

**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): November 10, 2025**

**Larimar Therapeutics, Inc.**

(Exact name of Registrant as Specified in Its Charter)

**Delaware**  
(State or Other Jurisdiction  
of Incorporation)

**001-36510**  
(Commission File Number)

**20-3857670**  
(IRS Employer  
Identification No.)

**Three Bala Plaza East**  
**Bala Cynwyd, Pennsylvania**  
(Address of Principal Executive Offices)

**19004**  
(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 8.01 Other Events.**

On November 10, 2025, Larimar Therapeutics, Inc. (the "Company") posted on its website an updated slide presentation, which is attached as Exhibit 99.1 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.

<u>Exhibit No.</u>	<u>Document</u>
99.1	<a href="#">Larimar Therapeutics, Inc. Corporate Presentation, dated November 10, 2025*</a>
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

\* Filed herewith

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**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: November 10, 2025

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

*Name: Carole S. Ben-Maimon, M.D.*

*Title: President and Chief Executive Officer*

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# Larimar Therapeutics

## Corporate Deck

November 2025

## Forward-Looking Statements

This presentation 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 presentation 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 any 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 the timing of the BLA submission, the expectations of the timing of, and potential for, accelerated approval or accelerated access, time to launch and market and overall development plans 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, and Larimar's ability to timely implement the revised dosing regimen in its clinical program for nomlabofusp; 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 non-clinical or clinical trials, and assessments; delays in patient recruitment, including as a result of changes in clinical protocols and adverse events; 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](http://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.

# Nomlabofusp – First Potential Disease Modifying Therapy for Friedreich’s Ataxia

## Initial 50 mg Open Label Study Data Supports Therapeutic Potential of Nomlabofusp

### Increased skin FXN levels and consistent directional improvement in clinical outcomes

- 100% of participants with data at 6 months achieved skin FXN levels over 50% of median levels in healthy volunteers (which is similar to levels in asymptomatic carriers)
- mFARS (primary outcome measure in other clinical studies) median score improvement of 2.25 in OL study participants after 1 year relative to a worsening of a median 1.00 observed in FACOMS natural history reference population
- Consistent directional improvements observed after 1 year across 4 key clinical outcomes (mFARS, FARS-ADL, 9-HPT, MFIS) suggest a potential for clinical benefit relative to a worsening in the FACOMS reference population

### Long-term safety observations with daily nomlabofusp

- Of 39 participants in OL study (65 total participants who received at least 1 dose in all nomlabofusp studies):
  - 7 experienced anaphylaxis in the first 6 weeks of dosing; all returned to usual state of health after standard treatment
  - Of the 39 participants in the OL study, 10 did not have prior exposure to nomlabofusp; 1 of these 10 experienced anaphylaxis (this participant is one of the 7 previously described cases)
- Larimar is modifying its starting dose regimen to mitigate the risk of anaphylaxis.
- Nomlabofusp was generally well tolerated with long-term daily dosing including 14 on treatment for at least 6 months and 8 for over 1 year; most common AEs were mild/moderate local ISRs and did not lead to any withdrawals

### Continue targeting BLA submission Q2 2026

- The BLA will pursue accelerated approval based on increases in skin FXN levels as further demonstrated in this data
- Based on these compelling data, we continue to target the BLA filing for Q2 2026 and believe that nomlabofusp could be the first disease modifying therapy for patients with FA
- \$175.4 million cash and investments as of September 30, 2025, with projected cash runway into Q4 2026



FXN: frataxin; FACOMS: Friedreich's Ataxia Clinical Outcome Measures Study; AE: Adverse events; ISRs: Injection site reactions; BLA: Biologics License Application

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

<b>Genetic defect on both alleles lowers frataxin levels</b>	Most patients with FA only produce ~20-40% of normal frataxin (FXN) levels depending on the tissue, sampling technique, and assay considered*
<b>Affects ~20,000 patients globally</b>	~5,000 patients in the U.S., with most remaining patients in Europe ~70% of patients present before age 14
<b>Progressive disease</b>	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
<b>Unmet Medical Need</b>	The only treatment currently approved for FA does not address frataxin deficiency



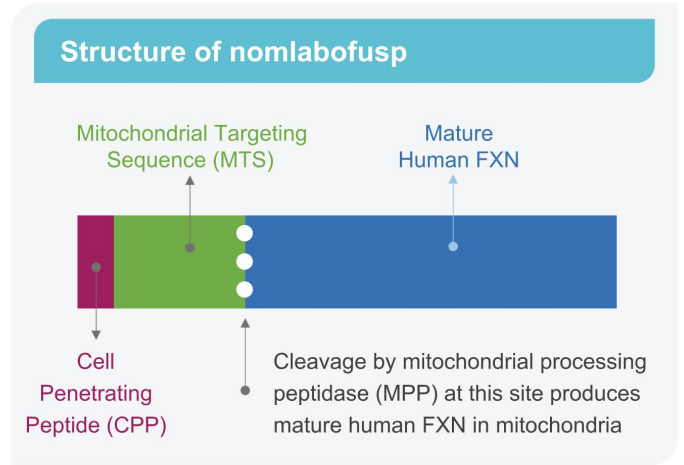
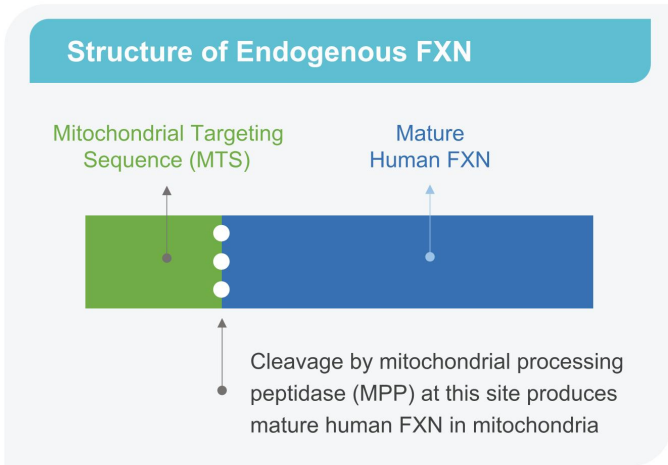
Larimar is developing nomlabofusp, the first potential disease modifying therapy designed to systemically address the underlying FXN deficiency in FA



\* 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)



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

## FXN Levels Clearly 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



\*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.



## Nomlabofusp Long-term Open Label Study

# Expanding Open Label Study\*: Now Includes Adolescents and Participants not in Prior Nomlabofusp Studies

## Patient Population

Initially, participation in a prior Phase 1 or Phase 2 trial required

Expanded study criteria to include:

- Adolescents (12-17 yrs) from the PK run-in study
- Participants not in prior studies

Plan to enroll children (2 to 11 yrs) directly in study

25 mg nomlabofusp

Participants switched from 25 mg to 50 mg dose from Nov 2024 to Q1 2025

50 mg nomlabofusp\*\*\*

Daily subcutaneous injections self-administered or by a caregiver

## Key Study Objectives

- Safety and tolerability
- Long-term PK
- Skin FXN concentrations
- Clinical efficacy measures compared to FACOMS\*\* database

\*\*\*Larimar is modifying the starting dosing regimen to include:

- Antihistamines 5 days prior to first dose and for 90 days after first dose
- 5 mg test dose followed by a 25 mg dose 1 hour later; then 25 mg daily for first 30 days; after 30 days the dose will be increased to 50 mg once daily
- Continue dispensing epinephrine auto-injector such as Epi-Pen, to be administered in the event of anaphylaxis

Larimar provided FDA full data update including safety, FXN and clinical data, and FDA agreed with our approach

