

Larimar Therapeutics

Nomlabofusp Regulatory Update

June 2025

Forward-Looking Statements

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Written FDA Recommendations on Safety Database for the Nomlabofusp BLA Submission for Friedreich's Ataxia Program

Interactions with FDA over the past year have provided clear expectations for the path to BLA submission

OLE Study

At least 30 participants with continuous exposure for 6 months

A subset of at least 10 participants with continuous exposure for 1 year

A large majority of the exposure should be on the 50 mg dose

Based on these Recommendations, BLA Submission Seeking Accelerated Approval Expected Q2 2026

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FA: Friedreich's ataxia; OLE: Open-label extension; BLA: Biologics License Application; FDA: Food and Drug Administration

Clear FDA Expectations for Path to BLA Submission Seeking Accelerated Approval Planned in Q2 2026

Elements of BLA Submission	FDA Recommendations
Use of Skin FXN Concentrations as a Surrogate Endpoint	• Open to use of increases in skin FXN concentrations as a RLSE • Acknowledged submitted data appears to support a relationship between increased skin FXN and relevant tissues such as the heart, dorsal root ganglion, and skeletal muscle • Acceptability of increases in skin FXN for accelerated approval will be decided during future BLA review
Safety Database	• At least 30 participants with continuous exposure for 6-months • A subset of at least 10 participants with continuous exposure for 1-year • A large majority of the exposure should be on the 50 mg dose
Clinical Data Package and Global Phase 3 Study	• SAD and MAD Phase 1 studies established safety and tolerability • Phase 2 dose exploration study data and PK/PD data from ongoing OLE study supported 50 mg as the recommended dose • Long-term data from ongoing OLE study including increases in skin FXN concentrations and safety data • Global Phase 3 study, intended as the confirmatory study, to evaluate clinical outcomes including upright stability and mFARS expected to be underway at the time of BLA submission
Pharmacology and Toxicology	• Nonclinical data supporting the use of FXN as a novel surrogate endpoint • Complete toxicology package including juvenile toxicology study • Clinical data includes trends towards normalization of patient lipid profiles and gene expression
Chemistry Manufacturing and Controls	• Data supporting the lyophilized drug product with stability at room temperature • Data on batches manufactured at a commercial scale • Analytical methods and proposed specifications

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FXN: Frataxin; OLE: Open-label extension; BLA: Biologics License Application; FDA: Food and Drug Administration; RLSE: reasonably likely surrogate endpoint; SAD: Single ascending-dose ; MAD: Multiple ascending dose

Friedreich's Ataxia (FA): A rare and progressive disease



Genetic defect on both alleles lowers frataxin levels	Most patients with FA only produce ~20-40% of normal frataxin (FXN) levels depending on the tissue, sampling technique, and assay considered*
Affects ~20,000 patients globally	~5,000 patients in the U.S., with most remaining patients in the Europe ~70% of patients present before age 14
Progressive disease	Initial symptoms include unsteady posture and frequent falling, and patients are eventually confined to a wheelchair Life expectancy of 30-50 years with an early death usually caused by heart disease
Unmet Medical Need	The only treatment currently approved for FA does not address frataxin deficiency

Larimar is developing nomlabofusp, the first potential disease modifying therapy designed to systemically address the underlying FXN deficiency in FA

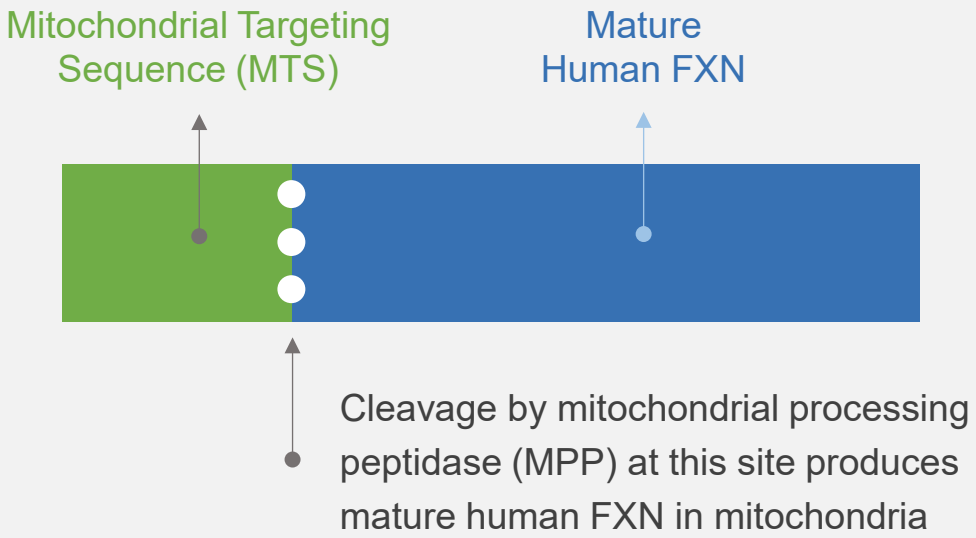
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* E.C. Deutsch et al. Molecular Genetics and Metabolism 101 (2010) 238–245.

