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): August 14, 2023

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 **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 August 14, 2023, 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.

Exhibit No.	Document
99.1	Larimar Therapeutics, Inc. Corporate Presentation, dated August 14, 2023*
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

* Filed 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: August 14, 2023

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

Corporate Presentation

August 2023

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 CTI-1601 and other planned product candidates, Larimar’s planned research and development efforts, including the timing of its CTI-1601 clinical trials 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 CTI-1601 clinical milestones and continued interactions with the FDA regarding the partial clinical hold; that preliminary clinical trial results may differ from final clinical trial results, that earlier non-clinical and clinical data and testing of CTI-1601 may not be predictive of the results or success of later clinical trials, and assessments; 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 CTI-1601’s manufacturing process; Larimar’s ability to obtain regulatory approvals for CTI-1601 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.

Investment Highlights

Novel protein replacement therapy platform	Clinical-stage biotechnology company focused on addressing unmet needs in Friedreich's ataxia (FA) and potentially other complex rare diseases based on a platform technology backed by a strong intellectual property portfolio
Potential first-ever therapy to increase frataxin levels	Lead candidate CTI-1601 is a recombinant fusion protein designed to directly address frataxin deficiency by delivering the protein to mitochondria. CTI-1601 has received Orphan Drug (US & EU), Rare Pediatric Disease (US), Fast Track (US), & PRIME (EU) designations
Completed Phase 1 proof-of-concept	Two double-blind, placebo-controlled Phase 1 trials in FA demonstrating CTI-1601 was **generally well tolerated** when dosed daily for up to 13 days; **dose-dependent increases in frataxin (FXN) levels** from baseline vs. placebo were observed in all evaluated tissues
Phase 2 and OLE studies with near-term catalysts	Ongoing Phase 2, placebo-controlled, 4-week dose exploration study in FA; 25 mg cohort data show CTI-1601 is generally well tolerated, increasing FXN levels from baseline vs. placebo in skin and buccal cells; **trial advancing to 50 mg cohort with data expected in 1H 2024; OLE trial with 25 mg daily dosing cleared for initiation in Q1 2024.** To potentially further escalate dose in Phase 2 study or the OLE study, submit Phase 2 data from 50 mg cohort to FDA due to continued partial clinical hold.
Strong financial foundation	$104.2 Million cash balance (June 30, 2023) with projected cash runway into Q4 2024

Larimar Therapeutics

Recent Progress Advances Long-Term Dosing Open Label Extension, and Phase 2 Dose Escalation of CTI-1601 for FA

FDA Clearance* **Second cohort evaluating 50 mg in Phase 2 trial**

Assesses safety, pharmacokinetics (PK), frataxin levels and dose response

Provides data for enhanced PK/frataxin modeling

Safety, PK and frataxin levels will inform on potential for additional cohorts

Top-line data expected in 1H 2024

FDA Clearance* **Open label extension (OLE) trial with 25 mg daily dosing**

Assesses long-term safety, PK, frataxin levels, efficacy outcomes and self-administration

Enables the comparison of clinical function with a matched set of untreated patients from the Friedreich's Ataxia Clinical Outcome Measures Study (FACOMS) database

Initial interim data expected in Q4 2024

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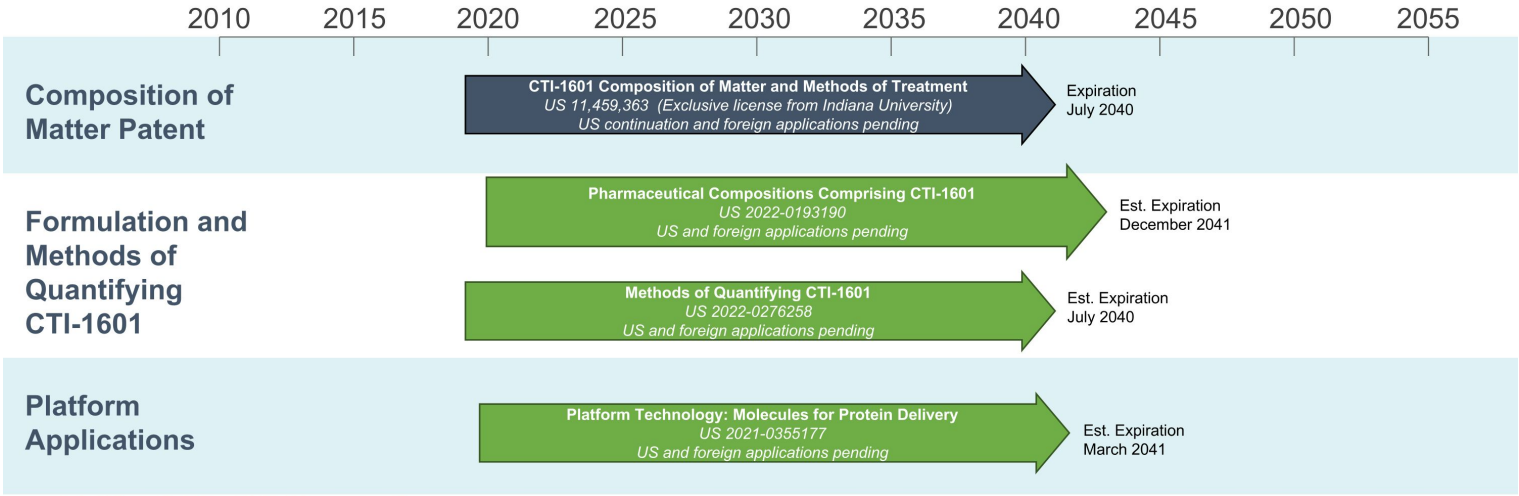
*Initiation of additional U.S. clinical trials or potential further dose escalation in these trials is contingent on FDA review of Phase 2 data from the 50 mg cohort and any available data from the OLE due to partial clinical hold