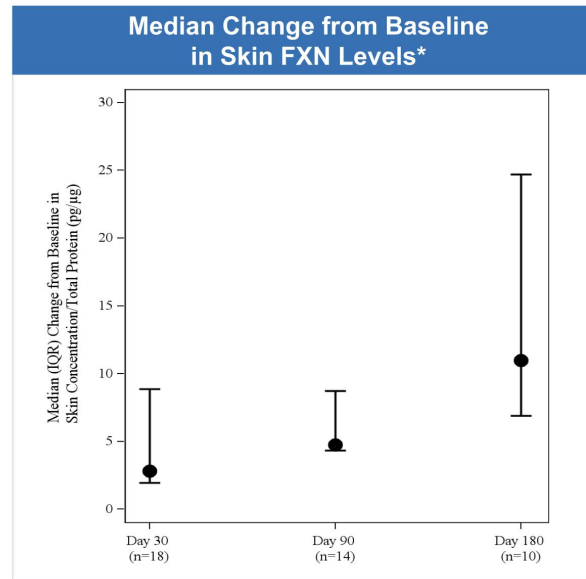
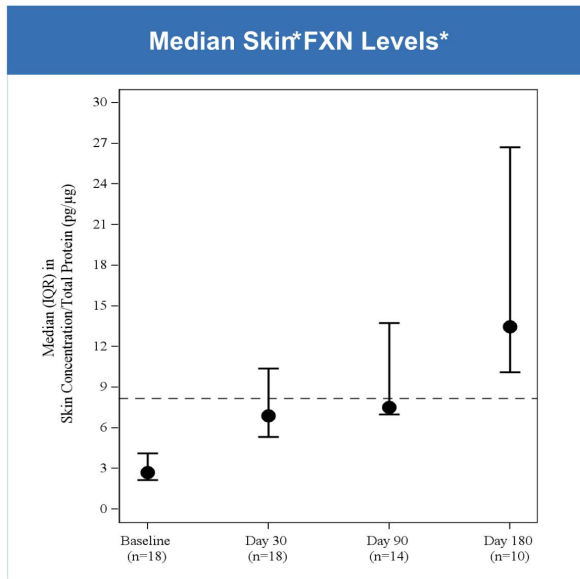


\*Due to inclusion of participants who have not participated in prior nomlabofusp clinical studies, this study is now referred to as Open Label Study (previously called the Open Label Extension study)

\*\*FACOMS: Friedreich's Ataxia Clinical Outcome Measures Study

# Increases in Skin FXN Levels are Sustained Over Time

100% of Participants at Day 180 had Skin FXN Levels >50% of Healthy Volunteers



Dotted Line indicates 50% of healthy volunteers FXN level

\*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 25<sup>th</sup> and 75<sup>th</sup> percentiles. Data include all participants with quantifiable FXN levels at baseline and at least 1 post-baseline FXN level.

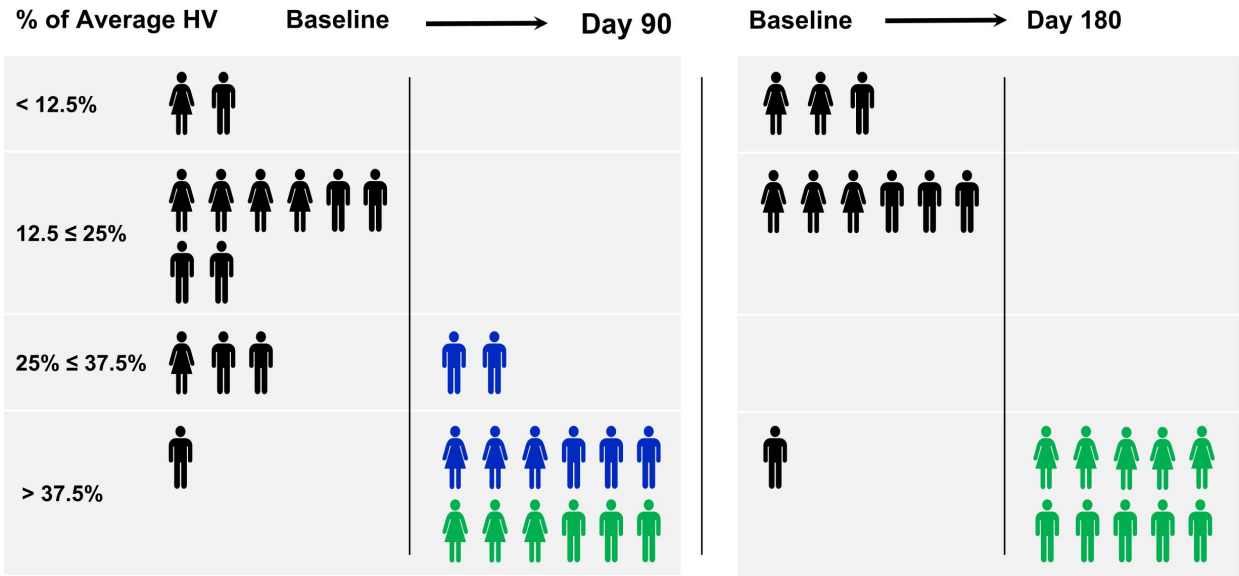
## 100% of OL Study Participants on Nomlabofusp Achieved FXN Levels by Day 180 that are Over 50% of Healthy Volunteers

Percentage of Participants* with Skin FXN Levels > 8.2 pg/μg** (50% of the median FXN concentration found in healthy volunteers)			
Baseline	Day 30	Day 90	Day 180
<b>0%</b> 0/18	<b>33%</b> 6/18	<b>43%</b> 6/14	<b>100%</b> 10/10



\*Data include all participants with quantifiable levels at each measurement point who had received 25 mg, 50 mg or had the dose increased from 25 mg to 50 mg  
\*\*8.2 pg/μg represents 50% of the median FXN concentration

# Skin FXN Levels Achieve Higher % of Healthy Volunteers' FXN Levels\* Following Daily Nomlabofusp



\*% of average healthy volunteers (HV) 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)

Data include all participants with quantifiable FXN levels at baseline and Day 90/Day 180



Baseline as a percentage of average FXN level in HV



FXN levels increased from baseline and reached 25% to < 50% of average FXN level in HV



FXN levels increased from baseline and reached > 50% of average FXN level in HV

## Absolute Skin FXN Levels Increase Over Time with Nomlabofusp\* Treatment in the Open Label Study

Statistic	Baseline	Day 30	Day 90	Day 180
<i>N</i>	18	18	14	10
<b>Median (IQR)</b>	<b>2.70 (2.14, 4.13)</b>	<b>6.87 (5.34, 10.37)</b>	<b>7.50 (6.66, 13.73)</b>	<b>13.44 (10.10, 26.71)</b>
(Min, Max)	(1.5, 6.3)	(1.5, 76.4)	(5.6, 37.1)	(8.7, 92.9)

- FDA is open to use of increases in skin FXN concentrations as a reasonably likely surrogate endpoint
- FDA 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



FXN = frataxin; IQR = interquartile range

Note: Median skin FXN levels in Larimar's noninterventional healthy volunteer study= 16.34 pg/μg

\* Data include all participants with quantifiable FXN levels at each measurement point who had received 25 mg, 50 mg or had the dose increased from 25 mg to 50 mg

## Disease Characteristics – OL Study & FACOMS Reference Population

	Nomlabofusp*	FACOMS
<b>Age of screening (years)</b>		
n	38	370
Mean (SD)	30.2 (10.94)	27.5 (9.30)
Min, Max	12, 55	12, 54
<b>Age of symptom onset (years)</b>		
n	38	370
Mean (SD)	12.7 (6.09)	13.8 (5.50)
Min, Max	5, 30	5,30
<b>Baseline mFARS Total Score</b>		
n	38	370
Mean (SD)	55.7 (17.05)	49.7 (14.5)
Min, Max	23.3, 85.5	23.3, 80.5

