# 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): October 30, 2024**

# Larimar Therapeutics, Inc.

**(Exact name of Registrant as Specified in Its Charter)**

| **Delaware** | **001-36510** | **20-3857670** |
|---|---|---|
| **(State or Other Jurisdiction of Incorporation)** | **(Commission File Number)** | **(IRS Employer Identification No.)** |
| **Three Bala Plaza East**<br>**Bala Cynwyd, Pennsylvania** | | **19004** |
| **(Address of Principal Executive Offices)** | | **(Zip Code)** |

**Registrant's Telephone Number, Including Area Code: (844) 511-9056**

**(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, par value $0.001 per share | LRMR | 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 October 30, 2024, Larimar Therapeutics, Inc. (the "***Company***") announced its financial results and operational highlights for the third quarter ended September 30, 2024. A copy of the press release is being furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

The information furnished pursuant to this Item 2.02, including Exhibit 99.1 attached hereto, is intended to be furnished and 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 filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

**Item 8.01 Other Events.**

On October 30, 2024, the Company posted on its website an updated slide presentation, which is attached as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference. Representatives of the Company will use the presentation in various meetings with investors, analysts and other parties from time to time.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

Below is a list of exhibits included with this Current Report on Form 8-K.

| Exhibit No. | Document |
|---|---|
| 99.1 | Press Release issued by Larimar Therapeutics, Inc. on October 30, 2024* |
| 99.2 | Larimar Therapeutics, Inc. Corporate Presentation, dated October 30, 2024 |
| 104 | Cover Page Interactive Data File (embedded within the Inline XBRL document) |

* Furnished herewith

**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.

Larimar Therapeutics, Inc.

Date: October 30, 2024

By: /s/ Carole S. Ben-Maimon, M.D.

*Name: Carole S. Ben-Maimon, M.D.*
*Title: President and Chief Executive Officer*

**Exhibit 99.1**

## Larimar Therapeutics Reports Third Quarter 2024 Operating and Financial Results

- *Nomlabofusp program update expected mid-December to include available safety, pharmacokinetic (PK) and frataxin data, as well as available clinical outcomes observations from patients with Friedreich's ataxia (FA) receiving 25 mg of nomlabofusp daily for 30-180 days in ongoing open label extension (OLE) study*
- *Initiation of PK run-in study in adolescents on track by year-end 2024*
- *Initiation of global confirmatory/registration study planned mid-2025*
- *Biologics License Application (BLA) submission for nomlabofusp targeted for 2H 2025 to support potential accelerated approval*
- *Strong balance sheet of $203.7 million cash, cash equivalents and marketable securities as of September 30, 2024, with projected cash runway into 2026*

**Bala Cynwyd, PA,** October 30, 2024 – Larimar Therapeutics, Inc. (Larimar) (Nasdaq: LRMR), a clinical-stage biotechnology company focused on developing treatments for complex rare diseases, today reported its third quarter 2024 operating and financial results.

"Our nomlabofusp program continues to advance, with the potential to be the first frataxin protein replacement therapy for patients with FA. All sites are activated with ongoing enrollment in our OLE study evaluating the long-term safety, PK and frataxin levels in patients with FA following daily subcutaneous administration. In mid-December, we plan to provide a development program update that will include available safety, PK, and frataxin data from patients receiving 25 mg of nomlabofusp daily for up to 180 days in our OLE study. We expect to also provide an update on enrollment," said Carole Ben-Maimon, MD, President, and Chief Executive Officer of Larimar. "In November, we look forward to presenting at the International Congress for Ataxia Research (ICAR) meeting new data on results from our completed dose exploration study including exploratory gene and lipid expression results following nomlabofusp treatment. In addition, we will also be presenting two posters with data from patients participating in our Phase 1 single ascending dose (SAD) and multiple ascending dose (MAD) studies and Phase 2 dose exploration study. One poster will provide patient data on baseline disease characteristics and baseline tissue frataxin levels, and the other will present the relationship between dose, PK and tissue frataxin levels using modeling and simulation. We remain on track to initiate a PK run-in study in adolescent patients with FA in the fourth quarter of this year which is the first step towards evaluating nomlabofusp treatment in pediatric patients."

Dr. Ben-Maimon continued, "On the regulatory front, we were pleased to recently receive Innovative Licensing and Access Pathway (ILAP) designation from the Medicines and Healthcare Products Regulatory Agency (MHRA) which aims to facilitate patient access by accelerating time to market in the U.K. We also held our first meetings with the Food and Drug Administration (FDA) as part of the Support for Clinical Trials Advancing Rare Disease Therapeutics (START) pilot program and appreciate the dialogue and interaction designed to help advance our development program. In parallel, we began work to further understand the continued areas of unmet need in the FA therapeutic landscape from the perspective of physicians, payers, and most importantly, patients. We will use this information to develop our commercial approach and to refine our market entry strategy. Finally, we continue scaling up our manufacturing efforts and collecting required data to support a potential accelerated approval path. Our targeted BLA submission remains on track for the second half of 2025."

**Recent Highlights**

- Today, Larimar announced that it will provide a nomlabofusp development program update in mid-December 2024 that will include available safety, PK and frataxin data, as well as available clinical outcomes observations from patients currently receiving a daily 25 mg dose of nomlabofusp for approximately 30 to 180 days in the OLE study. An update on enrollment in the OLE study will also be provided.
- Larimar recently received ILAP designation from the MHRA for nomlabofusp for the treatment of adults and children with FA. ILAP aims to facilitate patient access to novel treatments by accelerating time to market through opportunities for enhanced engagements with U.K. regulatory authorities and other stakeholders. Along with the receipt of the ILAP designation, nomlabofusp has already been granted orphan drug designations in the U.S. and the European Union (EU), Fast Track and Rare Pediatric Disease designations in the U.S., PRIME designation in the EU, and selected to be in the START pilot program by the FDA.
- Larimar is on track to initiate by year-end a PK run-in study in an initial cohort of 12-15 adolescents (12 to 17 years of age) with FA. Initiation of a second cohort of 12-15 children (2 to 11 years of age) is planned to follow next year. Study participants will be randomized 2:1 to receive either nomlabofusp or placebo daily. Following assessment of safety and exposure data of each cohort in the PK run-in study, participants will be eligible to screen for the OLE study.

- Larimar is on track for a planned initiation of a global confirmatory/registration study planned mid-2025 with potential sites in the U.S., Europe, U.K., Canada, and Australia. Larimar continues to target BLA submission for the second half of 2025 to support accelerated approval.
- In September 2024, Larimar announced that data from the Company's nomlabofusp Phase 1 studies and Phase 2 dose exploration study, some of which has been previously disclosed, will be presented at the ICAR meeting being held November 12-15, 2024, in London, U.K.

**Third Quarter 2024 Financial Results**
As of September 30, 2024, the Company had cash, cash equivalents and marketable securities totaling $203.7 million, which provides projected cash runway into 2026.

*Third quarter of 2024 compared to the third quarter of 2023*

The Company reported a net loss for the third quarter of 2024 of $15.5 million, or $0.24 per share, compared to a net loss of $9.1 million, or $0.21 per share, for the third quarter of 2023.

Research and development expenses for the third quarter of 2024 were $13.9 million compared to $6.6 million for the third quarter of 2023. The increase in research and development expenses was primarily driven by an increase of $3.8 million in nomlabofusp manufacturing costs including lyophilization development, production scaling costs and manufacturing costs related to producing doses to be used in ongoing and planned clinical trials, an increase of $1.1 million in personnel expense due to increased headcount, an increase of $0.9 million in assay development costs, an increase of $0.6 million in clinical costs primarily associated with the OLE study which began dosing patients in the first quarter of 2024, an increase of $0.3 million of professional fees related to consulting costs, an increase of $0.2 million in stock compensation costs associated with 2024 grants and an increase of $0.2 million in internal lab costs.

General and administrative expenses were $4.3 million in the third quarter of 2024 compared to $3.8 million in the third quarter of 2023. The increase in general and administrative expenses was primarily driven by an increase of $0.4 million in personnel expense and an increase of $0.2 million in professional fees primarily related to consulting costs related to commercial activity and other public company related expenses.

*Nine months ended September 30, 2024 compared to the nine months ended September 30, 2023*

The Company reported a net loss for the 9-month period ending September 30, 2024 of $51.8 million, or $0.86 per share, compared to a net loss of $24.0 million, or $0.55 per share, for the 9-month period ending September 30, 2023.

Research and development expenses for the 9-month period ending September 30, 2024 were $46.5 million compared to $17.0 million for the 9-month period ending September 30, 2023. The increase in research and development expenses was primarily driven by an increase of $20.2 million in nomlabofusp manufacturing costs including lyophilization development, production scaling costs and manufacturing costs related to producing doses to be used in ongoing and planned clinical trials, an increase of $3.2 million in personnel expense due to increased headcount, an increase of $2.9 million in clinical costs primarily associated with the OLE study which began dosing patients in the first quarter of 2024, increase of $0.9 million in assay development costs, an increase of $0.8 million related to the Track-FA program, an increase of $0.5 million in stock compensation costs associated with 2024 grants, an increase of $0.5 million in internal lab costs and an increase of $0.3 million of professional fees related to consulting costs.

General and administrative expenses for the 9-month period ending September 30, 2024 were $13.1 million compared to $10.6 million for the 9-month period ending September 30, 2023. The increase in general and administrative expenses was primarily driven by an increase of $1.0 million in personnel expense, an increase of $1.0 million in professional fees primarily related to consulting costs related to commercial activity and other public company related expenses, an increase of $0.3 million of other expense related to computer software, information technology services and recruiting and an increase of $0.2 million in stock compensation costs associated with 2024 grants.

