therapy

Weill Cornell Medicine

Sequential dosing

Sponsored research agreement evaluating intra-cisternal administration of LX2006 following systemic dosing in large animal models.

Apertura GENE THERAPY

Blood Brain Barrier-Crossing Capsid

Option agreement providing the opportunity to secure a license to a novel IV, BBB-crossing capsid.

Vivet THERAPEUTICS

Novel immune suppression strategies

Option agreement providing the opportunity to secure an exclusive license to VTX-PID, an IgG-degrading enzyme.

IgG = immunoglobulin G

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Unlocking the full spectrum of FA

Neurological burden can span the full continuum

Cardiomyopathy Spectrum

No cardiomyopathy	Mild CM	Moderate CM	Advanced CM
Neuro-predominant disease	Diagnosed cardiac involvement	Moderate cardiac disease	Greater cardiac disease burden

Potential label-broadening opportunity for LX2006 pending additional mFARS data

LX2006 FA-CM Opportunity
Potential disease-modifying gene therapy for FA cardiomyopathy

Future Multimodal Platform Potential

Complementary modalities with potential standalone, sequential or combined use with LX2006

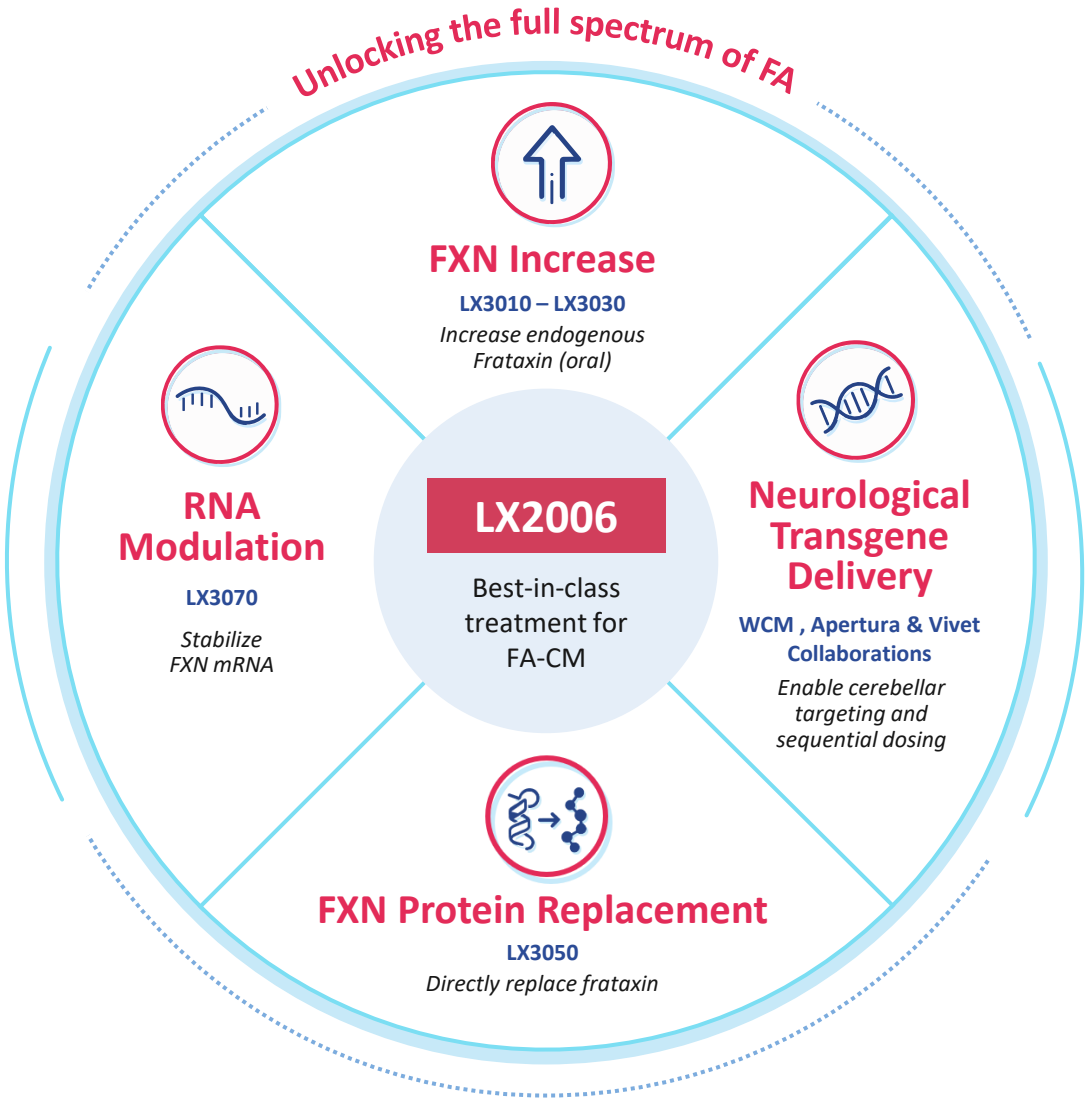
Potential reach regardless of cardiomyopathy status or stage

- **Gene therapy**
- **Small molecules**
- **Protein replacement**
- **RNA-based**
- **Neuro-targeted collaborations**

LX2006 has the potential to serve as the cardiac foundation of a broader multimodal FA platform addressing both cardiac and neurological disease

FA = Friedreich ataxia; FA-CM = Friedreich ataxia cardiomyopathy; CM = cardiomyopathy; mFARS = modified Friedreich Ataxia Rating Scale

Multiple opportunities to address the full spectrum of FA with LX2006 as the backbone



Building the leading FA platform through focus, breadth and disciplined execution

Execute SUNRISE-FA 2

SUNRISE-FA 2 remains the highest operational and capital-allocation priority

Expand the platform

Mantle and research collaborations add complementary approaches across cardiac and neurological FA

Select strongest opportunity

Predefined development gates will determine which CNS candidates receive further investment

These transactions will advance Lexeo's objective of building the best-in-class FA platform, with complementary therapeutic approaches that provide a breadth of opportunity unmatched in the FA landscape

FA = Friedreich ataxia

Thank you