	Nomlabofusp*	FACOMS
<b>Baseline FARS-ADL Overall Score</b>		
n	38	370
Mean (SD)	17.5 (6.84)	14.2 (5.70)
Min, Max	2, 27	2, 27
<b>Baseline 9-HPT Average Time of Dominant Hand(s)</b>		
n	34	370
Mean (SD)	95.4 (67.65)	124.8 (51.90)
Min, Max	35.8, 277.3	36.7, 276.5
<b>Baseline MFIS Overall Score</b>		
n	38	370
Mean (SD)	33.2 (15.05)	31.8 (15.60)
Min, Max	2, 79	2, 78

FACOMS longitudinal natural history study (N = 955) includes participants with confirmed FA diagnosis

Larimar identified participants from the FACOMS dataset with similar range of baseline characteristics of participants in the OL study using data recorded over the last 4 years for each participant

## Improvements Across Clinical Outcomes with Nomlabofusp Relative to Worsening in FACOMS Study Supports Potential Clinical Benefits

		mFARS [0- 93]		FARS-ADL [0- 36]		9-HPT Dominant Hand		MFIS [0- 84]	
	Statistic	Nomlabofusp	FACOMS <sup>1</sup>	Nomlabofusp	FACOMS <sup>1</sup>	Nomlabofusp	FACOMS <sup>1</sup>	Nomlabofusp	FACOMS <sup>1</sup>
Baseline	Median (IQR)	<b>54.75</b> (41.2, 71.0)	<b>50.00</b> (37.0, 61.0)	<b>17.75</b> (13.0, 24.5)	<b>14.50</b> (10.0, 18.5)	<b>71.95</b> (49.6, 114.8)	<b>113.50</b> (86.5, 148.5)	<b>34.00</b> (20.0, 34.0)	<b>32.00</b> (21.0, 42.0)
	n	38	370	38	370	34	370	38	370
Change from Baseline at 1 year	Median (IQR)	<b>-2.25</b> (-3.75, -0.25)	<b>1.00</b> (-1.5, 4.0)	<b>-0.50</b> (-2.0, 1.0)	<b>0.50</b> (-1.0, 2.5)	<b>-7.40</b> (-38.8, -2.5)	<b>3.40</b> (-4.5, 18.0)	<b>-6.50</b> (-17.5, 4.0)	<b>1.50<sup>2</sup></b> (-9.5, 11.0)
	n	8	185	8	237	7	219	8	136



IQR = interquartile range

<sup>1</sup> Based on the range of baseline characteristics of participants in the OL study, Larimar identified patients from the FACOMS dataset with similar characteristics using data recorded over the last 4 years for each patient

<sup>2</sup> Modified Fatigue scale presented here is at Month 24 because it was not assessed at Month 12

## Nomlabofusp Safety Observations with Long-term Treatment

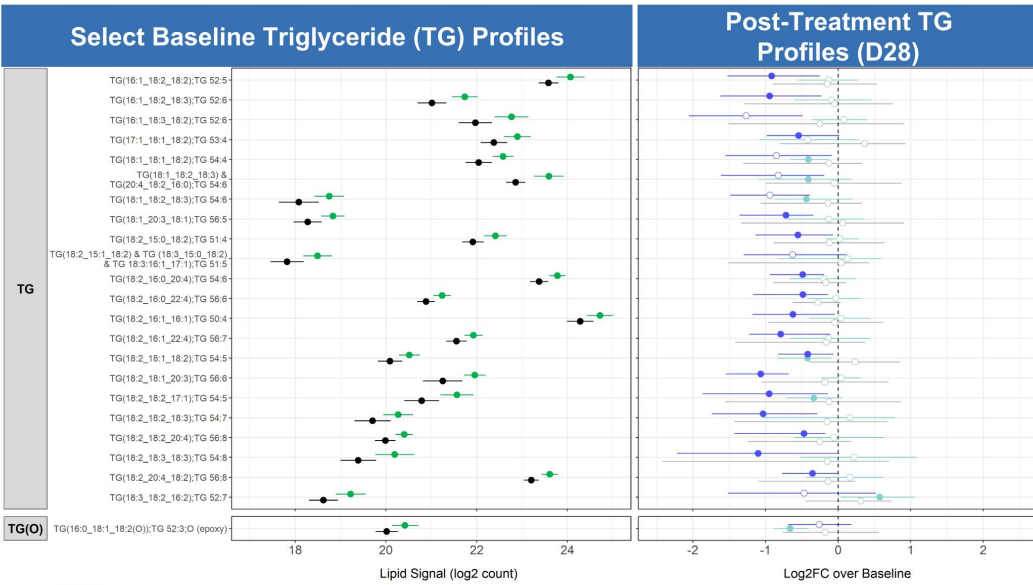
- 7 of 39 participants in OL study (65 total participants received at least 1 dose of nomlabofusp across all studies) experienced anaphylaxis
  - Most events occurred on the initial day of administration, and all occurred within the first 6 weeks of dosing
  - All returned to usual state of health after standard treatment
- Of the 39 participants in the OL study, 10 did not have prior exposure to nomlabofusp; 1 of these 10 experienced anaphylaxis (this participant is one of the 7 previously described cases)
- Nomlabofusp with long-term daily dosing was generally well tolerated, including 14 on treatment for at least 6 months and 8 for over 1 year
- Most common AEs were mild/moderate local ISRs and did not lead to any withdrawals
- Larimar is modifying the starting dose regimen to include:
  - Antihistamines 5 days prior to first dose and for 90 days after first dose
  - 5 mg test dose followed by a 25 mg dose 1 hour later and then 25 mg daily for the first 30 days; after 30 days the dose will be increased to 50 mg daily
  - Continue dispensing epinephrine auto-injector, such as EpiPen, to be administered in the event of anaphylaxis
- Larimar provided the FDA a full data update including the safety, FXN, and clinical data. FDA agreed with the new dosing regimen and Larimar is implementing the change



## Key Clinical Data From Prior Studies

# Interest from FDA in Exploring the Correlation Between Lipids and FXN Concentrations

Decreases in elevated lipids in adults with FA\* observed after nomlabofusp treatment



\*Samples from **Phase 2 dose exploration study** evaluating nomlabofusp 25 mg (Cohort 1) and 50 mg (Cohort 2) or placebo via subcutaneous injection daily for 14 days followed by alternate day administration for 14 days. Plasma samples were collected before, during, and after treatment for lipid profiling. Healthy volunteer (HV) data is from Larimar's non-interventional HV study

Data presented at the International Congress for Ataxia Research, November 2024



## Nomlabofusp PK Profile Consistent Across Studies

### Long-term PK Profile Consistent with Phase 1 and Phase 2 Studies

- Rapid absorption after subcutaneous administration
- Steady state reached by Day 30 at both the 25 mg and 50 mg doses with no further accumulation
- Pharmacokinetic profile consistent with Phase 1 and Phase 2 studies

### Adolescent PK Profile Consistent with Adult

- Adolescents 12 to 17 years of age received a weight-based equivalent of 50 mg for 7 days
- Exposure and PK in 9 adolescents 12 to 17 years of age on nomlabofusp was similar to adults on 50 mg of nomlabofusp

# Global Phase 3 Double-blind Placebo-controlled Study

## Patient Population

- Ambulatory participants
- 2 - 40 years of age (~2/3 under 21 years of age)
- n = 100 – 150

Placebo

50 mg nomlabofusp

Daily subcutaneous injections self-administered or by a caregiver

← 18 months of treatment →

## Key Study Objectives

- Safety and tolerability
- Upright stability (U.S.) and mFARS (Europe) as primary outcome measures