**About Larimar Therapeutics**
Larimar Therapeutics, Inc. (Nasdaq: LRMR), is a clinical-stage biotechnology company focused on developing treatments for complex rare diseases. Larimar's lead compound, nomlabofusp, is being developed as a potential treatment for Friedreich's ataxia. Larimar also plans to use its intracellular delivery platform to design other fusion proteins to target additional rare diseases characterized by deficiencies in intracellular bioactive compounds. For more information, please visit: https://larimartx.com.

**Forward-Looking Statements**
This press release contains forward-looking statements that are based on Larimar's management's beliefs and assumptions and on information currently available to management. All statements contained in this release other than statements of historical fact are forward-looking statements, including but not limited to statements regarding Larimar's ability to develop and commercialize nomlabofusp and other planned product candidates, Larimar's planned research and development efforts, including the timing of its nomlabofusp clinical trials, interactions and filings with the FDA, expectations regarding potential for accelerated approval or accelerated access and time to market and overall development plan and other matters regarding Larimar's business strategies, ability to raise capital, use of capital, results of operations and financial position, and plans and objectives for future operations.

In some cases, you can identify forward-looking statements by the words "may," "will," "could," "would," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue," "ongoing" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements involve risks, uncertainties and other factors that may cause actual results, performance, or achievements to be materially different from the information expressed or implied by these forward-looking statements. These risks, uncertainties and other factors include, among others, the success, cost and timing of Larimar's product development activities, nonclinical studies and clinical trials, including nomlabofusp clinical milestones and continued interactions with the FDA; that preliminary clinical trial results may differ from final clinical trial results, that earlier non-clinical and clinical data and testing of nomlabofusp may not be predictive of the results or success of later clinical trials, and assessments; that the FDA may not ultimately agree with Larimar's nomlabofusp development strategy; the potential impact of public health crises on Larimar's future clinical trials, manufacturing, regulatory, nonclinical study timelines and operations, and general economic conditions; Larimar's ability and the ability of third-party manufacturers Larimar engages, to optimize and

scale nomlabofusp's manufacturing process; Larimar's ability to obtain regulatory approvals for nomlabofusp and future product candidates; Larimar's ability to develop sales and marketing capabilities, whether alone or with potential future collaborators, and to successfully commercialize any approved product candidates; Larimar's ability to raise the necessary capital to conduct its product development activities; and other risks described in the filings made by Larimar with the Securities and Exchange Commission (SEC), including but not limited to Larimar's periodic reports, including the annual report on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, filed with or furnished to the SEC and available at www.sec.gov. These forward-looking statements are based on a combination of facts and factors currently known by Larimar and its projections of the future, about which it cannot be certain. As a result, the forward-looking statements may not prove to be accurate. The forward-looking statements in this press release represent Larimar's management's views only as of the date hereof. Larimar undertakes no obligation to update any forward-looking statements for any reason, except as required by law.

**Investor Contact:**
Joyce Allaire
LifeSci Advisors
jallaire@lifesciadvisors.com
(212) 915-2569

**Company Contact:**
Michael Celano
Chief Financial Officer
mcelano@larimartx.com
(484) 414-2715

**Larimar Therapeutics, Inc.**

Condensed Consolidated Balance Sheet

(unaudited)

| | September 30, 2024 | December 31, 2023 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 35,067 | $ 26,749 |
| Short-term marketable securities | 168,640 | 60,041 |
| Prepaid expenses and other current assets | 9,549 | 3,385 |
| Total current assets | 213,256 | 90,175 |
| Property and equipment, net | 779 | 684 |
| Operating lease right-of-use assets | 3,026 | 3,078 |
| Restricted cash | 1,339 | 1,339 |
| Other assets | 621 | 659 |
| Total assets | $ 219,021 | $ 95,935 |
| **Liabilities and Stockholders' Equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 1,686 | $ 1,283 |
| Accrued expenses | 13,573 | 7,386 |
| Operating lease liabilities, current | 1,026 | 837 |
| Total current liabilities | 16,285 | 9,506 |
| Operating lease liabilities | 4,336 | 4,709 |
| Total liabilities | 20,621 | 14,215 |
| Commitments and contingencies | | |
| Stockholders' equity: | | |
| Preferred stock; $0.001 par value per share; 5,000,000 shares authorized as of September 30, 2024 and December 31, 2023; no shares issued and outstanding as of September 30, 2024 and December 31, 2023 | — | — |
| Common stock, $0.001 par value per share; 115,000,000 shares authorized as of September 30, 2024 and December 31, 2023; 63,806,628 and 43,909,069 shares issued and outstanding as of September 30, 2024 and December 31, 2023, respectively | 64 | 43 |
| Additional paid-in capital | 438,312 | 270,150 |
| Accumulated deficit | (240,334) | (188,554) |

| | | |
|---|---|---|
| Accumulated other comprehensive gain | 358 | 81 |
| Total stockholders' equity | 198,400 | 81,720 |
| Total liabilities and stockholders' equity | $ 219,021 | $ 95,935 |

**Larimar Therapeutics, Inc.**

Condensed Consolidated Statements of Operations

(In thousands, except share and per share data)

(unaudited)

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2024 | 2023 | 2024 | 2023 |
| Operating expenses: | | | | |
| Research and development | $ 13,919 | $ 6,585 | $ 46,540 | $ 17,022 |
| General and administrative | 4,345 | 3,754 | 13,057 | 10,574 |
| Total operating expenses | 18,264 | 10,339 | 59,597 | 27,596 |
| Loss from operations | (18,264) | (10,339) | (59,597) | (27,596) |
| Other income, net | 2,765 | 1,275 | 7,817 | 3,640 |
| Net loss | $ (15,499) | $ (9,064) | $ (51,780) | $ (23,956) |
| Net loss per share, basic and diluted | $ (0.24) | $ (0.21) | $ (0.86) | $ (0.55) |
| Weighted average common shares outstanding, basic and diluted | 63,806,158 | 43,903,738 | 60,399,697 | 43,899,670 |
| Comprehensive loss: | | | | |
| Net loss | $ (15,499) | $ (9,064) | $ (51,780) | $ (23,956) |
| Other comprehensive gain (loss): | | | | |
| Unrealized gain (loss) on marketable securities | 508 | (5) | 277 | 38 |
| Total other comprehensive gain (loss) | 508 | (5) | 277 | 38 |
| Total comprehensive loss | $ (14,991) | $ (9,069) | $ (51,503) | $ (23,918) |

Exhibit 99.2

# Larimar Therapeutics

## Corporate Deck

October 2024

# Forward-Looking Statements

This presentation contains forward-looking statements that are based on the beliefs and assumptions of Larimar Therapeutics, Inc. ( “Company”) and on information currently available to management. All statements contained in this presentation other than statements of historical fact are forward-looking statements, including but not limited to Larimar’s ability to develop and commercialize nomlabofusp (CTI-1601) and other planned product candidates, Larimar’s planned research and development efforts, including the timing of its nomlabofusp clinical trials, expectations with respect to the FDA START pilot program, interactions with the FDA, expectations regarding potential for accelerated approval or accelerated access and time to market and overall development plan and other matters regarding Larimar’s business strategies, ability to raise capital, use of capital, results of operations and financial position, and plans and objectives for future operations.