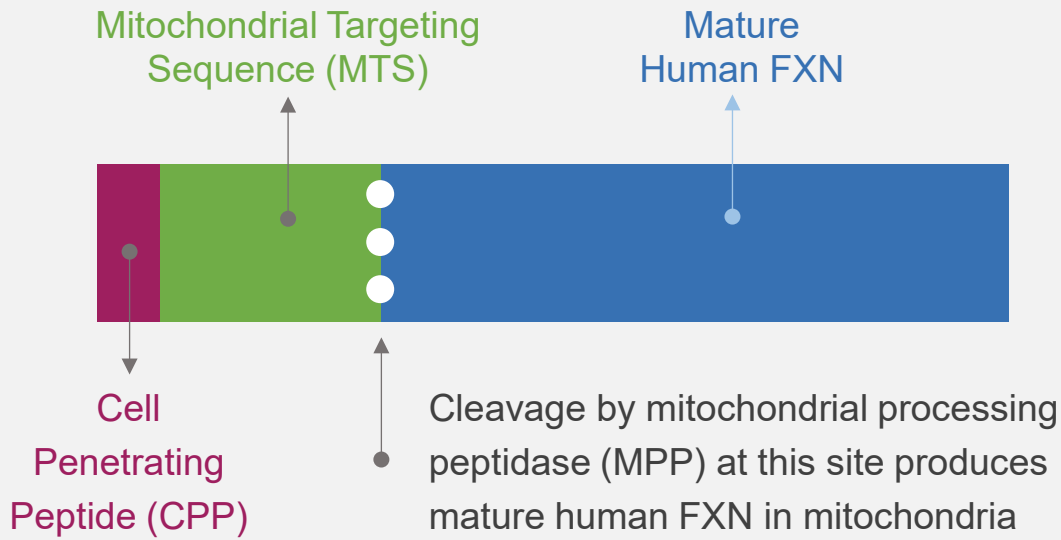
Nomlabofusp is Designed to Deliver Additional Frataxin

Nomlabofusp (CTI-1601) maintains the cleavage site between the MTS and mature human frataxin (FXN)

STRUCTURE OF ENDOGENOUS FXN



STRUCTURE OF NOMLABOFUSP



The presence of the cleavage site allows the CPP and MTS to be removed by mitochondrial processing peptidase to produce mature human FXN in the mitochondria

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Open-label Extension: 25 mg Completed, Dosing at 50 mg Continues

Long-term data from 50 mg dose expected September 2025

Key Eligibility Criteria

Previous participation in Phase 1 or Phase 2 trials

Nomlabofusp or placebo arms; most received nomlabofusp

Daily subcutaneous injections self-administered or by a caregiver

25 mg nomlabofusp

50 mg nomlabofusp

- All 7 sites activated and enrolling
- Patients switched from 25 mg to 50 mg dose from Nov 2024 to Q1 2025
- Adolescents (12-17 yrs) and children (2-11 yrs) from the PK run-in study will be eligible to screen for the OLE

Key Study Objectives

- Safety and tolerability
- Long-term PK
- Tissue FXN concentrations
- Clinical efficacy measures compared to FACOMS* database once enrollment is complete