Qualifying sites in U.S., Europe, U.K., Canada, and Australia

# Potential Path to Bring Nomlabofusp to Patients Worldwide

## Open Label Study

Plan to continue enrolling participants on new starting dose regimen with long-term 50 mg dose, including adolescents and those new to a nomlabofusp study

Continue introducing lyophilized dosage form

Planning to enroll children (2 - 11 yrs of age) directly into the study

## Global Phase 3 Study\*

Received feedback from FDA and EMA on study protocol

Sites in the U.S., Europe, U.K., Canada, and Australia currently being qualified



## Next Steps

Update on open label study status and regulatory discussions in Q1 2026

BLA submission seeking accelerated approval targeted in Q2 2026

U.S. launch targeted for early 2027

Received FDA Agreement on strategy for potency testing of nomlabofusp; commercial scale PPQ in progress

**START Pilot**  
(US)

**Orphan Drug**  
(US & EU)

**Rare Pediatric Disease**  
(US)

**Fast Track**  
(US)

**PRIME**  
(EU)

**ILAP**  
(UK-MHRA)



\*Study will initiate with participants 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

BLA based on skin FXN levels as potential surrogate endpoint

## Positive long-term data

Increased skin FXN levels similar to asymptomatic carriers and consistent directional improvement across 4 key clinical outcome measures

## BLA submission seeking accelerated approval targeted Q2 2026

U.S. launch targeted for early 2027

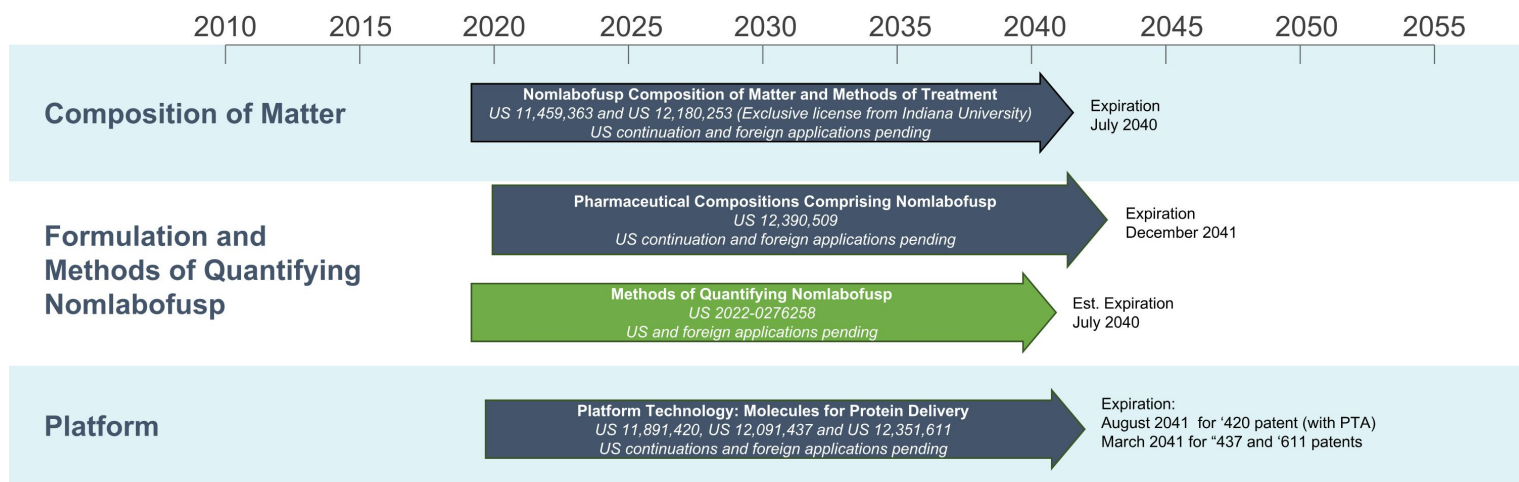


# Larimar Therapeutics

Appendix

# 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 and patents 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



## Mitochondrial Localization and Preclinical Data

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



- 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

# Nomlabofusp Extends Survival in FXN-deficient KO Mice

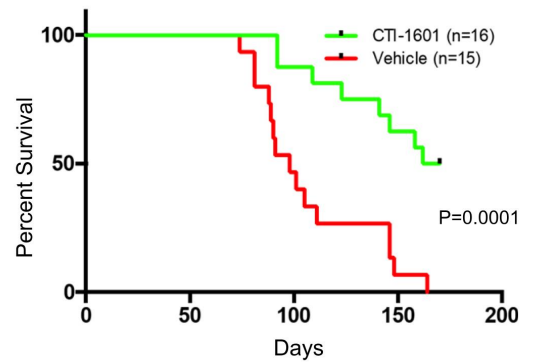
Initial proof-of-concept for FXN replacement therapy in cardiac mouse model of FA

## 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

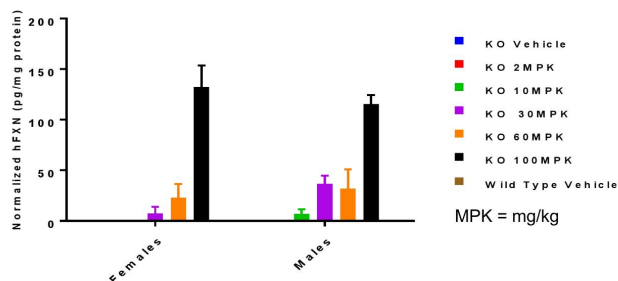
Single dose level: 10 mg/kg nomlabofusp or vehicle given intraperitoneally three times per week

- ✓ 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.

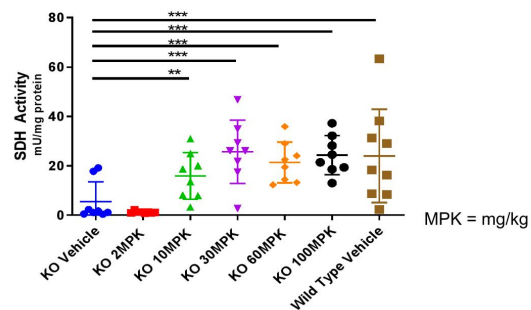
## Mitochondrial FXN (Heart)



Mitochondria hFXN concentration increases dose-dependently  
Given subcutaneously, nomlabofusp functionally replaces hFXN in mitochondria of KO mice



## SDH Activity (Muscle)

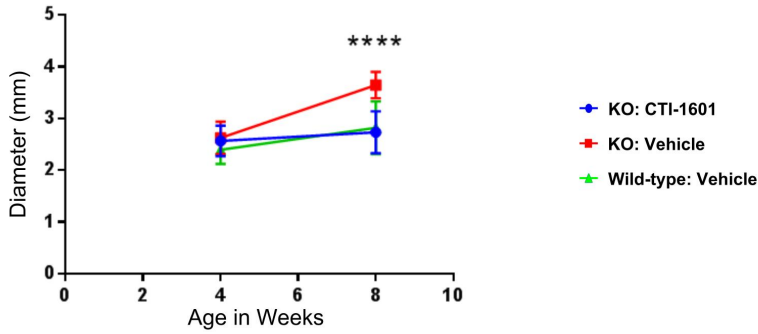


Succinate dehydrogenase (SDH) activity, which is indicative of mitochondrial function, increases in a dose-dependent manner after administration of nomlabofusp; activity plateaus at 30 mg/kg and is equivalent to activity in wild type

# Nomlabofusp Prevents Left Ventricle Dilation in KO Mice

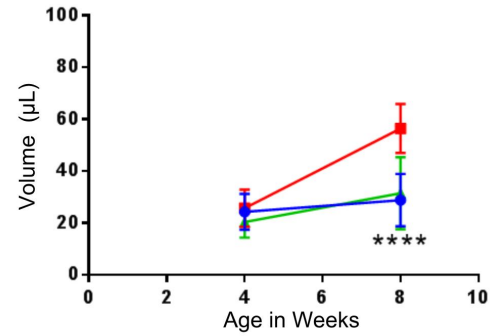
**Study Design** – Cardiac and skeletal muscle FXN knockout mice (MCK-CRE) were treated at 10 mg/kg every other day at Jackson Laboratories (Bar Harbor, ME). Echocardiograms were performed pre-dose and post dose.