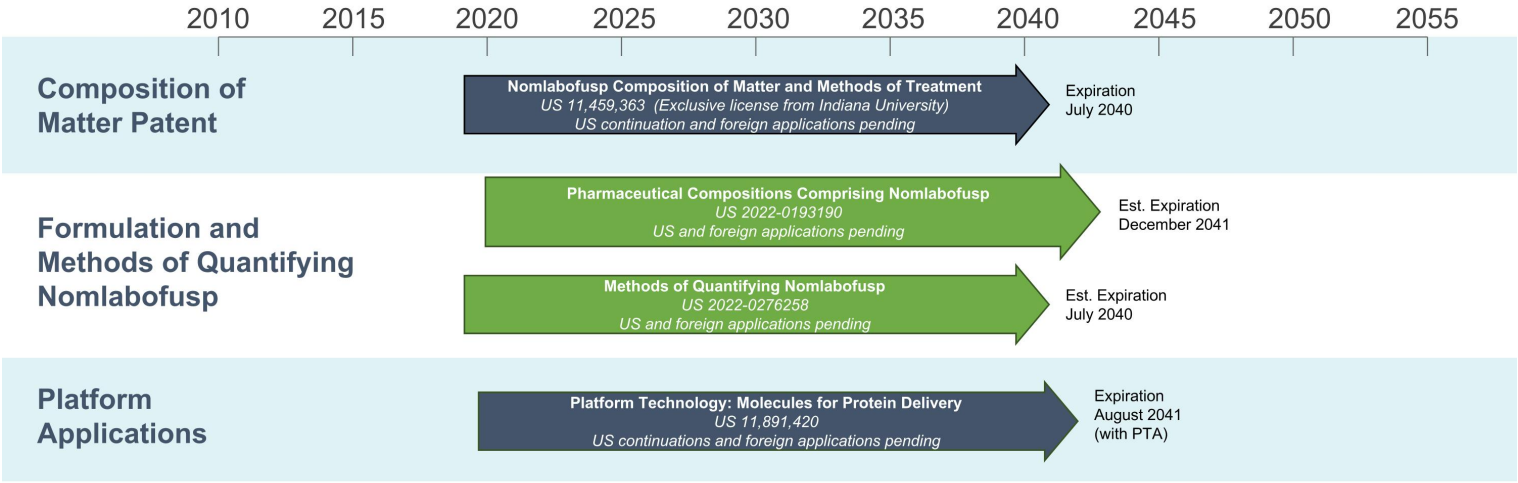
In some cases, you can identify forward-looking statements by the words “may,” “will,” “could,” “would,” “should,” “expect,” “intend,” “plan,” “anticipate,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “ongoing” or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements involve risks, uncertainties and other factors that may cause actual results, performance, or achievements to be materially different from the information expressed or implied by these forward-looking statements. These risks, uncertainties and other factors include, among others, the success, cost and timing of Larimar’s product development activities, nonclinical studies and clinical trials, including nomlabofusp clinical milestones and continued interactions with the FDA; that preliminary clinical trial results may differ from final clinical trial results, that earlier non-clinical and clinical data and testing of nomlabofusp may not be predictive of the results or success of later clinical trials, and assessments; that the FDA may not ultimately agree with Larimar’s nomlabofusp development strategy; the potential impact of public health crises on Larimar’s future clinical trials, manufacturing, regulatory, nonclinical study timelines and operations, and general economic conditions; Larimar’s ability and the ability of third-party manufacturers Larimar engages, to optimize and scale nomlabofusp’s manufacturing process; Larimar’s ability to obtain regulatory approvals for nomlabofusp and future product candidates; Larimar’s ability to develop sales and marketing capabilities, whether alone or with potential future collaborators, and to successfully commercialize any approved product candidates; Larimar’s ability to raise the necessary capital to conduct its product development activities; and other risks described in the filings made by Larimar with the Securities and Exchange Commission (SEC), including but not limited to Larimar’s periodic reports, including the annual report on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, filed with or furnished to the SEC and available at www.sec.gov. These forward-looking statements are based on a combination of facts and factors currently known by Larimar and its projections of the future, about which it cannot be certain. As a result, the forward-looking statements may not prove to be accurate. The forward-looking statements in this presentation represent Larimar’s management’s views only as of the date hereof. Larimar undertakes no obligation to update any forward-looking statements for any reason, except as required by law.

# Clinical-Stage Novel Protein Replacement Therapy Platform

| | |
|---|---|
| **Potential first therapy to increase frataxin levels** | Lead candidate nomlabofusp is a recombinant fusion protein designed to directly address frataxin deficiency in patients with FA by delivering the protein to mitochondria. Granted Orphan Drug (US & EU), Rare Pediatric Disease (US), Fast Track (US), PRIME (EU) and ILAP (UK-MHRA) designations. Selected by FDA to participate in its START pilot program |
| **Consistent Phase 1 and Phase 2 findings** | Nomlabofusp was generally well tolerated and demonstrated dose-dependent increases in frataxin (FXN) levels from baseline in skin and buccal cells in a completed 4-week placebo-controlled Phase 2 study and a completed multiple ascending dose Phase 1 study |
| **Plan to pursue accelerated approval with FDA** | FDA acknowledgement that FXN deficiency appears to be critical to the pathogenic mechanism of FA, and that there continues to be an unmet need for treatments that address the underlying disease pathophysiology. Discussions to support an accelerated approval are ongoing. BLA submission targeted for 2H 2025 |
| **Clinical program** | Dosed first adult patient in OLE with 25 mg daily in Q1 2024; All 7 OLE sites activated; continuing to enroll patients<br>Available data on enrolled patients in the ongoing OLE study and development program update expected mid-Dec 2024<br>Plans to initiate PK run-in study in adolescents by end of 2024; transition adolescents into OLE after assessment of safety and exposure data in the adolescent cohort<br>Dose escalation to 50 mg currently planned following further characterization of FXN PD at 25 mg dose |
| **Strong financial foundation** | Approximately $204 million in cash and investments as of 9/30/24<br>Provides projected cash runway into 2026 |

# Larimar Technology is Supported by a Strong IP Portfolio

## Granted nomlabofusp (CTI-1601) composition of matter patent extends into 2040




### Additional nomlabofusp IP protection

- US and foreign pending applications cover key biomarkers, analytical tools and methods of treatment for additional disease indications for nomlabofusp
- Nomlabofusp should be eligible for **12 years of market exclusivity** upon approval in the US (independent of patents) and at least **10 years of market exclusivity** upon approval in EU (independent of patents)

Granted Pending

# 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 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 EU
~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

**No approved therapies increase frataxin levels**

Only treatment approved for FA does not address frataxin deficiency

Larimar Therapeutics

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

# **Strong Relationship with FARA –** Joined FARA's TRACK-FA Neuroimaging Consortium as an Industry Partner

**TRACK-FA** collects natural history data to establish disease specific neuroimaging biomarkers for potential use in clinical trials. Larimar will have access to all study data for use in regulatory filings, as appropriate

**FARA provides industry with several key items**

- Assistance with patient recruitment and education
- Access to Global Patient Registry with demographic and clinical information on more than 1,000 FA patients
- Sponsored a Patient-Focused Drug Development Meeting in 2017 resulting in a publication titled "The Voice of the Patient"

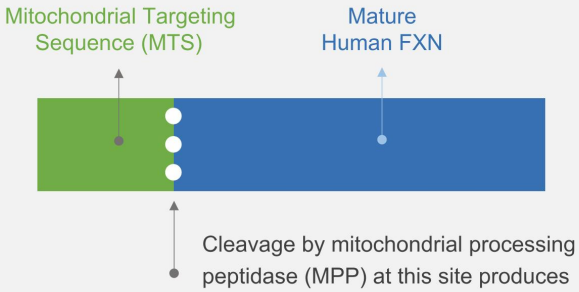
FARA Friedreich's Ataxia Research Alliance

National, non-profit organization dedicated to the pursuit of scientific research leading to treatments and a cure for FA

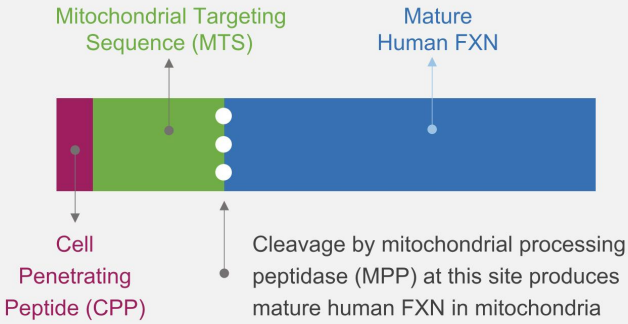
# Nomlabofusp is Designed to Deliver Additional Frataxin

**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**

Larimar Therapeutics

# FXN Levels Predict Disease Progression in FA

**Lower FXN levels are associated with earlier onset of disease, faster rate of disease progression, and shorter time to loss of ambulation**

### Median Age of Onset and Rate of Disease Progression in Relation to FXN Levels

| **FXN Level*** (% of Normal Level) | **Age of Onset** (Years) | **FARS**** (Change/Year) |
|---|---|---|
| 11.2 | 7 | 2.9 |
| 22.0 | 11 | 2.1 |
| 31.0 | 16 | 2.0 |
| 48.7 | 19 | 1.6 |

Adapted from H.L.Plasterer et al. PLoS ONE 2013 8(5):e63958

### Median Age of Onset Predicts Time to Loss of Ambulation

| **Age of Onset** (Years) | **Median Time to Loss of Ambulation** (Years) |
|---|---|
| < 15 | 11.5 |
| 15 to 24 | 18.3 |
| > 24 | 23.5 |

Adapted from C. Rummey et al. EClinicalMedicine. 2020 18:100213

Larimar Therapeutics

*FXN levels measured in peripheral blood mononuclear cells (PBMCs). FXN levels as measured by % of normal demonstrated to be equivalent in PBMCs, buccal cells, and whole blood.
**FARS: Friedreich's ataxia rating score, measures disease progression with a higher score indicating a greater level of disability.

# Completed Ph 2 Dose Exploration Study (25 & 50 mg Cohorts)

**Goal: Further characterize PK/PD and assess safety to inform long-term dose and dose regimen**

**28-day Treatment Period - nomlabofusp (CTI-1601) or placebo**

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|

= Subcutaneous administration of nomlabofusp (CTI-1601) or placebo

= No Administration

| Study Details | |
|---|---|
| **Population** | Ambulatory and non-ambulatory Friedreich's ataxia patients ≥18 years of age<br>Nomlabofusp (CTI-1601) treatment naïve or participated (if eligible) in a previous Larimar study |
| **Dose** | **Cohort 1:** 25 mg<br>**Cohort 2:** 50 mg |
| **Key Endpoints** | Frataxin levels in peripheral tissue, PK, safety and tolerability; other exploratory endpoints include lipids and gene expression levels |
| **Number of Patients** | **Cohort 1:** Enrolled 13 participants (9 on nomlabofusp; 4 on placebo)<br>**Cohort 2:** Enrolled 15 participants (10 on nomlabofusp; 5 on placebo) |
| **Key Results** | Generally well tolerated; most common adverse events were mild and moderate injection site reactions<br>Dose dependent increases of frataxin levels in tissues tested (skin and buccal cells)<br>Baseline FXN levels in skin cells in the 50 mg cohort were < 17% of the average of healthy volunteers. After daily dosing for 14 days, FXN levels increased to 33% to 59% of the average of the healthy volunteers |