Larimar Technology is Supported by a Strong IP Portfolio

Granted CTI-1601 composition of matter patent extends into 2040



Additional CTI-1601 IP protection

- CTI-1601 pending applications cover key biomarkers, analytical tools and methods of treatment for additional disease indications
- CTI-1601 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)

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Granted Pending

Friedreich's Ataxia (FA)

Rare and Progressive Disease

Caused by genetic defect resulting in low levels of frataxin

- Patients with FA only produce ~20-40% of normal frataxin levels depending on the tissue, sampling technique, and assay considered[1]
- Affects ~20,000 patients globally, with ~5,000 patients in the U.S. and majority of the remaining patients in the EU

Approximately 70% of patients present before age 14

- Initial symptoms may include unsteady posture, frequent falling and progressive difficulty in walking. By the time symptoms occur, heart damage may have already occurred. Progressive disease: symptoms worsen and patients are eventually confined to a wheelchair with speech becoming hesitant and jerky (often referred to as "scanning speech")

Life expectancy of 30-50 years

- Early death usually caused by heart disease

No available therapies increase frataxin levels

- Only treatment approved for FA does not address frataxin deficiency

LRMR continues to have a strong relationship with Friedreich's Ataxia Research Alliance

- Dedicated FA patient advocacy group focused on treatments for FA

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

FXN Levels Determine 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

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

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

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

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

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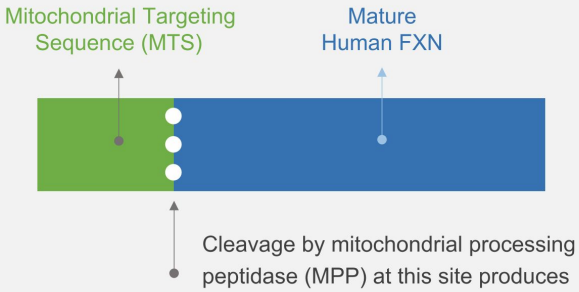
*FARS: Friedreich's ataxia rating scale, measures disease progression with a higher score indicating a greater level of disability; **FXN levels measured in peripheral blood mononuclear cells (PBMCs). FXN levels demonstrated to be equivalent in PBMCs, buccal cells, and whole blood.

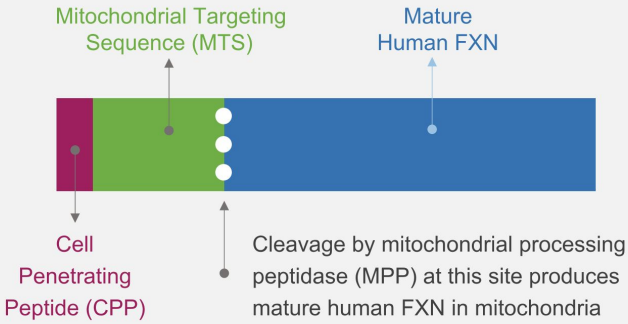
CTI-1601 is Designed to Deliver Additional Frataxin (FXN)

CTI-1601 maintains the cleavage site between the MTS and mature human FXN

STRUCTURE OF ENDOGENOUS FXN



STRUCTURE OF CTI-1601



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

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Completed Phase 1 Multiple Ascending Dose Study

Treatment Schedules for Each Cohort

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 CTI-1601 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 CTI-1601 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 CTI-1601 or placebo

= No Administration

FXN Level Sampling Days Presented for Each Cohort

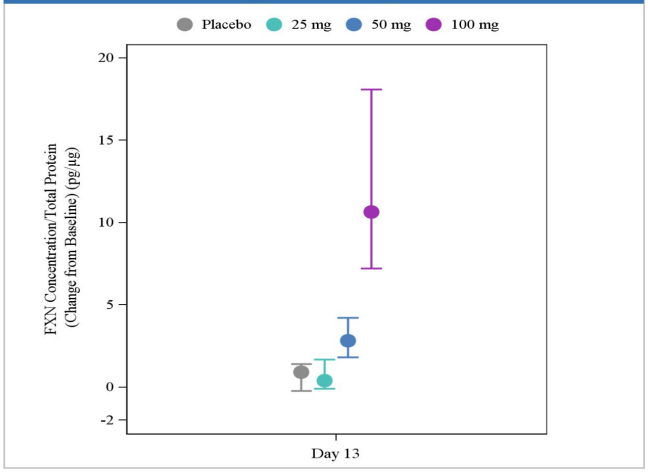
Cohort 1 Sampling Days	
Buccal Cells	Baseline, Day 4, Day 13
Skin	Baseline, Day 13
Platelets	Baseline, Day 4, Day 13