## Left Ventricle Internal Diameter (Systole)



Left ventricular (LV) diameter 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)

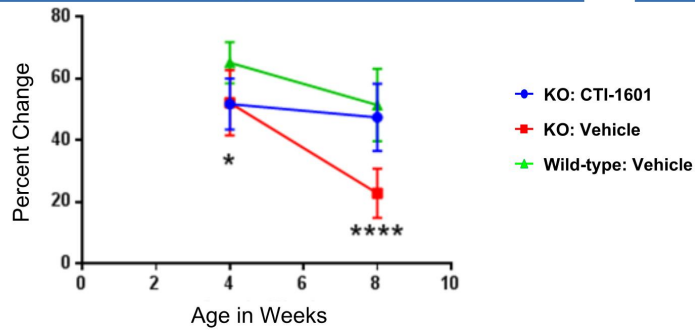


Nomlabofusp-treated mice have similar LV volume as wild type; echocardiogram shows significant differences between vehicle and nomlabofusp treated (10 mg/kg every other day) KO mice

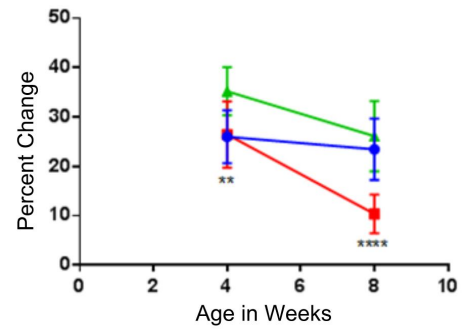
# Nomlabofusp Preserves Left Ventricle Function in KO Mice

**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

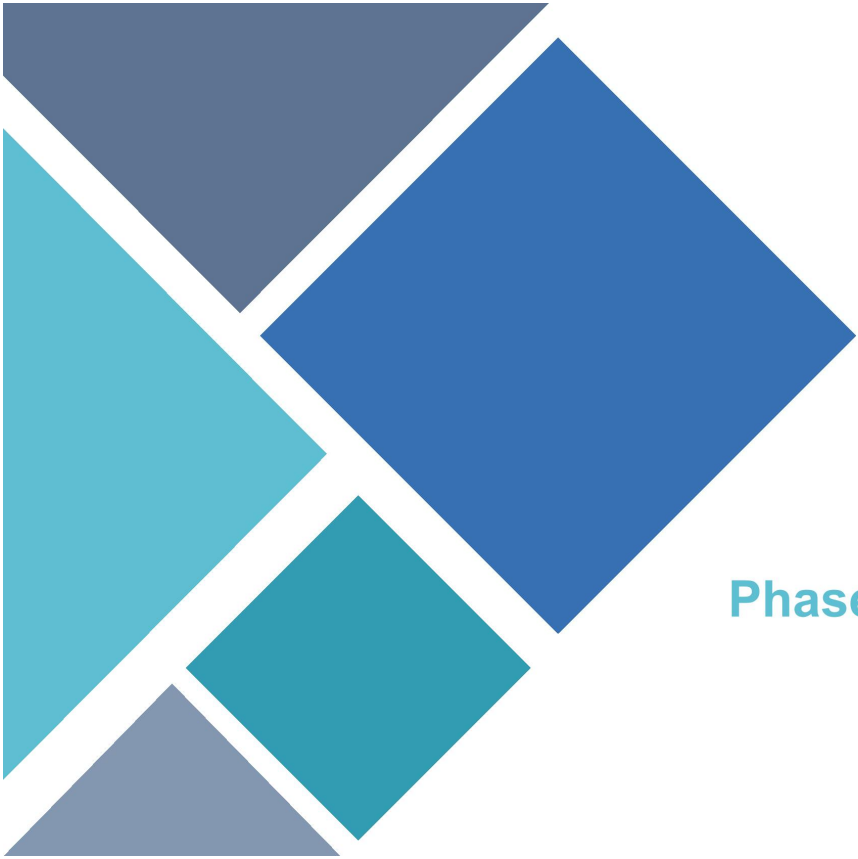


## Left Ventricle Fractional Shortening



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



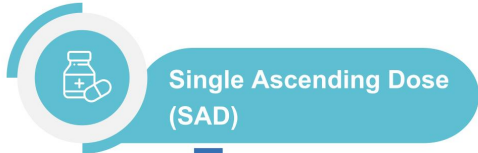
## Phase 1 Clinical Data

# 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



### Single Ascending Dose (SAD)

Eligible patients from SAD trial could enroll in MAD trial

**Number of subjects:** 28

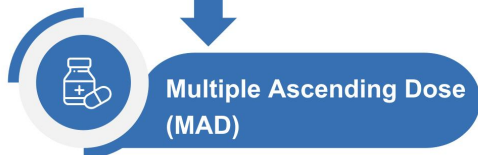
**Dose levels:** 25 mg, 50 mg, 75 mg and 100 mg (subcutaneous administration)

**Treatment Duration:** 1 day

**1° Endpoint:** Safety and tolerability

**2° Endpoints:** PK; PD; FXN levels; multiple exploratory

**Status:** Complete



### Multiple Ascending Dose (MAD)

**Number of Subjects:** 27

**Dose Range:** 25 mg, 50 mg, 100 mg (subcutaneous administration)

**Treatment Regimen:** Multiple increasing doses administered subcutaneously over 13 days

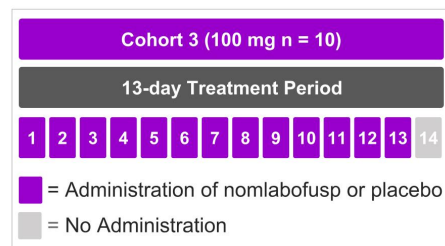
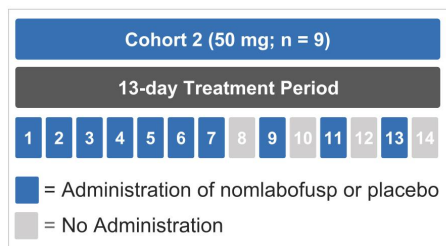
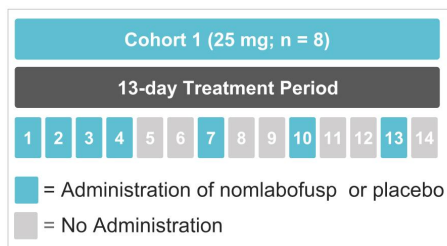
**1° Endpoint:** Safety and tolerability

**2° Endpoints:** PK; PD; FXN levels (buccal cells, platelets, optional skin biopsies); multiple exploratory

**Status:** Complete

# Completed Phase 1 Multiple Ascending Dose Study

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



## FXN Level Sampling Days Presented for Each Cohort

**Cohort 1 Sampling Days**

<b>Buccal Cells</b>	Baseline, Day 4, Day 13
<b>Skin</b>	Baseline, Day 13
<b>Platelets</b>	Baseline, Day 4, Day 13