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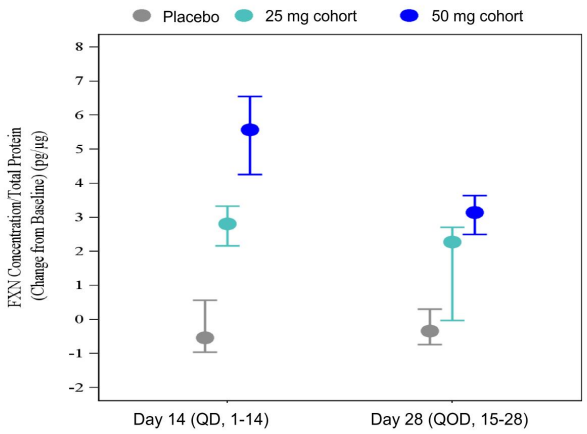
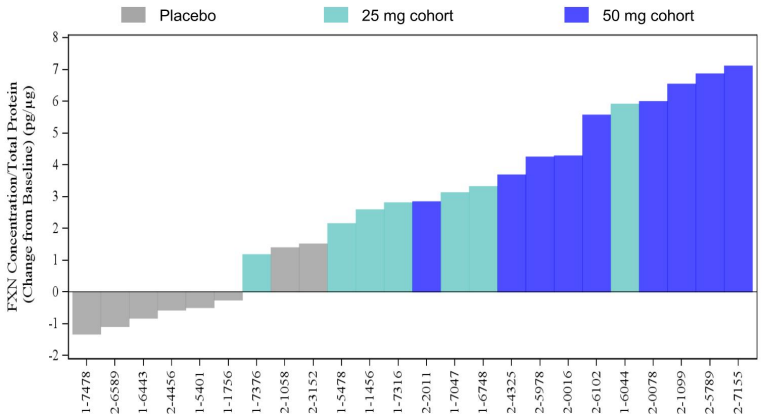
# Dose-Dependent Increase in FXN Levels in Skin Cells

**Participants dosed daily for 14 days, then every other day until day 28**

## Skin Cells
## FXN Levels* Change from Baseline**




## FXN Levels* in Skin Cells
## Change from Baseline at Day 14

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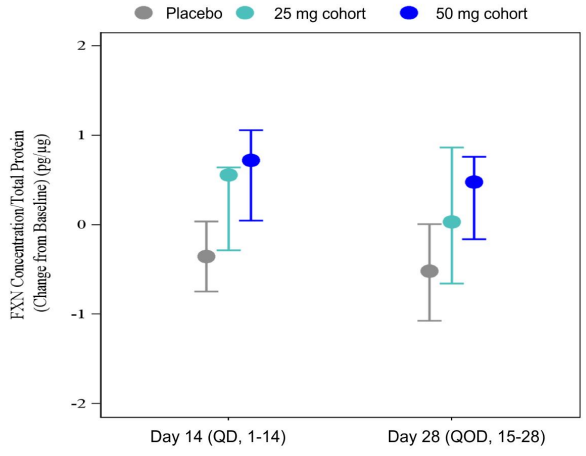
*FXN levels measured via detection of peptide derived from mature FXN; FXN concentrations are normalized to total cellular protein content in each sample. Data represent median and 25th and 75th percentiles. Only participants with quantifiable levels at both baseline and Day 14 are included in the figures.
**Median baseline FXN levels in patients were 3.5 pg/µg for the placebo, 3.7 pg/µg for the 25 mg cohort and 2.1 pg/µg for the 50 mg cohort.

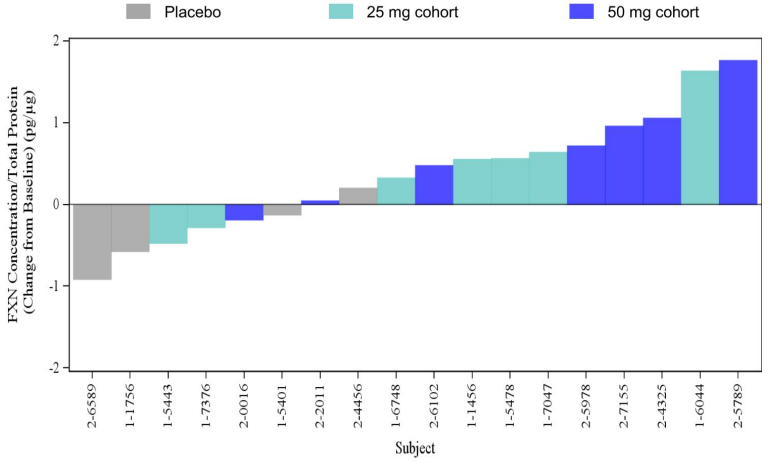
# Dose-Dependent Increase in FXN Levels in Buccal Cells

**Participants dosed daily for 14 days, then every other day until day 28**

## Buccal Cells
## FXN Levels* Change from Baseline**

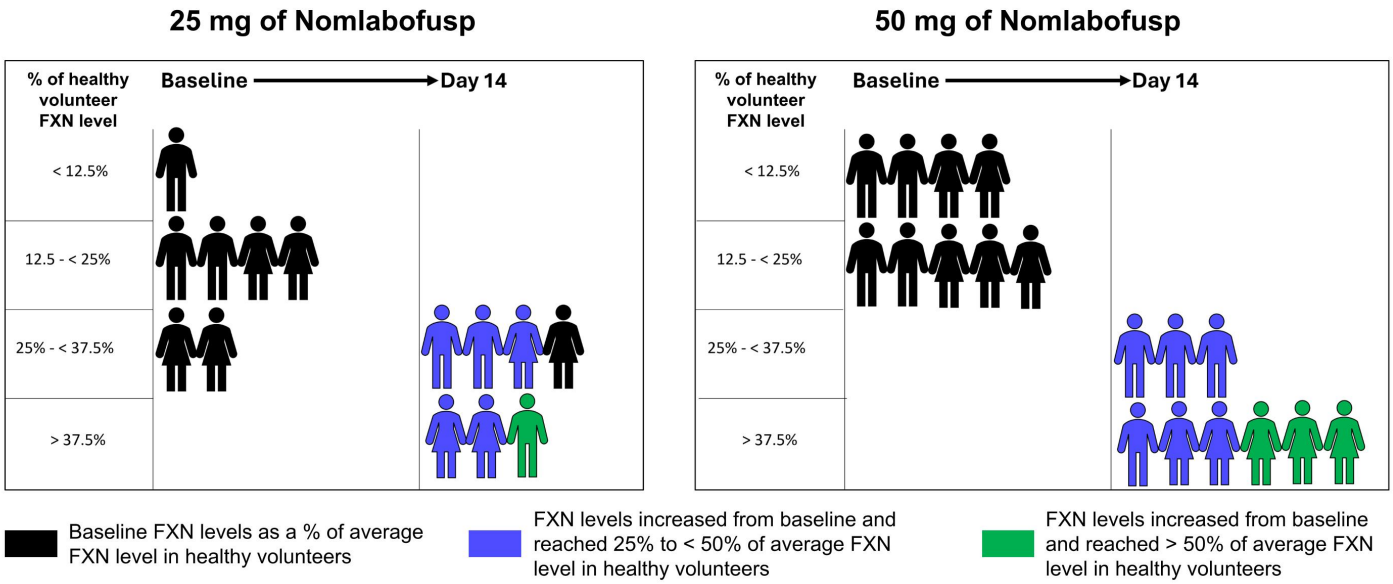



## FXN Levels* in Buccal Cells
## Change from Baseline at Day 14



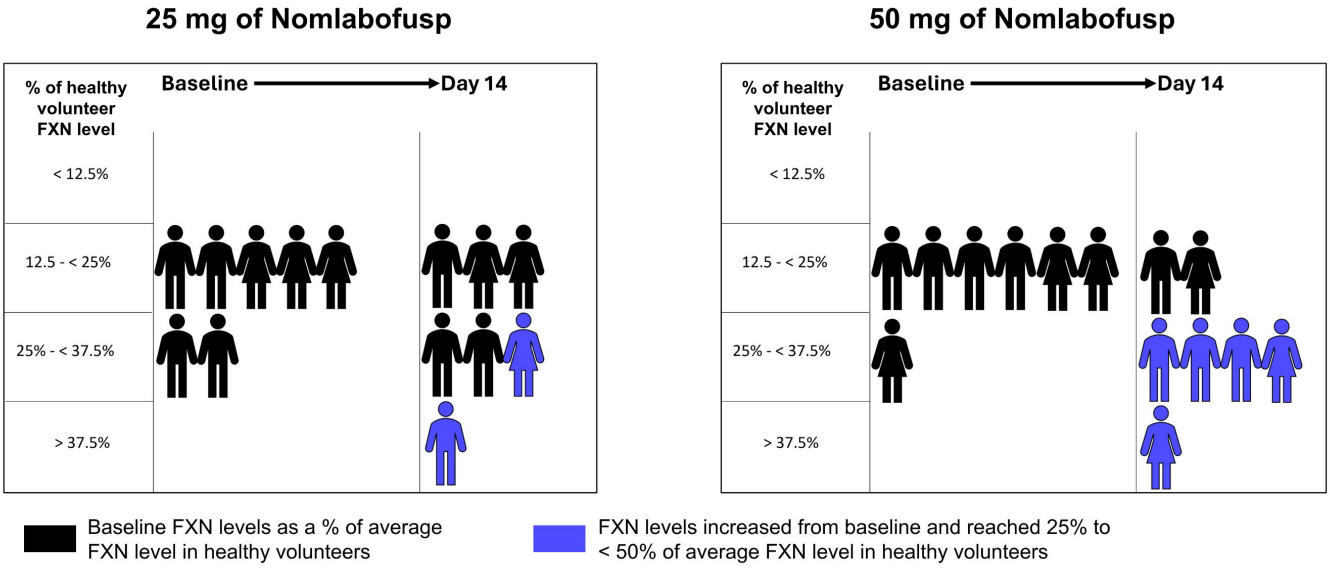

*FXN levels measured via detection of peptide derived from mature FXN; FXN concentrations are normalized to total cellular protein content in each sample. Data represent median and 25th and 75th percentiles. Only participants with quantifiable levels at both baseline and Day 14 are included in the figures.
**Median baseline FXN level in patients were 2.1 pg/µg for the placebo, 1.8 pg/µg for the 25 mg cohort and 1.6 pg/µg for the 50 mg cohort.