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

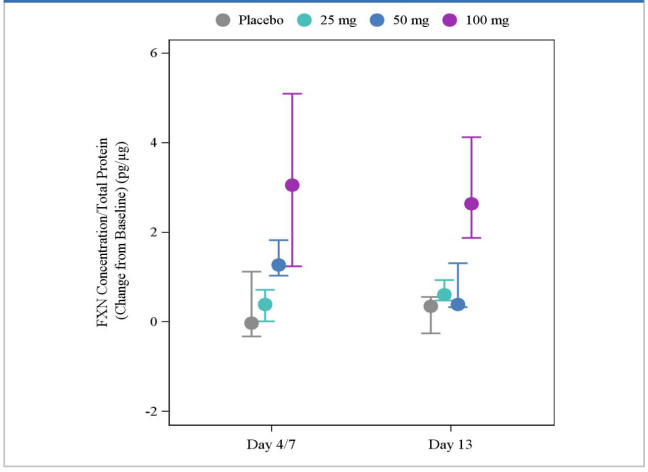
Cohort 3 Sampling Days	
Buccal Cells	Baseline, Day 7, Day 13
Skin	Baseline, Day 13
Platelets	Baseline, Day 7, Day 13

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

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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; 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; Sample collection days varied in each cohort per the trial protocol

Phase 2 Dose Exploration Study Advancing to 50 mg Cohort

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

Treatment Schedule

28-day Treatment Period

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
= Administration of CTI-1601 or placebo																											
= No Administration																											

Study Details

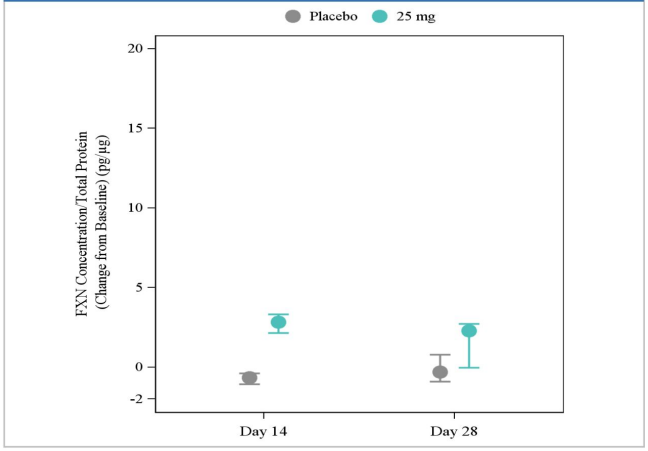
Population	Ambulatory and non-ambulatory Friedreich's ataxia patients ≥18 years of age. CTI-1601 treatment naïve or participated (if eligible) in a previous Larimar study.
Dose	**Cohort 1:** 25 mg **Cohort 2:** 50 mg
Key Endpoints	Frataxin levels in peripheral tissue, PK, safety and tolerability. Other endpoints include lipid profiles and gene expression data.
Number of Patients	**Cohort 1:** Enrolled 13 participants (9 on CTI-1601; 4 on placebo). **Cohort 2:** Designed to enroll ~12-15 participants randomized 2:1 to receive CTI-1601 or placebo.
Timing	Dosing in Cohort 1 is complete. Cohort 2 has been cleared for initiation. Top-line data from Cohort 2 expected in 1H 2024.

Increases in FXN Levels in Phase 2 Trial's 25 mg Cohort

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

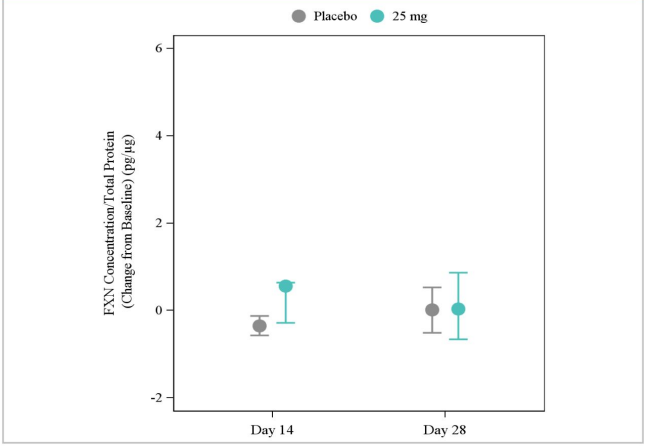
Skin Cells FXN* Change from Baseline**

Median placebo-adjusted increase from baseline of 3.5 pg/µg with 14 days daily dosing



Buccal Cells FXN* Change from Baseline**

Median placebo-adjusted increase from baseline of 0.9 pg/µg with 14 days daily dosing



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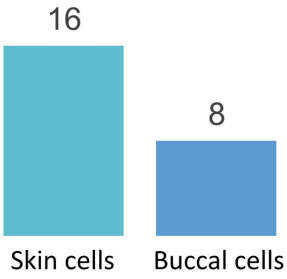
*FXN levels measured via detection of peptide derived from mature FXN; FXN concentrations are normalized to total cellular protein content in each sample; Data represent median and 25th and 75th percentiles.

** Median baseline from all of the patients were approximately 3.7 pg/µg for skin cells, and 1.9 pg/µg for buccal cells

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

Recently completed non-interventional study measured FXN in homozygous healthy volunteers

Median Frataxin Concentration (pg/µg)
in Homozygous Healthy Volunteers (n = 60)



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)

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 CTI-1601; 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
.