**Cohort 2 Sampling Days**

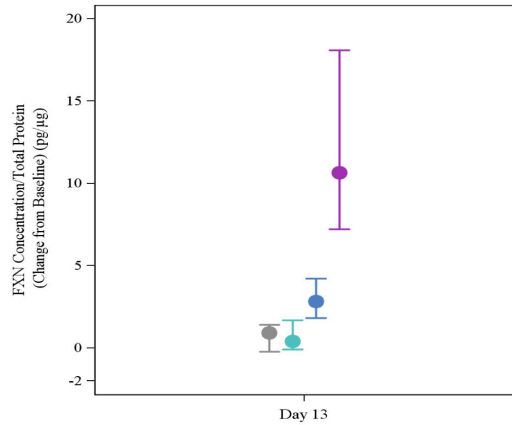
<b>Buccal Cells</b>	Baseline, Day 7, Day 13
<b>Skin</b>	Baseline, Day 13
<b>Platelets</b>	Baseline, Day 7, Day 13

**Cohort 3 Sampling Days**

<b>Buccal Cells</b>	Baseline, Day 7, Day 13
<b>Skin</b>	Baseline, Day 13
<b>Platelets</b>	Baseline, Day 7, Day 13

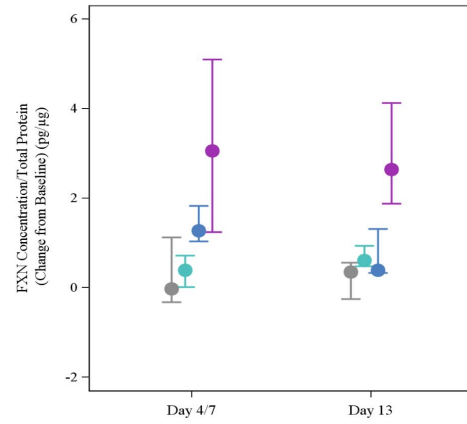
# Dose Dependent Increases in FXN Levels Observed in Skin and Buccal Cells in Phase 1

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



Placebo: Participants randomized to placebo in each cohort  
 25 mg: Dosed daily for 4 days, every third day thereafter

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



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 25<sup>th</sup> and 75<sup>th</sup> 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;

# 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)
<b>Sex</b>							
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)
<b>Age (years)</b>							
	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
<b>Race</b>							
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)
<b>Ethnicity</b>							
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)

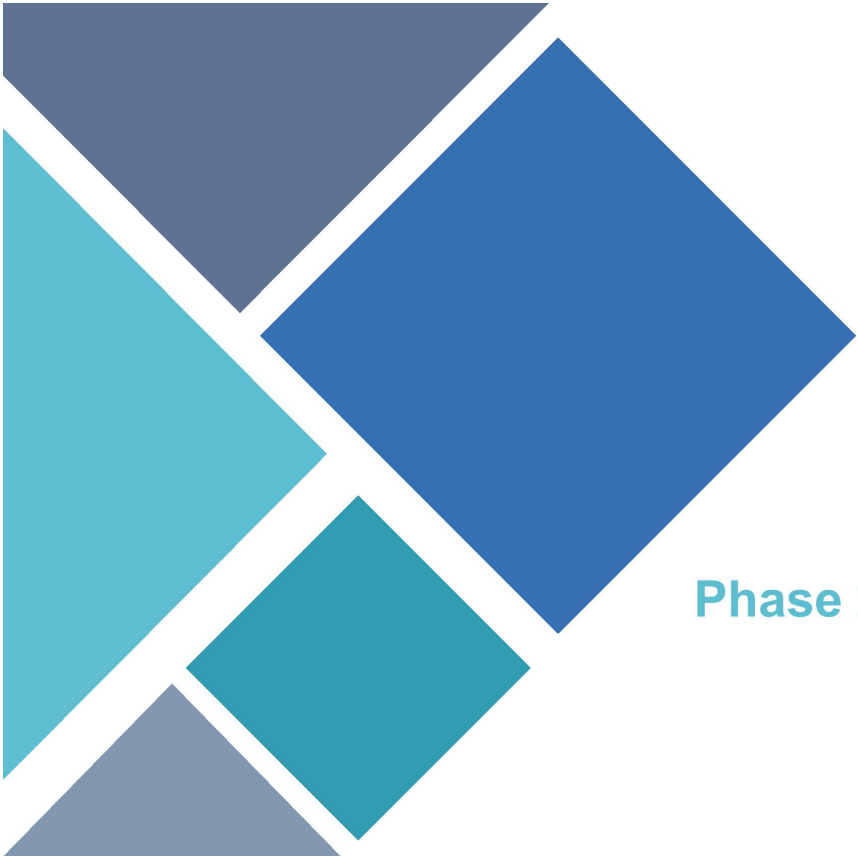
# MAD Trial Patient Disease Characteristics

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)
<b>Age at Symptom Onset</b>							
	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
<b>Age at Diagnosis</b>							
	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
<b>Assistive Device</b>							
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)

**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 Dose Exploration Data



## 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



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

  = No Administration

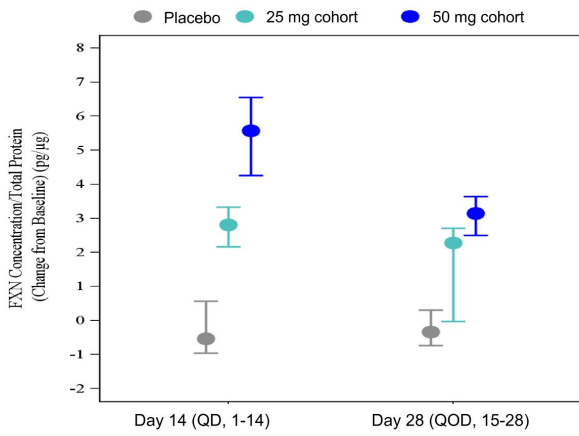
### Study Details

<b>Population</b>	Ambulatory and non-ambulatory Friedreich's ataxia patients ≥18 years of age Nomlabofusp (CTI-1601) treatment naïve or participated (if eligible) in a previous Larimar study
<b>Dose</b>	<b>Cohort 1:</b> 25 mg <b>Cohort 2:</b> 50 mg
<b>Key Endpoints</b>	Frataxin levels in peripheral tissue, PK, safety and tolerability; other exploratory endpoints include lipids and gene expression levels
<b>Number of Patients</b>	<b>Cohort 1:</b> Enrolled 13 participants (9 on nomlabofusp; 4 on placebo) <b>Cohort 2:</b> Enrolled 15 participants (10 on nomlabofusp; 5 on placebo)
<b>Key Results</b>	Generally well tolerated; most common adverse events were mild and moderate injection site reactions Dose dependent increases of frataxin levels in tissues tested (skin and buccal cells) 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

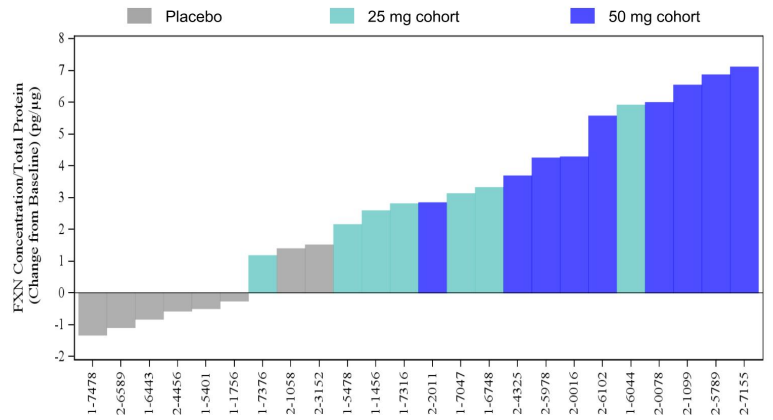
# Dose-Dependent Increase in FXN Levels in Skin Cells