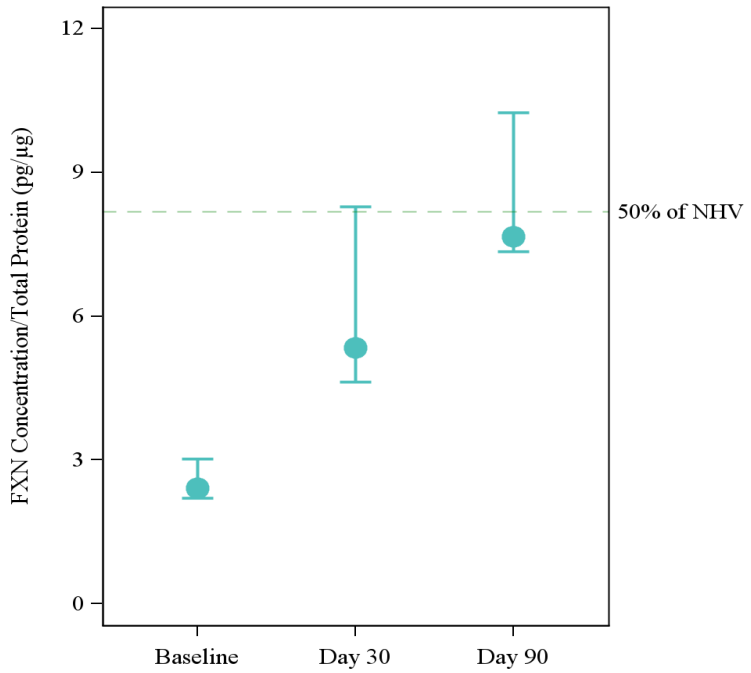
Screening Period ≤ 42 days** → Treatment Period Planned for ≥ 1 year → Potential extensions

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*FACOMS: Friedreich's Ataxia Clinical Outcome Measures Study.
**Estimated screening period may be extended for those study participants who have not been on a stable regimen of omaveloxolone for at least six months.

Nomlabofusp 25 mg Daily Increased Skin FXN Levels in the OLE Study

Absolute FXN Levels



Time dependent increase in skin FXN levels

Mean % of healthy volunteers

16% at baseline
(9.33% min, 24.48% max)

↓

72% at Day 90
(43.86 % min, 160.61 % max)

Skin FXN levels as a % of healthy volunteers are higher at Day 90 vs. baseline in subjects

FXN levels measured via detection of peptide derived from mature FXN; FXN concentrations are normalized to total cellular protein content in each sample.
Data represent median and 25th and 75th percentiles. Only participants with quantifiable levels at all measurement points are included. 50% of normal healthy volunteer (NHV) FXN level is 8.17pg/µg from the noninterventional healthy volunteer study (N=60).
Mean % of healthy volunteers is the mean of all the participants FXN levels relative to the mean FXN levels in skin cells (16.34 pg/µg) and in buccal cells (8.24 pg/µg) from the noninterventional healthy volunteer study (N=60).

Observed Trends Towards Improvement in Clinical Outcomes at Day 90 in OLE After Daily 25 mg Nomlabofusp

Visit	Statistic	**mFARS** 93-Point Scale	**FARS-ADL** 36-Point Scale	**Modified Fatigue Impact Scale** 84-Point Scale	**9 Hole Peg Test Dominant Hand** Time (Seconds)
		N = 8	N = 8	N = 8	N = 8
Baseline	Mean (SD)	55.81 (13.296)	18.13 (6.064)	27.1 (14.23)	130.91 (99.366)
	Median (IQR)	53.5 (47.5, 68.3)	17.0 (12.8, 23.8)	29.5 (18, 38)	89.5 (48.7, 227.8)
	(Min, Max)	(35.0, 73.0)	(11.0, 27.0)	(2, 45)	(38.0, 277.3)
Day 90	Mean (SD)	55.13 (14.829)	15.88 (6.249)	18.5 (15.68)	113.11 (95.586)
	Median (IQR)	53.3 (43.8, 66.0)	14.8 (11.0, 21.3)	17.0 (5, 32)	67.15 (48.4, 176.7)
	(Min, Max)	(35.3, 79.5)	(8.0, 25.0)	(0, 42)	(33.50, 287.00)
Change from Baseline at Day 90	**Mean (SD)**	**-0.69 (3.983)**	**-2.25 (3.082)**	**-8.6 (12.24)**	**-17.79 (27.450)**
	Median (IQR)	**-1.17 (-3.8, 1.2)**	**-2.25 (-3.8, 0.3)**	**-3.5 (-19, -3)**	**-9.00 (-32.0, 1.7)**
	(Min, Max)	**(-5.0, 7.0)**	**(-8.0, 1.5)**	**(-28, 9)**	**(-73.5, 9.8)**