Clinical Data Indicate CTI-1601 is Generally Well Tolerated

CTI-1601 administered to 37 different adults with FA in multiple studies

35 of 37 clinical trial participants dosed with CTI-1601 completed their respective study
One Phase 2 participant withdrew due to an allergic reaction that resolved with standard treatment
One Phase 1 participant in the 50 mg cohort withdrew due to mild-to-moderate nausea and vomiting

No serious adverse events or important medical events in any CTI-1601 clinical trial
One severe adverse event (allergic reaction that resolved with standard treatment referenced above)

Most common adverse events (AEs) were mild and moderate injection site reactions (ISRs)
No study discontinuations due to ISRs and all resolved without intervention
ISRs in 100% of CTI-1601-treated participants and 40% of placebo-treated participants across all trials

In MAD study, except for ISRs, number & severity of AEs did not increase with increasing dose

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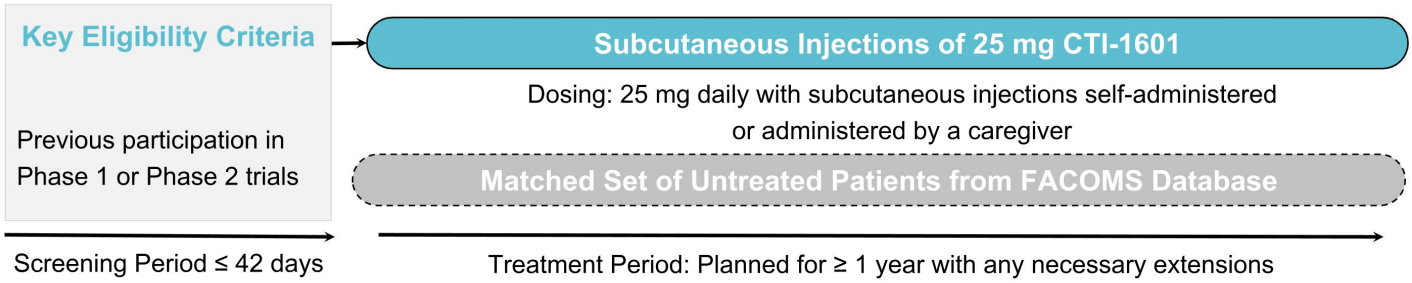
Open-label Extension Trial: Initiation Expected in Q1 2024

Preliminary interim data expected in Q4 2024



Safety and Pharmacodynamic Objectives

- Evaluate safety and tolerability
- Evaluate long-term PK
- Evaluate tissue frataxin concentrations
- Evaluate lipid profiles and gene expression data

Other Objectives

- Assess measures of clinical function

FACOMS: Friedreich's Ataxia Clinical Outcome Measures Study

CTI-1601 Clinical Development Plan

Top-line data from 50 mg cohort of Phase 2 dose exploration trial expected in 1H 2024

Ongoing and Planned Trials* Include:

Phase 2, four-week dose exploration study intended to identify dose and dose regimen for long-term studies. Advancing to 50 mg cohort.

Open-label extension trial with 25 mg daily dosing for eligible patients who participated in SAD, MAD, and/or four-week dose exploration studies. Initiation expected Q1 2024.

MAD trial in patients 2 to 17 years of age**. Participants eligible to screen for OLE trial.

Global double-blind placebo-controlled pivotal trial***

*Initiation of additional U.S. clinical trials or potential further dose escalation in the Phase 2 or OLE trials is contingent on submission to FDA of additional data from adult patients due to partial clinical hold.
**Company is planning discussions with FDA on how to best include patients 2 to 17 years of age in clinical development
***Company plans to initiate discussions with FDA on appropriate pivotal trial endpoints, including value of FXN levels. Also, the Company is planning discussions with regulators & investigators outside the U.S. to expand clinical program to international geographies.

CTI-1601 is a Competitively Differentiated FA Treatment Approach*

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

REATA PHARMACEUTICALS Biogen

CTI-1601 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	**CTI-1601**	**Larimar**	**Recombinant frataxin protein**	**Phase II**
Mitochondrial Oxidative Stress Modifier	Omaveloxolone (SKYCLARYS™)	Reata Pharma/Biogen	Nrf2 Activator	Approved
	Vatiquinone	PTC Therapeutics	15-Lipoxygenase Inhibitor	Phase III
	Epicatechin	Epirium Bio	Acetylcholinesterase Agonist	Phase II
	MIB-626	MetroBiotech	NAD+ Precursor	Phase II
Gene Expression Regulator	Resveratrol	Jupiter Neurosciences	P450 Enzyme Inhibitor	Phase II
	Etravirine	Frategene	Frataxin Pathway Modifier	Phase II
	DT-216	Design Therapeutics	GeneTAC	Phase I
Pathway Modifier	Leriglitazone	Minoryx	PPAR Gamma Agonist	Phase II
	Dimethyl Fumarate	Ixchel Pharma	Fumaric Acid Derivative	Phase I
Gene Therapy	LX2006	Lexeo Therapeutics	Frataxin Gene Replacement	Phase I/II

Larimar Therapeutics

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

Summary: CTI-1601 Cleared by FDA to Advance Clinical Development

CTI-1601	Generally well tolerated Dose-dependent increases in FXN levels in all evaluated tissues in Phase 1 Increases in FXN from baseline compared to placebo in all evaluated tissues (skin and buccal cells) in Phase 2
Regulatory Updates	Phase 2 dose exploration trial of CTI-1601 in FA cleared to proceed to 50 mg cohort Open label extension trial with 25 mg daily dosing cleared for initiation Beginning preparations to expand CTI-1601 clinical program to ex-U.S. geographies
Expected Milestones	**Q3 2023**: Initiation of 50 mg cohort in Phase 2 dose exploration trial **Q1 2024:** Initiation of open-label extension trial **1H 2024:** Top-line data from Phase 2 trial's 50 mg cohort **Q4 2024:** Interim data from open-label extension trial