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

**FXN Levels\* in Skin Cells  
Change from Baseline\*\***



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

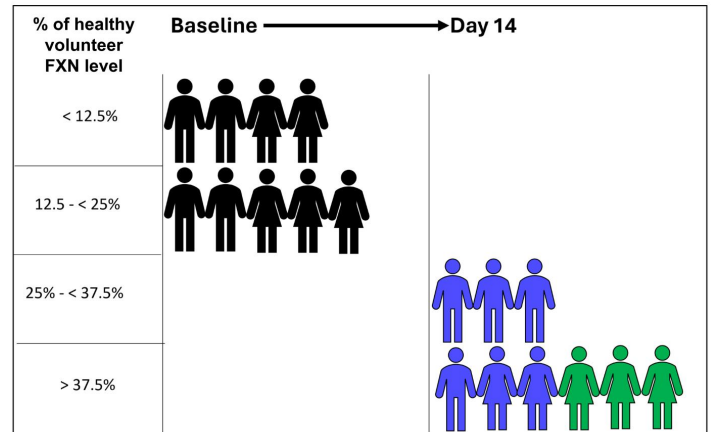
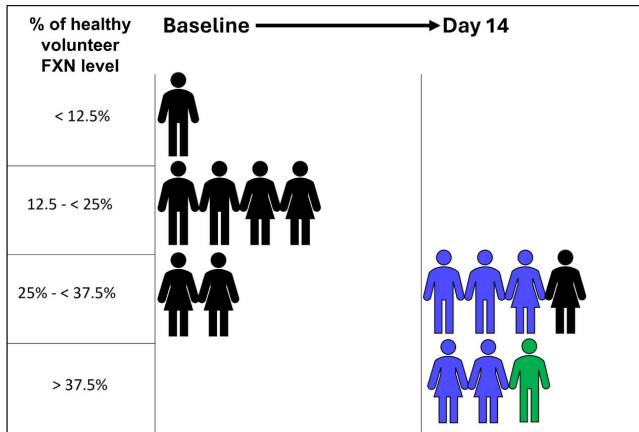


\*FXN levels measured via detection of peptide derived from mature FXN; FXN concentrations are normalized to total cellular protein content in each sample. Data represent median and 25<sup>th</sup> and 75<sup>th</sup> percentiles. Only participants with quantifiable levels at both baseline and Day 14 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.

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

## 25 mg of Nomlabofusp

## 50 mg of Nomlabofusp



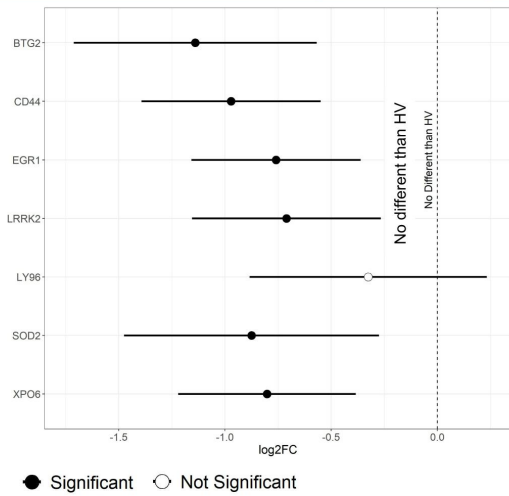
Baseline FXN levels as a % of average FXN level in healthy volunteers
  FXN levels increased from baseline and reached 25% to < 50% of average FXN level in healthy volunteers
  FXN levels increased from baseline and reached > 50% of average FXN level in healthy volunteers



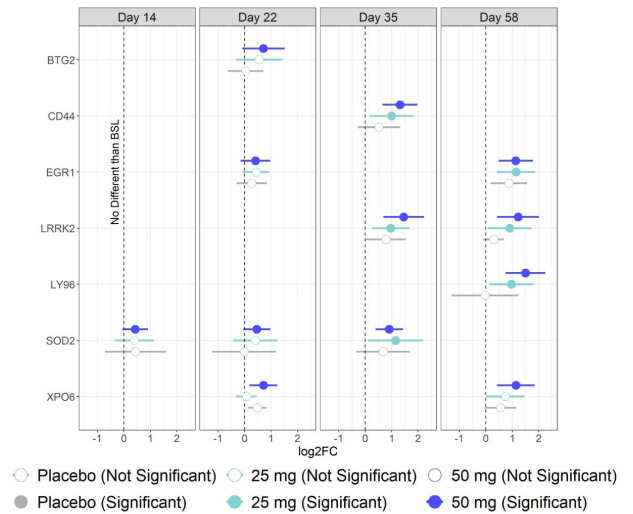
Only participants with quantifiable levels at baseline and day 14 are included in the figures.  
 \*% of healthy volunteer FXN level is calculated by dividing each participant's FXN level by the average FXN level (16.34 pg/ $\mu$ g) from the noninterventional healthy volunteer study (N=60).

# Increase Towards Normal Gene Expression in Adults with FA\* Observed After Nomlabofusp Treatment

## Select Baseline Gene Expression Patients with FA\* vs. Healthy Volunteers (HV)\*\*



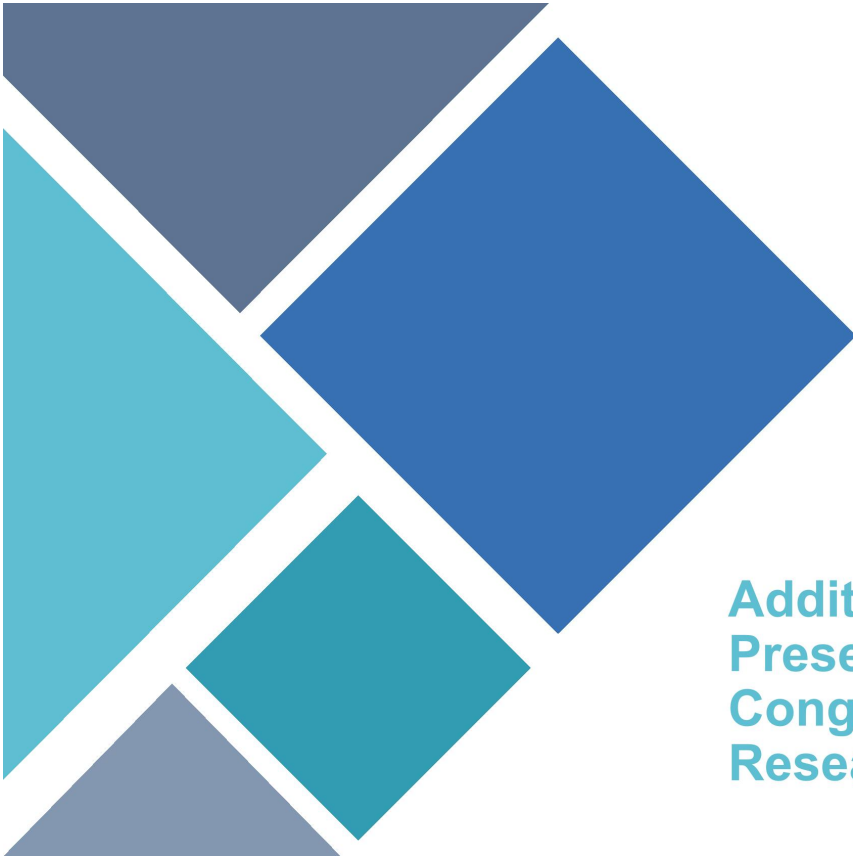
## Post-treatment Changes in Gene Expression From Baseline



Data presented at the International Congress for Ataxia Research, November 2024

\*Samples from Phase 2 dose exploration study evaluating nomlabofusp 25 mg (Cohort 1) and 50 mg (Cohort 2) or placebo via subcutaneous injection daily for 14 days followed by alternate day administration for 14 days. Buccal samples were collected before, during, and after treatment for gene expression profiling