Timed 25-Foot Walk is not presented due to participants' ambulatory status

Nomlabofusp is Generally Well-Tolerated with Long-Term Treatment

First potential disease modifying therapy to treat FA, a rare and progressive neurodegenerative disease

Safety Data

- Nomlabofusp has been generally well tolerated
- Includes some participants on treatment for up to 15 months
- Most common adverse events are local injection site reactions, with most being mild, brief in duration, and self-limited
- No participant has withdrawn from the study due to injection site reactions
- Anaphylaxis has been deemed an adverse drug reaction likely related to nomlabofusp by the Larimar Safety Team
- Participants with prior exposure who have been off treatment for some time seem to be more likely to develop an allergic reaction
- Premedication with antihistamines starting 5 days prior to the first dose and continuing for the first month in this population

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Recent Updates to the OLE Study Design

Commercial Formulation	Introduction of lyophilized drug product formulation (stable at room temperature) intended for commercialization
Antihistamine Premedication	Premedication with antihistamines starting 5 days prior to the first dose and continuing for the first month in participants with prior exposure who have been off treatment for some time
Adolescent Expansion	Inclusion of adolescents (12-17 yrs of age) from the PK run-in study
Program Expansion	Inclusion of participants who have not participated in prior nomlabofusp clinical trials

Due to inclusion of participants who have not participated in prior nomlabofusp clinical trials, this study will now be referred to as Open Label Study

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START Pilot Program Continues to Expedite the Clinical and Regulatory Development of Nomlabofusp

START Pilot Program
Support for Clinical Trials Advancing Rare Disease Therapeutics

1 of 7 novel drugs development programs selected by FDA

A new milestone-driven program launched by the FDA in September 2023

Designed to accelerate the development of novel therapies for rare diseases

Sponsors selected can benefit from:
- more frequent and rapid ad-hoc FDA interactions
- help facilitating the development of programs to pre-BLA meeting stage
- guidance on generating high-quality and reliable data intended to support a BLA

CDER Selection Based On

Demonstrated development **program readiness**

Potential to address serious and unmet medical need in a **rare neurodegenerative condition**

Alignment of CMC development timelines with clinical development plans

Proposed plan where **enhanced communication can improve efficiency of product development**

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FDA: Food and Drug Administration; CDER: Center for Drug Evaluation and Research; CMC: Chemistry, Manufacturing, and Controls

Potential Path to Bring Nomlabofusp to Patients Worldwide

Open Label Study

Continuing to enroll participants on 50 mg dose

Plan to introduce lyophilized dosage form mid-2025

Plan to enroll patients who have not participated in a prior nomlabofusp trial

Considering enrolling children 2 - 11 yrs of age directly into the study

Data expected Sept 2025
30-40 participants who received at least one dose of nomlabofusp

Adolescent PK Run-In Study

Dosing of adolescents (12-17 yrs of age) at weight-based dose expected to match PK of adult 50 mg dose completed

Participants eligible to transition into OLE

Ongoing screening and enrollment of patients into the OLE study

Adolescent data expected Sept 2025
14 participants, some on placebo

Global Phase 3 Study

Received feedback from FDA and EMA on study protocol

Potential sites in the U.S., Europe, U.K., Canada, and Australia

Study Design*

- Double-blind placebo-controlled study
- Ambulatory patients (n = 100 – 150) weighted to younger patients
- Includes patients 2 - 40 yrs
- 18 months dosing
- Upright stability and mFARS as primary outcome measures

Next Steps

BLA submission to seek accelerated approval planned for Q2 2026

U.S. launch planned for early 2027

*Study will initiate with subjects 12-40 yrs of age and will change to 2-40 yrs when dose is confirmed in children 2-11 yrs of age

Nomlabofusp Advancing Towards BLA Submission for FA

First potential disease modifying therapy
Designed to systemically address FXN deficiency in FA

FDA clarity on key BLA elements
Skin FXN concentrations as a surrogate endpoint

Safety database of at least 30 for 6-mos, and a subset of at least 10 for 1-year; large majority of exposure should be on the 50 mg dose

Long-term data from the OLE & PK and safety data from adolescent PK-run in study
Expected in September 2025

BLA submission seeking accelerated Approval expected Q2 2026
To include data from adults & children

U.S. launch planned for early 2027

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$157.5 M in cash and investments as of March 31, 2025, with projected cash runway into Q2 2026