Record 1 of 0

Recruiting

A First-in-Human, Open-Label, Dose-Escalation Study to Evaluate the Safety and Tolerability of Gene Therapy with TTX-381 for the Ocular Manifestations Associated with Neuronal Ceroid Lipofuscinosis Type 2 (CLN2) Disease

ClinicalTrials.gov ID NCT05791864

Sponsor Tern Therapeutics, LLC

Information provided by Tern Therapeutics, LLC (Responsible Party)

Last Update Posted 2025-03-25

Study Details Tab

Study Overview

Brief Summary

This is a first-in-human, open-label, single ascending dose study of TTX-381 for the treatment of ocular manifestations of CLN2 (Batten disease).

Detailed Description

This is a first-in-human, open-label, single ascending dose study of TTX-381, a gene therapy for the potential treatment of ocular manifestations of CLN2 (Batten disease). TTX-381 is being studied as a potential treatment of ocular manifestations of neuronal ceroid lipofuscinosis type 2 (CLN2) disease. Children with CLN2 disease have a non-working gene (set of instructions) that causes an enzyme called tripeptidyl-peptidase 1 (TPP1) to be missing or not working in their bodies. Without enough TPP1, cells

cannot break down certain molecules in the body, so these storage materials build up and start to hurt the body, particularly the central nervous system (the brain and spine) and retinal cells (eyes); cause seizures; and change how children with CLN2 disease grow, act, think, and see. After eligibility has been confirmed, the participant's eyes will be assigned as the treated eye and the control fellow eye. Due to the symmetry in the clinical course of CLN2 ocular disease, untreated fellow eyes will serve as controls for the contralateral, treated eyes. Participants will be followed in this study for 5 years after TTX-381 administration.

Official Title

A First-in-Human, Open-Label, Dose-Escalation Study to Evaluate the Safety and Tolerability of Gene Therapy with TTX-381 for the Ocular Manifestations Associated with Neuronal Ceroid Lipofuscinosis Type 2 (CLN2) Disease

Conditions

Neuronal Ceroid Lipofuscinosis Type 2

Intervention / Treatment

- Genetic: TTX-381

Other Study ID Numbers

- TTX-381-1102
- 2021-000173-92 (EudraCT Number)

Study Start (Actual)

2023-05-17

Primary Completion (Estimated)

2026-07-30

Study Completion (Estimated)

2030-07-30

Enrollment (Estimated)

16

Study Type

Interventional

Phase

Phase 1
Phase 2

Resource links provided by the National Library of Medicine

MedlinePlus (https://medlineplus.gov/) related topics: Genes and Gene Therapy (https://medlineplus.gov/genesandgenetherapy.html)

Genetic and Rare Diseases Information Center (https://rarediseases.info.nih.gov/gard) resources: Adult Neuronal Ceroid Lipofuscinosis (https://rarediseases.info.nih.gov/diseases/10973/adult-neuronal-ceroid-lipofuscinosis) Neuronal Ceroid Lipofuscinosis (https://rarediseases.info.nih.gov/diseases/10739/neuronal-ceroid-lipofuscinosis)

FDA Drug and Device Resources (https://www.clinicaltrials.gov/fda-links)

Contacts and Locations

This section provides contact details for people who can answer questions about joining this study, and information on where this study is taking place.

To learn more, please see the Contacts and Locations section in How to Read a Study Record (https://www.clinicaltrials.gov/study-basics/how-to-read-study-record#contacts-and-locations).

Study Contact

Name: Tern Therapeutics Patient Advocacy
Phone Number:
202-644-8488
Email: patientadvocacy@terntx.com

This study has 1 location

United Kingdom

London, United Kingdom, Wc1N 3JH
Recruiting
Greater Ormond Street Hospital
Contact:
research.ophthalmology@gosh.nhs.uk

Contact: Robert Henderson, MD

Participation Criteria

Researchers look for people who fit a certain description, called eligibility criteria. Some examples of these criteria are a person's general health condition or prior treatments.