Investment Highlights

Novel protein replacement therapy platform	Clinical-stage biotechnology company focused on addressing unmet needs in Friedreich's ataxia (FA) and potentially other complex rare diseases based on a platform technology backed by a strong intellectual property portfolio
Potential first-ever therapy to increase frataxin levels	Lead candidate CTI-1601 is a recombinant fusion protein designed to directly address frataxin deficiency by delivering the protein to mitochondria. CTI-1601 has received Orphan Drug (US & EU), Rare Pediatric Disease (US), Fast Track (US), & PRIME (EU) designations
Completed Phase 1 proof-of-concept	Two double-blind, placebo-controlled Phase 1 trials in FA demonstrating CTI-1601 was **generally well tolerated** when dosed daily for up to 13 days; **dose-dependent increases in frataxin (FXN) levels** from baseline vs. placebo were observed in all evaluated tissues
Phase 2 and OLE studies with near-term catalysts	Ongoing Phase 2, placebo-controlled, 4-week dose exploration study in FA; 25 mg cohort data show CTI-1601 is generally well tolerated, increasing FXN levels from baseline vs. placebo in skin and buccal cells; **trial advancing to 50 mg cohort with data expected in 1H 2024; OLE trial with 25 mg daily dosing cleared for initiation in Q1 2024.** To potentially further escalate dose in Phase 2 study or the OLE study, submit Phase 2 data from 50 mg cohort to FDA due to continued partial clinical hold.
Strong financial foundation	$104.2 Million cash balance (June 30, 2023) with projected cash runway into Q4 2024

Larimar Therapeutics


Larimar
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August 2023 Corporate Update
THANK YOU

Larimar Therapeutics

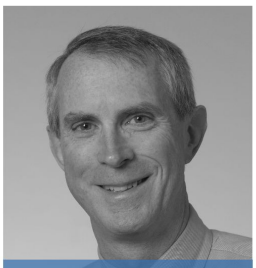
Appendix

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

Strong Relationship with FARA

Company has strong relationship with Friedreich's Ataxia Research Alliance (FARA)

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

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

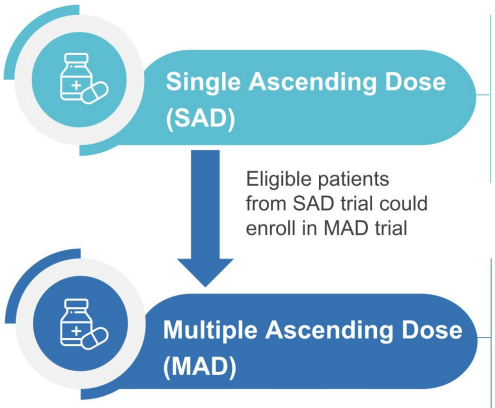
Additional Phase 1 Data

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

Larimar Therapeutics

Completed Phase 1 Multiple Ascending Dose Study

Treatment Schedules for Each Cohort

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 CTI-1601 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 CTI-1601 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 CTI-1601 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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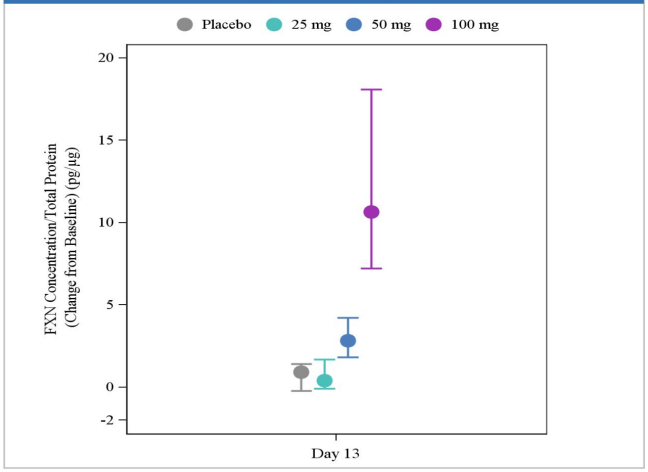
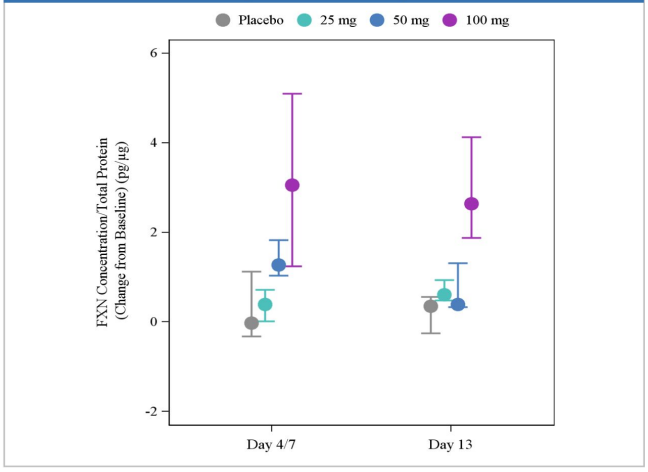
Dose Dependent Increases in FXN Levels Observed in Skin and Buccal Cells in Phase 1

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

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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; FXN levels from baseline, Day 4, & Day 13 measurements are shown for data derived from the 25 mg cohort; FXN levels from baseline, Day 7 & Day 13 measurements are shown for data derived from the 50 & 100 mg cohorts; Sample collection days varied in each cohort per the trial protocol

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)

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

Repeated subcutaneous injections of CTI-1601 were generally well tolerated in Phase 1 MAD trial

Summary of MAD trial safety data:

Repeated doses (25 mg, 50 mg, and 100 mg) of CTI-1601 or placebo were administered subcutaneously.