# Skin Cell FXN Levels Achieve Higher % of Healthy Volunteers* Following 14 days of Daily Nomlabofusp




Only participants with quantifiable levels at baseline and day 14 are included in the figures.
*% of healthy volunteer FXN level is calculated by dividing each participant's FXN level by the average FXN level (16.34 pg/µg) from the noninterventional healthy volunteer study (N=60).

# Buccal Cell FXN Levels Achieve Higher % of Healthy Volunteers* Following 14 days of Daily Nomlabofusp




Only participants with quantifiable levels at baseline and day 14 are included in the figures.
*% of healthy volunteer FXN level is calculated by dividing each participant's FXN level by the average FXN level (8.24 pg/µg) from Larimar's noninterventional healthy volunteer study (N=60).

# Nomlabofusp: Predictable Pharmacokinetics

1. Quick absorption after subcutaneous administration
2. Dose-proportional increases in exposure observed
3. Pharmacokinetic profile consistent with Phase 1 studies

# Open-label Extension Study: Dosed first patient in Q1 2024

**Available data on enrolled patients in ongoing OLE and development program update expected in mid-Dec 2024**

## Key Eligibility Criteria

Previous participation in Phase 1 or Phase 2 trials

**Daily subcutaneous injection of 25 mg nomlabofusp;**
self-administered or by a caregiver
**Plan to increase dose to 50 mg daily**

- All 7 sites activated
- First patient dosed in March 2024
- Continuing to enroll patients
- Amending study to include adolescents (12-17 yrs) and children (2-11 yrs) after completion of PK run-in study

## Key Study Objectives

- Safety and tolerability
- Long-term PK
- Dose escalation to 50 mg currently planned following further characterization of FXN pharmacodynamics at 25 mg dose
- Tissue FXN concentrations and potential use as surrogate endpoint to support accelerated approval
- Clinical efficacy measures compared to the matched set of untreated patients from FACOMS* database

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

*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 Clinical Development Plan

## Intend to pursue accelerated approval pathway with potential BLA submission targeted for 2H 2025
## Selected by FDA to participate in its START pilot program


Ongoing open-label extension study with 25 mg daily dosing for eligible patients who participated in SAD, MAD, and/or four-week dose exploration studies

Available data on enrolled patients in ongoing OLE expected in mid-December 2024

Plans to Initiate PK run-in study in adolescents (12-17 yrs) before year end 2024, followed by children (2-11 yrs) in 1H 2025

Participants completing the PK run-in study eligible to transition into OLE after assessment of safety and exposure data in the adolescent cohort

Planned global double-blind placebo-controlled confirmatory/registration study targeted to be initiated by mid- 2025*

BLA submission targeted for 2H 2025

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*Company initiated discussions with FDA on the potential use of FXN levels to support accelerated approval. Also, the Company is planning discussions with regulators and investigators outside the U.S. to expand clinical program to international geographies.

# Nomlabofusp is a Competitively Differentiated Treatment Approach*

**$7.3B** Acquisition supports the **robust market potential** for FA treatments

REATA PHARMACEUTICALS Biogen

**Nomlabofusp** is a potential **first-and-only protein replacement therapy** designed to address the underlying cause of FA

| Approach | Product | Company | Mechanism of Action | Clinical Status |
|---|---|---|---|---|
| **Protein replacement** | **Nomlabofusp (CTI-1601)** | **Larimar** | **Recombinant frataxin protein** | **Phase II** |
| **Mitochondrial Oxidative Stress Modifier** | Omaveloxolone (SKYCLARYS™) | Reata Pharma/Biogen | Nrf2 Activator | Approved (US and EU) |
| | Vatiquinone | PTC Therapeutics | 15-Lipoxygenase Inhibitor | Phase III |
| **Gene Expression Regulator** | DT-216P2 (new formulation) | Design Therapeutics | GeneTAC | Pre-clinical |
| **Gene Therapy** | LX2006 | Lexeo Therapeutics | Frataxin Gene Replacement | Phase I/II |

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*Competitive landscape focuses on clinical-stage, industry-sponsored programs from public companies

# Positive Ph2 Data, OLE Updates & Initiating in Adolescents

| | |
|---|---|
| **Consistent Ph 1 and Ph 2 Findings** | Nomlabofusp is generally well tolerated at doses tested up to 4 weeks<br>Dose-dependent increases in FXN levels from baseline in evaluated tissues (skin and buccal cells)<br>Baseline FXN levels in skin cells in the 50 mg cohort were < 17% of the average of healthy volunteers. After daily dosing for 14 days, FXN levels increased to 33% to 59% |
| **Clinical & Regulatory Updates** | Plans to Initiate PK run-in study in adolescents by end of 2024; transition adolescents into OLE after PK study<br>Pursuing clinical sites in the U.S., Europe, the U.K., Canada. and Australia for planned initiation of registration/confirmatory study targeted for mid- 2025<br>Selected by FDA to participate in its START pilot program<br>Initiated discussions with FDA regarding use of FXN as a surrogate endpoint to support accelerated approval |
| **2024/2025 Milestones** | **Nov 2024:** Three posters on Ph1 and Ph 2 dose exploration data at International Congress for Ataxia Research in London (Nov 12-15, 2024)<br>**Mid-Dec 2024:** Available data on enrolled patients in ongoing OLE and development program update<br>**Q4 2024:** Initiate PK run-in study in adolescents (ages 12-17 years old)<br>**1H 2025:** Initiate PK run-in study in children (ages 2-11 years old)<br>**Mid 2025:** Initiate global confirmatory/registration study<br>**2H 2025:** BLA submission; intend to pursue accelerated approval |

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# Clinical-Stage Novel Protein Replacement Therapy Platform

| | |
|---|---|
| **Potential first therapy to increase frataxin levels** | Lead candidate nomlabofusp is a recombinant fusion protein designed to directly address frataxin deficiency in patients with FA by delivering the protein to mitochondria. Granted Orphan Drug (US & EU), Rare Pediatric Disease (US), Fast Track (US), PRIME (EU) and ILAP (UK-MHRA) designations. Selected by FDA to participate in its START pilot program |
| **Consistent Phase 1 and Phase 2 findings** | Nomlabofusp was generally well tolerated and demonstrated dose-dependent increases in frataxin (FXN) levels from baseline in skin and buccal cells in a completed 4-week placebo-controlled Phase 2 study and a completed multiple ascending dose Phase 1 study |
| **Plan to pursue accelerated approval with FDA** | FDA acknowledgement that FXN deficiency appears to be critical to the pathogenic mechanism of FA, and that there continues to be an unmet need for treatments that address the underlying disease pathophysiology. Discussions to support an accelerated approval are ongoing. BLA submission targeted for 2H 2025 |
| **Clinical program** | Dosed first adult patient in OLE with 25 mg daily in Q1 2024; All 7 OLE sites activated; continuing to enroll patients<br>Available data on enrolled patients in the ongoing OLE study and development program update expected mid-Dec 2024<br>Plans to initiate PK run-in study in adolescents by end of 2024; transition adolescents into OLE after assessment of safety and exposure data in the adolescent cohort<br>Dose escalation to 50 mg currently planned following further characterization of FXN PD at 25 mg dose |
| **Strong financial foundation** | Approximately $204 million in cash and investments as of 9/30/24<br>Provides projected cash runway into 2026 |

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Nomlabofusp (CTI-1601); FA: Friedreich's ataxia


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October 2024 Corporate Deck
THANK YOU

# Larimar Therapeutics

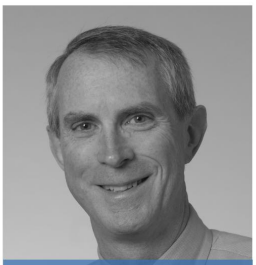
Appendix

# Scientific Advisory Board

**Giovanni Manfredi, MD, PhD**

Finbar and Marianne Kenny Professor in Clinical and Research Neurology at Weill Cornell Medicine.

Professor of Neuroscience at Weill Cornell Medicine.



**Mark Payne, MD**

Co-founder of Chondrial Therapeutics, which became Larimar Therapeutics, Inc.

Professor of Pediatrics at Indiana University School of Medicine

**Marni J. Falk, MD**

Executive Director of the Mitochondrial Medicine Frontier Program at The Children's Hospital of Philadelphia (CHOP)

Professor in the Division of Human Genetics, Department of Pediatrics at University of Pennsylvania Perelman School of Medicine

**Jill Ostrem, MD**

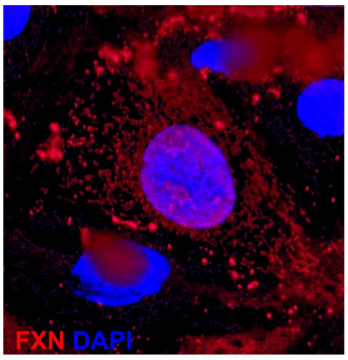
Medical Director and Division Chief of the University of California San Francisco (UCSF) Movement Disorders and Neuromodulation Center.