\*\*Data from Larimar's non-interventional healthy volunteer study



**Additional Phase 1 and 2 Data  
Presented at the International  
Congress for Ataxia  
Research, November 2024**

# Nomlabofusp Clinical Studies Included a Broad, Representative Population of Adults with FA

## Broad population of adults with FA included in Phase 1 and 2 Studies

Age of onset between 5 - 60 years with a median age of onset of 15 yrs

81% of participants had FXN levels at baseline less than 30% of healthy controls and 37% of participants had less than 20%

Over 50% of participants were non-ambulatory at baseline

*\*18 subjects participated in more than 1 study*

*\*\*Quantifiable buccal cell FXN levels relative to the median of healthy controls*

*\*\*\*Ambulatory status is based on the gait score (E7=5 vs. <5) of the upright stability subscore of the mFARS*



*\*\*\*\*Data presented at the International Congress for Ataxia Research, November 2024*

## Demographics and Baseline Disease Characteristics from Nomlabofusp Phase 1 and 2 Interventional Studies\*\*\*\*

	N*	Median	Mean	Min	Max
<b>Age</b>	61	28.0	31.9	19	69
<b>Age of Onset</b>	61	15.0	15.9	5	60
<b>Age of Diagnosis</b>	61	19.0	21.0	5	64
<b>Shorter GAA (GAA<sub>1</sub>)</b>	60	550.0	555.8	99	1000
<b>Longer GAA (GAA<sub>2</sub>)</b>	60	900.0	890.2	265	1300
<b>Frataxin, % of Control**</b>	57	24.4	23.9	8.7	61.9
<b>mFARS Score</b>	61	52.0	49.5	13.2	74.5
<b>Upright Stability Score</b>	61	32.0	26.9	7.0	35.0
<b>Dominant hand 9-hole peg test</b>	61	71.0	84.8	26.0	229.2
<b>T25-FW Test Score</b>	51	9.9	13.4	4.3	48.5
<b>Left Ventricular Mass (g)</b>	61	163.4	168.0	73.7	398.8
<b>LVEF %</b>	61	63.0	63.5	52	76
<b>Ambulatory Status***</b>					
No	36				
Yes	25				

# Pooled Data from Completed Phase 1 & 2 Studies Confirms Disease & FXN Relationships are Consistent with Literature

## Disease Characteristics by Quartiles Based on Buccal Cell FXN Levels at Baseline

Quartile	FXN Concentration* (pg/mcg)	Age at Symptom Onset**	Age at Diagnosis**	GAA <sub>1</sub> **	GAA <sub>2</sub> **
Q1 (N=14)	< 1.31	10.5	14.5	616.5	899.5
Q2 (N=14)	1.31 - <1.95	13.5	23.0	486.0	866.0
Q3 (N=14)	1.95 - <2.30	16.0	19.0	555.0	871.5
Q4 (N=15)	≥ 2.30	19.0	27.0	400.0	933.0

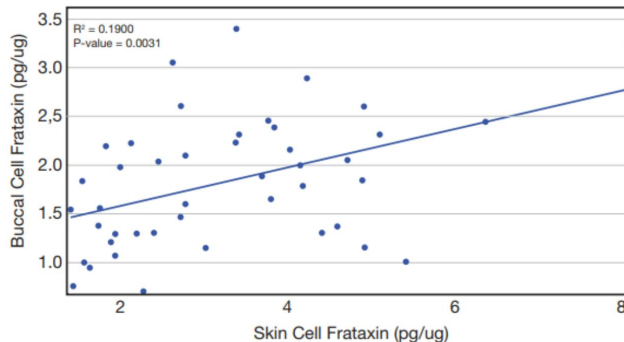
\*Quantifiable buccal cell frataxin levels

\*\*Median values

Median buccal cell FXN concentration in healthy controls = 8.1 ng/mcg

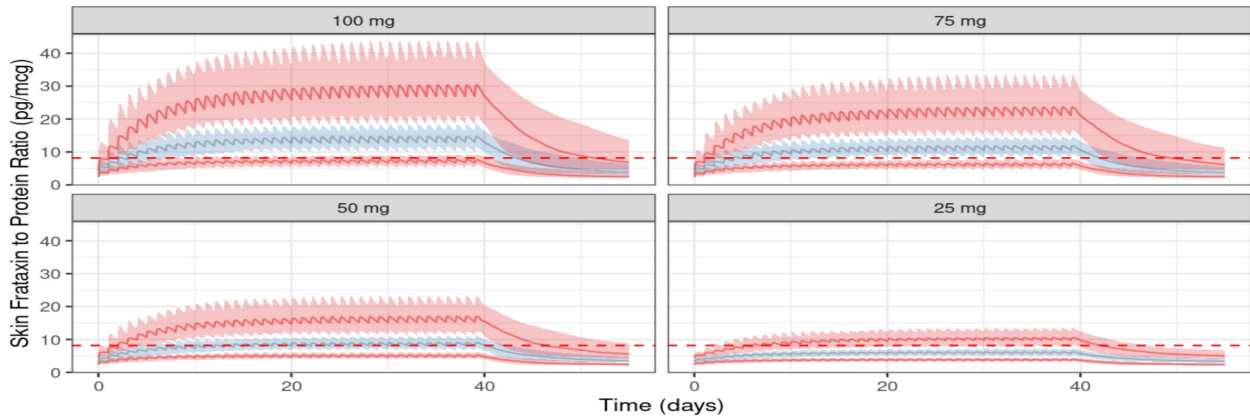
Buccal cell FXN levels correlated with age of onset and inversely correlated with the number of GAA repeats and rate of disease progression

## Baseline Buccal and Skin Cell FXN Levels



Buccal cell FXN levels correlated with skin cell FXN levels

# Modeling/Simulation Predicts\* 50mg Daily Can Achieve Skin FXN Levels $\geq$ 50% of Healthy Controls in Most Patients



**Dashed red line** – 50% the average skin FXN/protein ratio (8.17 pg/ug) in a non-interventional study in healthy controls (HC)  
**Blue line** – median of simulated values across trials  
**Red lines** – 10th and 90th percentiles  
**Shaded regions** – 95% confidence intervals of the corresponding percentiles (10th, 50th, and 90th).

Data presented at the International Congress for Ataxia Research, November 2024

**50 mg nomlabofusp daily was predicted to lead to:**  
 A median increase of 5.64 (2.3 – 13.5) pg/ $\mu$ g in FXN levels from baseline

Increase in skin FXN levels in 59% of simulated patients with FA to levels  $\geq$ 50% of average skin FXN levels in HC



\*PK/PD model was developed with data collected from 3 completed studies in adults with FA. A population of virtual FA patients (n = 100, 100 trials) receiving subcutaneous daily doses of 25, 50, 75, or 100 mg nomlabofusp for 40 days was simulated

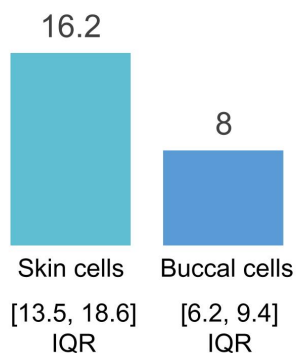


## Non-Interventional Study Data

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

Non-interventional study measured FXN in homozygous healthy volunteers

**Median Frataxin Concentration (pg/ $\mu$ g)  
in Homozygous Healthy Volunteers (n = 60)**



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

Lower FXN levels seen with typical onset<sup>2</sup> (5 to 15 years of age)

Higher FXN levels seen with late onset<sup>2</sup> (after 25 years of age)

Heterozygous carriers who show no signs of disease have buccal cell FXN levels of ~50% of unaffected healthy persons<sup>1</sup>



## FDA START Pilot Program

# 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**



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



FARA

## 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”



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