Message to the Friedreich Ataxia Community

LX2006 Program Update – Publication in JAMA Cardiology of Phase I/II Data

Dear Advocacy Partners and FA community members,

We are pleased to share that key data from the Phase I/II trials of LX2006 have been published in the *Journal of the American Medical Association (JAMA) Cardiology*. This paper describes results from two trials studying our investigational therapy LX2006: Lexeo's SUNRISE-FA study and a trial led by researchers at Weill Cornell Medicine. Since the two trials used a similar design, data from both could be combined to better understand the safety and potential effects of LX2006 across a total of 17 participants.

In FA, the heart muscle can become too thick (hypertrophy). Left ventricular mass index (LVMi) is a measure of how thick the main pumping chamber of the heart (the left ventricle) is. Both trials included adult participants with early signs of heart muscle disease as well as those with more advanced heart involvement.

Participants received a one-hour intravenous (IV) infusion of LX2006 and were followed for 6 to 36 months. Researchers studied different dose levels across three groups of participants.

While some of these data have been shared previously in updates and presentations, this publication brings additional comprehensive results together of the Phase I/II dataset in a peer-reviewed journal.

Highlights:

Heart-related findings:

- For participants who had abnormal or increased LVMi at the start of the studies, average LVMi decreased by about 28% at 6 months and 33% at 12 months in the mid- and high-dose groups (n=3). Some participants maintained these improvements for up to three years after treatment.
- The studies also looked at secondary cardiac biomarkers, which are additional measurements that help show how well the heart is functioning. These included

high-sensitivity troponin I (a marker of heart muscle injury) and lateral wall thickness (a measure of heart muscle structure). In most participants, these measures either improved or remained stable over time.

- Participants in the SUNRISE-FA trial (n=8) had heart tissue samples (cardiac biopsies) taken which measured levels of frataxin. All participants showed increased levels of frataxin in heart tissue three months after treatment compared to before treatment.

Neurologic findings:

- Participants in both studies completed the modified Friedreich Ataxia Rating Scale (mFARS), a test used to measure neurological function. LX2006 was associated with stabilization of mFARS scores over time, suggesting a potential effect on neurological symptoms.

Safety findings:

- LX2006 was generally well tolerated across the 17 participants who received treatment.
- No Grade 3 or higher serious adverse events have been reported to date. A serious adverse event is a medical event that is considered significant, such as one that requires hospitalization or is life-threatening. Grade 3 refers to more severe side-
- There was no clinically significant complement activation (an immune response that can cause inflammation if overactive) and only minimal, temporary increases in liver function tests (LFT), which measure how well the liver is working.
- One participant experienced asymptomatic myocarditis (inflammation of the heart muscle) about one year after treatment, which was possibly related to LX2006.

Next steps for the LX2006 program:

Lexeo Therapeutics is initiating the pivotal study SUNRISE-FA 2 for LX2006 to support accelerated approval. SUNRISE-FA 2 will be open to individuals living with Friedrich ataxia and heart muscle disease (cardiomyopathy).

Stay informed - join the early notification list for upcoming SUNRISE-FA 2 updates and details: SUNRISE-FA 2 Consent to Receive Information - Intellistack

We are grateful to the individuals living with FA, their families, caregivers, investigators, and advocacy partners who make this research possible.

The Lexeo Team