Carlin and Ellen Wiegner Endowed Professor of Neurology

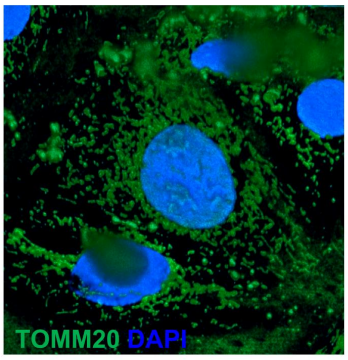
# Mitochondrial Localization and Preclinical Data

# Nomlabofusp Transduction of Cells In Vitro Leads to hFXN Located in Mitochondria

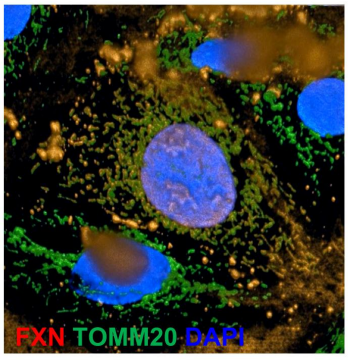
FXN staining




TOMM20 (mitochondria) staining




FXN co-localizes with TOMM20




- Rat cardiomyocytes (H9C2) were transduced with nomlabofusp
- Cells were fixed and analyzed by immunofluorescence microscopy to detect the presence of human frataxin (hFXN) and TOMM20 ( a mitochondrial outer membrane protein)
- Nuclei were stained with DAPI

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# Nomlabofusp Extends Survival in FXN-deficient KO Mice

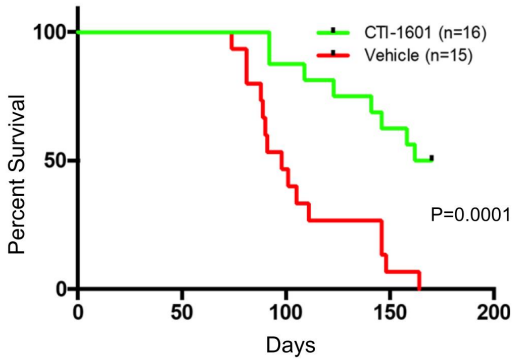
**Initial proof-of-concept for FXN replacement therapy in cardiac mouse model of FA**

### Median survival of MCK-Cre FXN-KO mice

- 166 days (nomlabofusp) vs. 98 days (Vehicle)
- Nomlabofusp administered 10 mg/kg SC every other day

### Survival beyond vehicle mean (107.5 days)

- 87.5% (nomlabofusp) vs. 33% (Vehicle)
- Demonstrates that nomlabofusp is capable of delivering sufficient amounts of FXN to mitochondria




**Nomlabofusp (CTI-1601) rescues a severe disease phenotype in a well-characterized cardiac mouse model of FA**

# Nomlabofusp Prevents Development of Ataxic Gait in Neurologic KO Mouse Model

## In-Vivo Efficacy Data in Pvalb-Cre FXN-KO Mouse Model

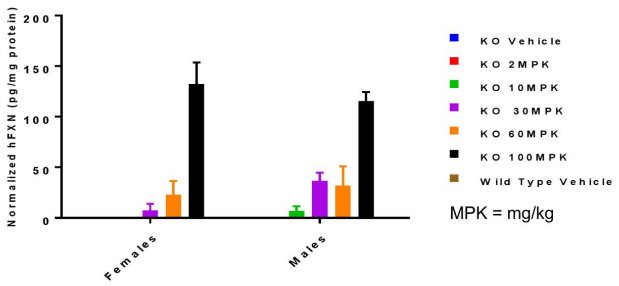
Single dose level: 10 mg/kg nomlabofusp or vehicle given intraperitoneally three times per week

- hFXN replacement with nomlabofusp **prevents development of ataxic gait**
- Nomlabofusp-treated mice **survive longer** than untreated mice
- Human frataxin **present in brain, dorsal root ganglia and spinal cord** demonstrating central nervous system penetration

# Nomlabofusp Delivers hFXN to Mitochondria and Restores SDH Activity in KO Mice

**Study Design** – Cardiac and skeletal muscle FXN knockout mice (MCK-CRE) were treated at varying SQ doses of nomlabofusp every other day for two weeks at Jackson Laboratories (Bar Harbor, ME). After dosing, animals were sacrificed, and heart and skeletal muscle were evaluated for hFXN concentration in mitochondrial extracts and SDH activity was assessed.

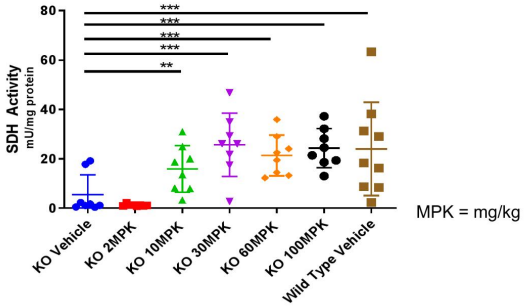
## Mitochondrial FXN (Heart)




Mitochondria hFXN concentration increases dose-dependently

Given subcutaneously, nomlabofusp functionally replaces hFXN in mitochondria of KO mice

## SDH Activity (Muscle)




Succinate dehydrogenase (SDH) activity, which is indicative of mitochondrial function, increases in a dose-dependent manner after administration of nomlabofusp; activity plateaus at 30 mg/kg and is equivalent to activity in wild type

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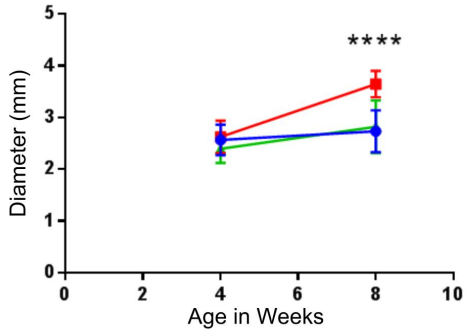
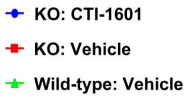
# Nomlabofusp Prevents Left Ventricle Dilation in KO Mice

**Study Design** – Cardiac and skeletal muscle FXN knockout mice (MCK-CRE) were treated at 10 mg/kg every other day at Jackson Laboratories (Bar Harbor, ME). Echocardiograms were performed pre-dose and post dose.

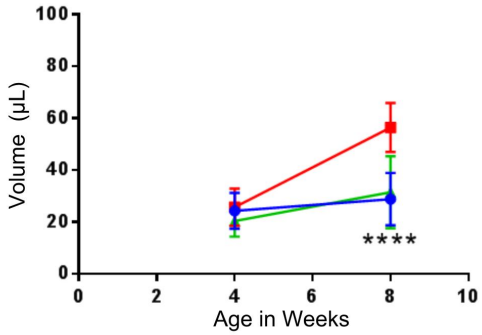
## Left Ventricle Internal Diameter (Systole)




Left ventricular (LV) volume increases in systole in untreated mice by 8 weeks (after 4 weeks of dosing with vehicle), but remains similar to wildtype when treated with nomlabofusp (10 mg/kg every other day)




## Left Ventricle Volume (Systole)




Nomlabofusp-treated mice have similar LV volume as wild type; echocardiogram shows significant differences between vehicle and nomlabofusp treated (10 mg/kg every other day) KO mice

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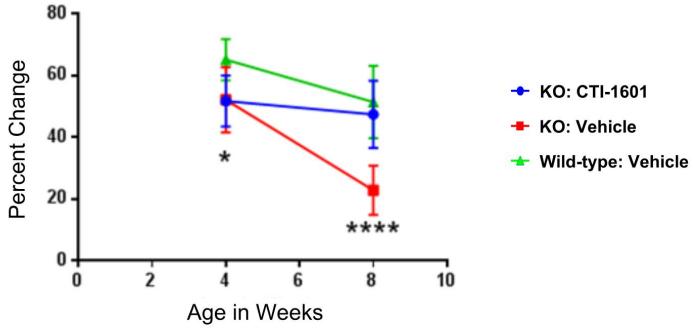
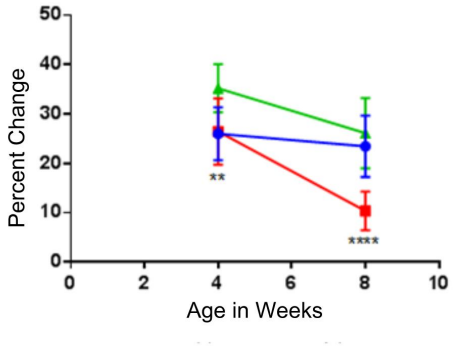
# Nomlabofusp Preserves Left Ventricle Function in KO Mice

**Study Design** – Cardiac and skeletal muscle FXN knockout mice (MCK-CRE) were treated at 10 mg/kg every other day at Jackson Laboratories (Bar Harbor, ME). Echocardiograms were performed pre-dose and post dose.