- No serious adverse events (SAEs), important medical events, or treatment-related severe adverse events were observed.
- Most common adverse events (AEs) were mild and moderate injection site reactions (ISR). At least one ISR was seen in 43% of patients receiving placebo, and all patients receiving CTI-1601 experienced ISRs.
- Most ISRs resolved within an hour after injection, and all ISRs resolved without intervention. There were no study discontinuations due to ISRs.
- Except for ISRs, the number & severity of AEs did not increase with increasing dose.

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

Additional Phase 2 Cohort 1 Data

Phase 2 Dose Exploration Study Advancing to 50 mg Cohort

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

Treatment Schedule

28-day Treatment Period

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
= Administration of CTI-1601 or placebo																											
= No Administration																											

Study Details

Population	Ambulatory and non-ambulatory Friedreich's ataxia patients ≥18 years of age. CTI-1601 treatment naïve or participated (if eligible) in a previous Larimar study.
Dose	**Cohort 1:** 25 mg **Cohort 2:** 50 mg
Key Endpoints	Frataxin levels in peripheral tissue, PK, PD, safety and tolerability. PD endpoints include lipid profiles and gene expression data.
Number of Patients	**Cohort 1:** Enrolled 13 participants (9 on CTI-1601; 4 on placebo). **Cohort 2:** Designed to enroll ~12-15 participants randomized 2:1 to receive CTI-1601 or placebo.
Timing	Dosing in Cohort 1 is complete. Cohort 2 has been cleared for initiation. Top-line data from Cohort 2 expected in 1H 2024.

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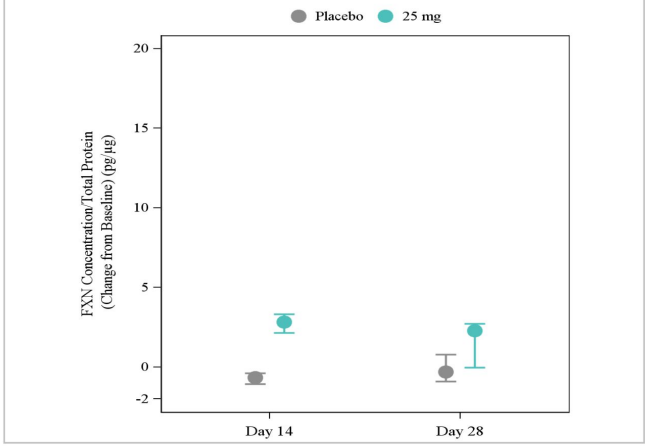
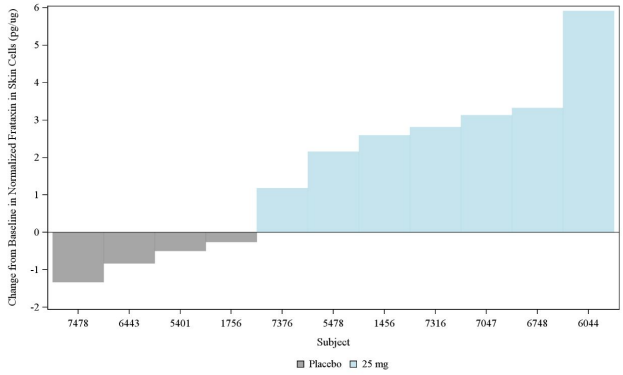
Increases in FXN Levels Observed in Skin Cells

Median placebo-adjusted increase from baseline of 3.5 pg/µg in skin with 14 days daily dosing

FXN* Change from Baseline (Skin Cells)



Day 14 FXN* Change from Baseline (Skin Cells)#

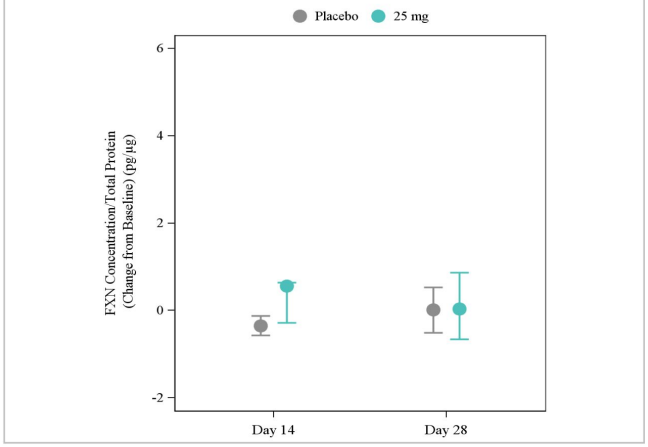


*FXN levels measured via detection of peptide derived from mature FXN; FXN concentrations are normalized to total cellular protein content in each sample; Data for left graph represent median and 25th and 75th percentiles.
#: One participant treated with CTI-1601 discontinued from study at Day 14 (Day 14 sample was not collected) and another treated with CTI-1601 had a FXN concentration value < lower limit of quantitation (LLOQ) at Day 14.