**Left Ventricle Ejection Function**




**Left Ventricle Fractional Shortening**




Left ventricular (LV) function drops significantly in vehicle treated mice by Week 8

Nomlabofusp-treated (10 mg/kg every other day) mice have similar LV function as wildtype; echocardiogram shows significant differences between vehicle and nomlabofusp treated KO mice

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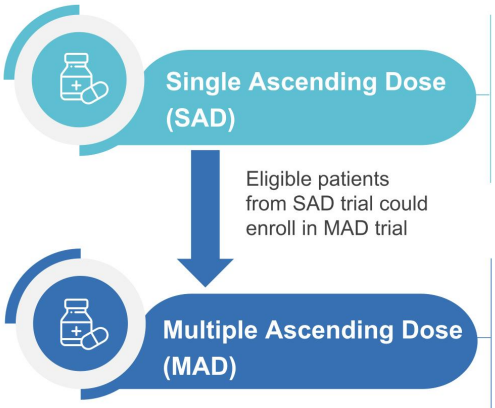
# Phase 1 Clinical Data

# CTI-1601: Phase 1 Clinical Program in Patients with FA

## Program consisted of double-blind, placebo controlled single- and multiple-ascending dose trials

**Phase 1 Development Plan**

- Two double-blind, placebo-controlled dosing trials in patients with FA
- Patient dosing began December 2019
- Safety Review Committee assessed all blinded data between each cohort to ensure patient safety




**Number of subjects:** 28
**Dose levels:** 25 mg, 50 mg, 75 mg and 100 mg (subcutaneous administration)
**Treatment Duration:** 1 day
**1º Endpoint:** Safety and tolerability
**2º Endpoints:** PK; PD; FXN levels; multiple exploratory
**Status:** Complete

**Number of Subjects:** 27
**Dose Range:** 25 mg, 50 mg, 100 mg (subcutaneous administration)
**Treatment Regimen:** Multiple increasing doses administered subcutaneously over 13 days
**1º Endpoint:** Safety and tolerability
**2º Endpoints:** PK; PD; FXN levels (buccal cells, platelets, optional skin biopsies); multiple exploratory
**Status:** Complete

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# Completed Phase 1 Multiple Ascending Dose Study

## Treatment Schedules for Each Cohort- nomlabofusp (CTI-1601) or placebo

**Cohort 1 (25 mg; n = 8)**

**13-day Treatment Period**

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|

= Administration of nomlabofusp or placebo

= No Administration

**Cohort 2 (50 mg; n = 9)**

**13-day Treatment Period**

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|

= Administration of nomlabofusp or placebo

= No Administration

**Cohort 3 (100 mg n = 10)**

**13-day Treatment Period**

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|

= Administration of nomlabofusp or placebo

= No Administration

## FXN Level Sampling Days Presented for Each Cohort

| Cohort 1 Sampling Days | |
|---|---|
| **Buccal Cells** | Baseline, Day 4, Day 13 |
| **Skin** | Baseline, Day 13 |
| **Platelets** | Baseline, Day 4, Day 13 |

| Cohort 2 Sampling Days | |
|---|---|
| **Buccal Cells** | Baseline, Day 7, Day 13 |
| **Skin** | Baseline, Day 13 |
| **Platelets** | Baseline, Day 7, Day 13 |

| Cohort 3 Sampling Days | |
|---|---|
| **Buccal Cells** | Baseline, Day 7, Day 13 |
| **Skin** | Baseline, Day 13 |
| **Platelets** | Baseline, Day 7, Day 13 |

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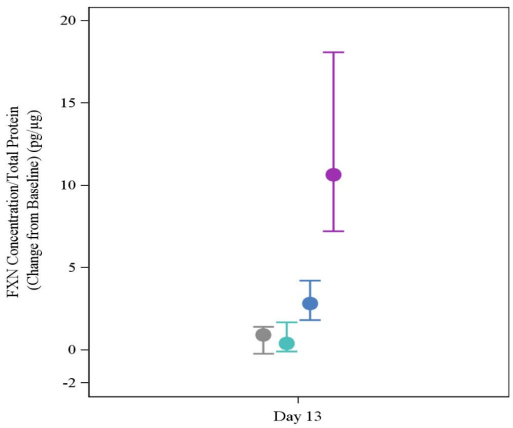
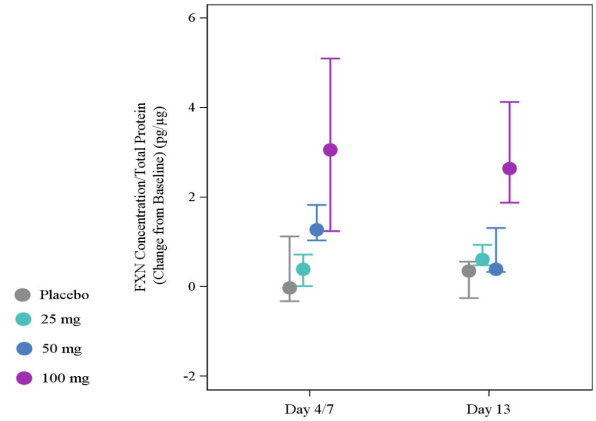
# Dose Dependent Increases in FXN Levels Observed in Skin and Buccal Cells in Phase 1

**FXN* Change from Baseline By Dose Group (Skin Cells)**




**FXN* Change from Baseline By Dose Group (Buccal Cells)**







**Placebo:** Participants randomized to placebo in each cohort
**25 mg:** Dosed daily for 4 days, every third day thereafter
**50 mg:** Dosed daily for 7 days, every other day thereafter
**100 mg:** Dosed daily for 13 days

*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; FXN levels from Day 4, & Day 13 measurements are shown for data derived from the 25 mg cohort; FXN levels from Day 7 & Day 13 measurements are shown for data derived from the 50 & 100 mg cohorts;

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# MAD Trial Patient Demographics

| Parameter | Statistic | All placebo (n=7) | 25 mg CTI-1601 (n=6) | 50 mg CTI-1601 (n=7) | 100 mg CTI-1601 (n=7) | All CTI-1601 (n=20) | Overall (n=27) |
|---|---|---|---|---|---|---|---|
| **Sex** | | | | | | | |
| Male | n (%) | 5 (71.4) | 3 ( 50.0) | 4 ( 57.1) | 3 ( 42.9) | 10 ( 50.0) | 15 (55.6) |
| Female | n (%) | 2 (28.6) | 3 ( 50.0) | 3 ( 42.9) | 4 ( 57.1) | 10 ( 50.0) | 12 (44.4) |
| **Age (years)** | | | | | | | |
| | Mean | 25.7 | 39.7 | 34.7 | 28.0 | 33.9 | 31.7 |
| | SD | 6.37 | 16.59 | 9.03 | 8.96 | 12.13 | 11.40 |
| | Median | 23 | 37 | 36 | 24 | 34 | 28 |
| | Min, Max | 20,36 | 21,65 | 19,47 | 20,44 | 19,65 | 19,65 |
| **Race** | | | | | | | |
| White | n (%) | 6 ( 85.7) | 6 (100.0) | 6 ( 85.7) | 6 ( 85.7) | 18 ( 90.0) | 24 (88.9) |
| Asian | n (%) | 0 | 0 | 1 ( 14.3) | 1 ( 14.3) | 2 ( 10.0) | 2 ( 7.4) |
| American Indian | n (%) | 1 ( 14.3) | 0 | 0 | 0 | 0 | 1 (3.7) |
| **Ethnicity** | | | | | | | |
| Hispanic/Latino | n (%) | 2 (28.6) | 0 | 0 | 0 | 0 | 2 (7.4) |
| Not Hispanic/Latino | n (%) | 5 (71.4) | 6 (100.0) | 7 (100.0) | 7 (100.0) | 20 (100.0) | 25 (92.6) |

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SD: Standard deviation

# MAD Trial Patient Disease Characteristics

| Parameter | Statistic | All placebo (n=7) | 25 mg CTI-1601 (n=6) | 50 mg CTI-1601 (n=7) | 100 mg CTI-1601 (n=7) | All CTI-1601 (n=20) | Overall (n=27) |
|---|---|---|---|---|---|---|---|
| **Age at Symptom Onset** | | | | | | | |
| | Mean | 14.1 | 24.0 | 19.3 | 11.9 | 18.1 | 17.1 |
| | SD | 5.34 | 14.48 | 6.21 | 6.72 | 10.37 | 9.39 |
| | Median | 15.0 | 18.0 | 19.0 | 10.0 | 18.0 | 16.0 |
| | Min, Max | 8,23 | 12,44 | 8,28 | 5,22 | 5,44 | 5,44 |
| **Age at Diagnosis** | | | | | | | |
| | Mean | 18.3 | 31.5 | 26.4 | 15.9 | 24.3 | 22.7 |
| | SD | 7.87 | 19.88 | 4.28 | 8.21 | 13.24 | 12.23 |
| | Median | 20.0 | 25.5 | 28.0 | 13.0 | 27.0 | 21.0 |
| | Min, Max | 9,32 | 14,64 | 17,30 | 5,27 | 5,64 | 5,64 |
| **Assistive Device** | | | | | | | |
| Walker | n (%) | 0 | 2 (33.3) | 3 (42.9) | 0 | 5 (25.0) | 5 (18.5) |
| Wheelchair | n (%) | 4 (57.1) | 3 (50.0) | 1 (14.3) | 6 (85.7) | 10 (50.0) | 14 (51.9) |
| Other | n (%) | 1 (14.3) | 0 | 1(14.3) | 0 | 1 (5.0) | 2 (7.4) |
| None | n (%) | 2 (28.6) | 1 (16.7) | 2 (28.6) | 1 (14.3) | 4 (20.0) | 6 (22.2) |

SD: Standard deviation

# PK analyses support evaluating once-daily and every-other-day dosing regimens for CTI-1601

## Summary of MAD Trial PK Analyses

- CTI-1601 was quickly absorbed after subcutaneous administration
- Dose-proportional increases in exposure observed with increasing doses of CTI-1601
- Mean half life of CTI-1601 in plasma was approximately 11 hours
- CTI-1601 appeared to be at or close to steady state exposure after 13 days of dosing 100 mg once daily

# Phase 2 Demographic/ Disease Characteristics and Additional Data

# Demographics – Phase 2 Trial

| | 25 mg Cohort | | | 50 mg Cohort | | |
|---|---|---|---|---|---|---|
| | Placebo *N = 4* | Nomlabofusp *N = 9* | Overall *N = 13* | Placebo *N = 5* | Nomlabofusp *N = 10* | Overall *N = 15* |
| **Age at Screening (Years)** | | | | | | |
| Mean (SD) | 34.0 (9.20) | 37.8 (14.93) | 36.6 (13.16) | 28.6 (4.67) | 28.1 (11.00) | 28.3 (9.17) |
| Median | 33 | 31 | 31 | 27 | 24 | 26 |
| Q1, Q3 | 27, 42 | 27, 42 | 27, 42 | 26, 30 | 21, 32 | 21, 32 |
| Min, Max | 25, 45 | 25, 69 | 25, 69 | 24, 36 | 19, 54 | 19, 54 |
| **Sex n (%)** | | | | | | |
| Male | 2 (50.0) | 5 (55.6) | 7 (53.8) | 1 (20.0) | 4 ( 40.0) | 5 (33.3) |
| Female | 2 (50.0) | 4 (44.4) | 6 (46.2) | 4 (80.0) | 6 ( 60.0) | 10 (66.7) |
| **Previously Treated with Nomlabofusp n (%)** | | | | | | |
| Yes | 1 ( 25.0) | 3 ( 33.3) | 4 ( 30.8) | 0 | 1 ( 10.0) | 1 ( 6.7) |
| No | 3 ( 75.0) | 6 ( 66.7) | 9 ( 69.2) | 5 (100.0) | 9 ( 90.0) | 14 ( 93.3) |

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# Disease Characteristics – Phase 2 Study

| | 25 mg Cohort | | | 50 mg Cohort | | |
|---|---|---|---|---|---|---|
| | Placebo *N = 4* | Nomlabofusp *N = 9* | Overall *N = 13* | Placebo *N = 5* | Nomlabofusp *N = 10* | Overall *N = 15* |
| **Age at Symptom Onset (Years)** | | | | | | |
| Mean (SD) | 14.5 (4.93) | 13.0 (10.47) | 13.5 (8.77) | 15.2 (7.26) | 13.7 (8.37) | 14.2 (7.78) |
| Median | 14.5 | 10 | 11 | 14 | 12.5 | 14 |
| Q1, Q3 | 11, 19 | 8, 13 | 9, 15 | 11, 16 | 7, 18 | 7, 18 |
| Min, Max | 9, 20 | 5, 38 | 5, 38 | 8, 27 | 5, 30 | 5, 30 |
| **Age at Diagnosis (Years)** | | | | | | |
| Mean (SD) | 17.5 (5.57) | 18.6 (11.20) | 18.2 (9.58) | 18.6 (6.80) | 16.6 (8.03) | 17.3 (7.46) |
| Median | 16.5 | 16 | 16 | 19 | 13.5 | 14 |
| Q1, Q3 | 14, 22 | 14, 20 | 14, 20 | 13, 20 | 10, 21 | 12, 21 |
| Min, Max | 12, 25 | 5, 42 | 5, 42 | 12, 29 | 9, 30 | 9, 30 |
| **Time Since Diagnosis (Years)** | | | | | | |
| Mean (SD) | 16.1 (5.97) | 18.5 (11.52) | 17.8 (9.94) | 9.5 (3.72) | 11.9 (7.05) | 11.1 (6.10) |
| Median | 13.42 | 14.32 | 13.5 | 11 | 11.26 | 11 |
| Q1, Q3 | 12.9, 19.3 | 12.8, 21.6 | 12.8, 21.6 | 5.8, 11.3 | 7.4, 15.3 | 5.8, 15.2 |
| Min, Max | 12.5, 25.0 | 5.4, 45.0 | 5.4, 45.0 | 5.6, 14.0 | 2.3, 25.1 | 2.3, 25.1 |

# Absolute Increases in Skin FXN Levels

**Dose response in tissue FXN concentrations and increases from baseline after dosing**

| Day 14 Skin FXN Levels | | | |
|---|---|---|---|
| Dose | Visit | Absolute Values (pg/µg) | |
| | | Median | Mean |
| 25 mg | Baseline | 3.70 | 3.38 |
| | Day 14 | 5.53 | 6.40 |
| | **Change from Baseline** | **2.81** | **3.02** |
| 50 mg | Baseline | 2.12 | 2.08 |
| | Day 14 | 7.40 | 7.32 |
| | **Change from Baseline** | **5.57** | **5.24** |

| Day 28 Skin FXN Levels | | | |
|---|---|---|---|
| Dose | Visit | Absolute Values (pg/µg) | |
| | | Median | Mean |
| 25 mg | Baseline | 3.70 | 3.38 |
| | Day 28 | 4.39 | 4.80 |
| | **Change from Baseline** | **2.28** | **1.41** |
| 50 mg | Baseline | 2.12 | 2.08 |
| | Day 28 | 5.23 | 5.24 |
| | **Change from Baseline** | **3.14** | **3.17** |

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Only participants with quantifiable levels at baseline and day 14 and day 28 are included in the tables.

# Absolute Increases in Buccal FXN Levels

**Dose response in tissue FXN concentrations and increases from baseline after dosing**

| Day 14 Buccal FXN Levels | | | |
|---|---|---|---|
| Dose | Visit | Absolute Values (pg/µg) | |
| | | Median | Mean |
| 25 mg | Baseline | 1.78 | 1.80 |
| | Day 14 | 2.24 | 2.22 |
| | **Change from Baseline** | **0.56** | **0.42** |
| 50 mg | Baseline | 1.61 | 1.69 |
| | Day 14 | 2.44 | 2.38 |
| | **Change from Baseline** | **0.72** | **0.69** |

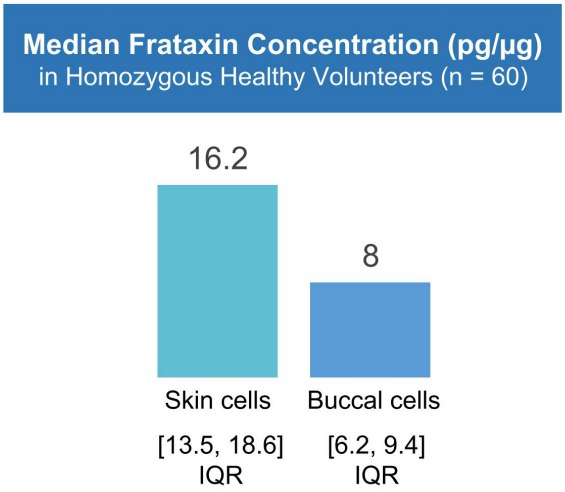
| Day 28 Buccal FXN Levels | | | |
|---|---|---|---|
| Dose | Visit | Absolute Values (pg/µg) | |
| | | Median | Mean |
| 25 mg | Baseline | 1.70 | 1.65 |
| | Day 28 | 1.73 | 1.76 |
| | **Change from Baseline** | **0.03** | **0.11** |
| 50 mg | Baseline | 1.76 | 1.77 |
| | Day 28 | 2.15 | 2.15 |
| | **Change from Baseline** | **0.48** | **0.38** |

Only participants with quantifiable levels at baseline and day 14 and day 28 are included in the tables.

# Non-Interventional Study Data

# CLIN-1601-002: Top-line Non-interventional Study Results

**Non-interventional study measured FXN in homozygous healthy volunteers**




Most patients with FA only produce ~20-40%[1] of normal frataxin levels depending on the tissue, sampling technique, and assay considered

Lower FXN levels seen with typical onset[2] (5 to 15 years of age)

Higher FXN levels seen with late onset[2] (after 25 years of age)

Heterozygous carriers who show no signs of disease have buccal cell FXN levels of ~50% of unaffected healthy persons[1]

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FXN concentrations were measured in skin and buccal cells from 60 homozygous healthy volunteers utilizing the same sampling technique and assay as clinical trials of nomlabofusp; FXN levels measured via detection of peptide derived from mature FXN; FXN concentrations normalized to total cellular protein content in each sample. 1. E.C. Deutsch et al. Molecular Genetics and Metabolism 101 (2010) 238–245. 2. Friedreich's Ataxia Research Alliance

# FDA START Pilot Program

# Nomlabofusp Selected by FDA for START Pilot Program

**Highlights FDA commitment to augment formal meetings with more rapid, ad-hoc communications to accelerate program development of rare diseases**

## START Pilot Program
Support for Clinical Trials Advancing Rare Disease Therapeutics

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

Designed to **accelerate development of novel therapies** intended to address unmet medical needs in **rare diseases**

**7 novel drugs selected**
- 3 products by CDER (nomlabofusp) for rare neurodegenerative conditions
- 4 products by CBER for cell and gene therapy

## CDER Selection Based On

Demonstrated development **program readiness** (e.g., sponsors who demonstrate the ability to move the program towards a marketing application)

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; CBER: Center for Biologics Evaluation and Research; CMC: Chemistry, Manufacturing, and Controls