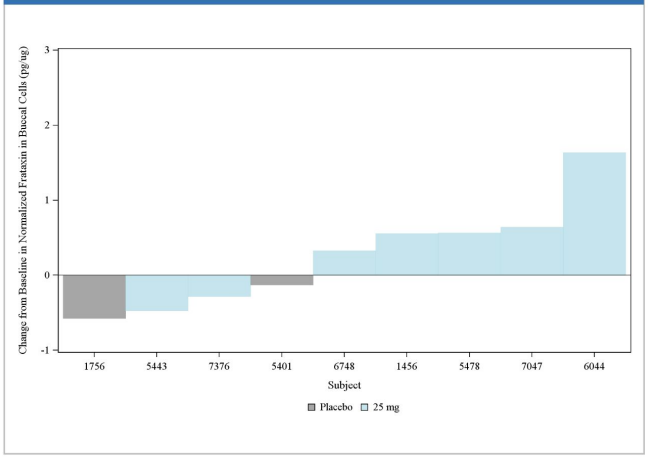
Increases in FXN Levels Observed in Buccal Cells

Median placebo-adjusted increase from baseline of 0.9 pg/µg in buccal cells with 14 days daily dosing

FXN* Change from Baseline (Buccal Cells)



Day 14 FXN* Change from Baseline (Buccal Cells)#



*FXN levels measured via detection of peptide derived from mature FXN; FXN concentrations are normalized to total cellular protein content in each sample; Data for left graph represent median and 25th and 75th percentiles.

#:One participant treated with CTI-1601 had a baseline value < lower limit of quantitation (LLOQ) and another participant treated with CTI-1601 had a baseline and Day 14 value < lower limit of quantitation (LLOQ); One participant treated with placebo had a FXN concentration value <LLOQ at baseline and another participant treated with placebo had a FXN concentration value <LLOQ at Day 14.

Demographics of Phase 2 (Cohort 1)

Demographics similar between Phase 1 and Phase 2 trials of CTI-1601

Parameter, n (%)	Placebo (N=4)	CTI-1601 25 mg (N=9)	Overall (N=13)
Mean Age (SD) (Years)	34.0 (9.20)	37.8 (14.93)	36.6 (13.16)
Male	2 (50.0%)	5 (55.6%)	7 (53.8%)
White	4 (100.0%)	8 (88.9%)	12 (92.3%)
Other	0	1 (11.1%)	1 (7.7%)
Not Hispanic or Latino	3 (75.0%)	8 (88.9%)	11 (84.6%)
Hispanic or Latino	1 (25.0%)	1 (11.1%)	2 (15.4%)
Mean BMI (SD) (kg/m^2)	23.66 (3.235)	25.26 (6.262)	24.77 (5.417%)
Previously participated in a CTI-1601 trial	1 (25.0%)	4 (44.4%)	5 (38.5%)

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Disease Characteristics (Phase 2 Cohort 1)

Parameter	Statistic	Placebo (N=4)	CTI-1601 (n=9)	Overall (n=13)
Age at Symptom Onset (years)				
	n	4	8	12
	Mean (SD)	14.5 (4.93)	13.0 (10.47)	13.5 (8.77)
	Median	14.5	10.0	11.0
	Q1, Q3	11, 19	8, 13	9, 15
	Min, Max	9, 20	5, 38	5, 38
Age at Diagnosis (years)				
	n	4	9	13
	Mean (SD)	17.5 (5.57)	18.6 (11.20)	18.2 (9.58)
	Median	16.5	16.0	16.0
	Q1, Q3	14, 22	14, 20	14, 20
	Min, Max	12, 25	5, 42	5, 42
Time Since Diagnosis (years)				
	n	4	9	13
	Mean (SD)	16.08 (5.965)	18.49 (11.523)	17.75 (9.938)
	Median	13.42	14.32	13.50
	Q1, Q3	12.9, 19.3	12.8, 21.6	12.8, 21.6
	Min, Max	12.5, 25.0	5.4, 45.0	5.4, 45.0

CTI-1601 appeared to be generally well tolerated in Phase 2 trial's 25 mg cohort

Summary of Phase 2 trial safety data (25 mg cohort):

25 mg CTI-1601 or placebo were administered subcutaneously daily for 14 days and then every other day until day 28. 13 participants were dosed in the trial (9 active, 4 placebo). Of the 9 CTI-1601-treated participants, 8 completed the trial with 1 withdrawing due to an allergic reaction to study drug, which resolved with standard treatment

- Data indicate CTI-1601 is generally well tolerated
- No serious adverse events. No important medical events. 1 severe adverse event (allergic reaction that resolved with standard treatment as referenced above).
- The most common adverse events were mild and moderate injection site reactions (at least one injection site reaction was seen in 50% of placebo participants and in 100% of CTI-1601 participants)

Pharmacokinetic Data

- Suggest steady state achieved by day 14

Preclinical Data

CTI-1601 Extends Survival in FXN-deficient KO Mice

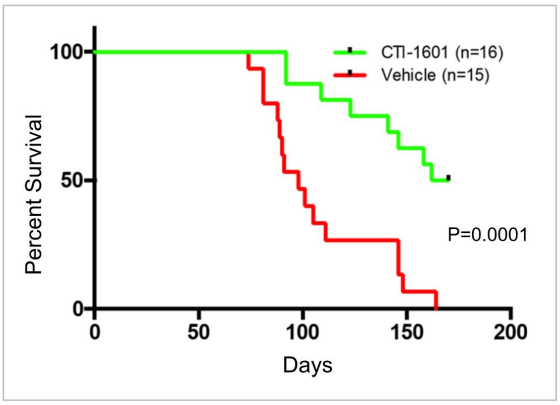
Initial Proof-of-Concept for FXN Replacement Therapy in Cardiac Mouse Model of FA

Median Survival of MCK-Cre FXN-KO Mice

- 166 days (CTI-1601) vs. 98 days (Vehicle)
- CTI-1601 was administered 10 mg/kg SC every other day

Survival beyond vehicle mean (107.5 days)

- 87.5% (CTI-1601) vs. 33% (Vehicle)
- Demonstrates that CTI-1601 is capable of delivering sufficient amounts of FXN to mitochondria



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

CTI-1601 Prevents The Development of Ataxic Gait in KO mice

In-Vivo Efficacy Data in Neurologic KO Mouse Model

Pvalb-Cre FXN-KO mouse

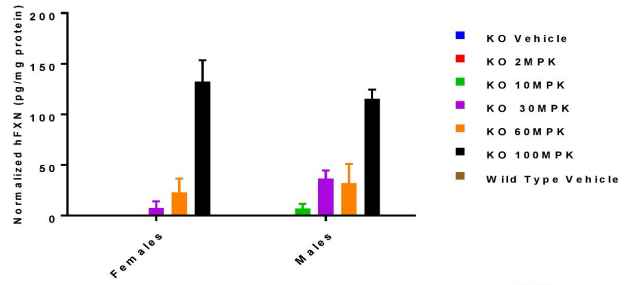
Single dose level: 10 mg/kg CTI-1601 or vehicle given intraperitoneally three times per week

- hFXN replacement with CTI-1601 **prevents the development of ataxic gait**
- CTI-1601-treated mice **survive longer** than untreated mice
- Human frataxin **present in brain, dorsal root ganglia and spinal cord** demonstrating central nervous system penetration

CTI-1601 Delivers hFXN to Mitochondria in KO Mice

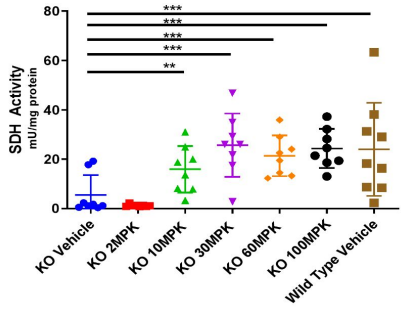
- hFXN concentration within mitochondria increases in a dose-dependent manner
- Given subcutaneously, CTI-1601 functionally replaces hFXN in mitochondria of KO mice
- Succinate dehydrogenase (SDH) activity, which is indicative of mitochondrial function, increases in a dose-dependent manner after administration of CTI-1601; activity plateaus at 30 mg/kg and is equivalent to activity in wild type animals
- Demonstrated normalization of gene expression in cardiac tissue

Normalized Mitochondrial FXN (Heart)



MPK = mg/kg

Normalized SDH Activity (Muscle)



MPK = mg/kg

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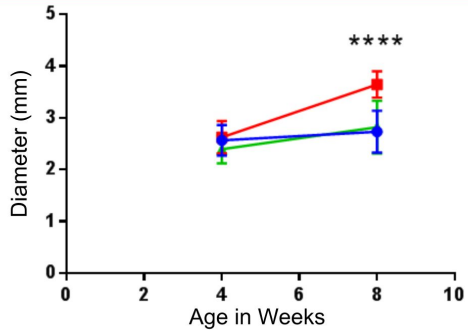
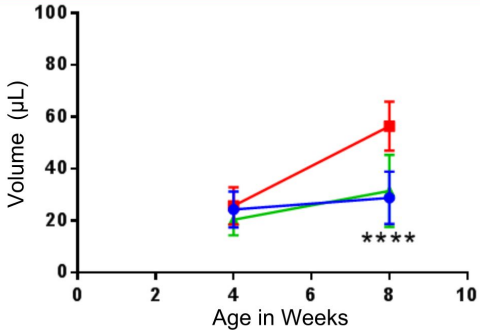
CTI-1601 Prevents Left Ventricle Dilation in KO Mice

- 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 CTI-1601 (10 mg/kg every other day)
- CTI-1601-treated mice have similar LV volume as healthy controls; echocardiogram shows significant differences between vehicle and CTI-1601 treated (10 mg/kg every other day) KO mice

Left Ventricle Internal Diameter (Systole)



Left Ventricle Volume (Systole)



KO: CTI-1601 KO: Vehicle Wild-type: Vehicle

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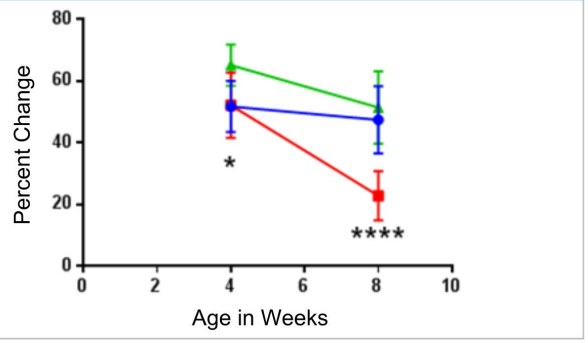
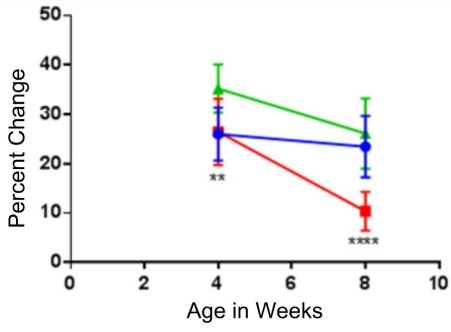
CTI-1601 Preserves Left Ventricle Function in KO Mice

- Left ventricular (LV) function drops significantly in vehicle treated mice by Week 8
- CTI-1601-treated (10 mg/kg every other day) mice have similar LV as healthy controls; echocardiogram shows significant differences between vehicle and CTI-1601 treated KO mice

Left Ventricle Ejection Function



Left Ventricle Fractional Shortening



KO: CTI-1601 KO: Vehicle Wild-type: Vehicle