For general information about clinical research, read Learn About Studies (https://www.clinicaltrials.gov/study-basics/learn-about-studies).

Eligibility Criteria

Description

Inclusion Criteria:

A participant is eligible to be included in the study only if all of the following criteria apply:

- Has biallelic CLN2 mutations.
- Has decreased leukocyte TPP1 activity.
- Has clinical signs or symptoms consistent with CLN2 disease (eg, developmental delay, developmental decline, seizure, vision loss, or other signs/symptoms) OR an older sibling with confirmed CLN2 diagnosis.
- Is currently receiving biweekly ICV ERT treatment with cerliponase alfa.
- Meets the following baseline disease condition according to age and CRT as assessed by SD-OCT and confirmed by CRC:

Participants in the phase of accelerated decline in CRT:

1. CRT at baseline ≤210 µm and
2. CRT at baseline ≥140 µm in both eyes and
3. Age ≤84 months,
    - Is willing to adhere to the protocol and 5-year visit schedule.
    - Sexually active female participants of childbearing potential (following menarche) or fertile male participants (following puberty) must be willing to use a medically accepted form of contraception from Screening Visit 2 until 6 weeks after vector administration.

OR

- Was previously administered TTX-381.
- Upon retrospective review, met the above criteria at the time of administration of TTX-381. IDMC may consider exceptions to this when weighing whether to retrospectively enroll a participant who has received TTX-381.
- Has been recommended for enrollment into the clinical trial by IDMC

Exclusion Criteria:

Participants are excluded from the study if any of the following criteria apply:

- Any ocular or systemic condition that, in the opinion of the investigator, would prevent administration and evaluation of the investigational product or interpretation of participant safety or study results (eg, significant lens or corneal opacities, glaucoma, amblyopia, gross retinal anatomical abnormality, etc).
- Difference in screening CRT measurement between the right and left eye >10µm.
- Prior Grade 3 or 4 hypersensitivity reaction, eg, bronchospasm and hypotension requiring intravenous treatment, cardiac dysfunction, anaphylaxis to ICV cerliponase alfa infusion.

- Any other contraindication to the administration of ICV cerliponase alfa, including ventriculo-peritoneal shunt, acute intracerebroventricular access device leakage, device failure, or device-related infection that would impact ability to receive ICV cerliponase alfa.
- Prior participation in a gene therapy study. A subject who has received subretinal TTX-381 under a compassionate use protocol may be enrolled if the PI, Medical Monitor, and Sponsor all agree that he/she can safely and successfully participate in the study and the IDMC has approved their enrollment.
- Prior participation in another ocular clinical trial, except an intravitreal cerliponase alfa trial where a subject has received a maximum of 3 injections and the PI, Medical Monitor, and Sponsor all agree that he/she can safely and successfully participate in the study after a washout period of 3 or more months.
- Prior intraocular injections of any kind, with the following two exceptions. A subject who has received a maximum of 3 intravitreal injections of cerliponase alfa may be enrolled in the study if the PI, Medical Monitor, and Sponsor all agree that he/she can safely and successfully participate in the study after a washout period of 3 or more months. A subject who has received subretinal TTX-381 under a compassionate use protocol may be enrolled if the PI, Medical Monitor, and Sponsor all agree that he/she can safely and successfully participate in the study and the IDMC has approved their enrollment.
- Participation in a nonocular clinical study with an investigational drug in the past 6 months prior to screening, except for intracerebroventricular cerliponase alfa.
- Ocular surgery within the prior 6 months except as above for subretinal TTX-381 administration.
- Prior bone marrow transplant. Use of the following medications within the 30 days prior to treatment: gemfibrozil, mycophenolate, prednisone or other steroids for the intended purpose of treating NCL (not including asthma indications), flupirtine.
- Known sensitivity or contraindications to medications planned for use in the peri-operative period.
- Contraindications to systemic immunosuppression.
- Severe renal insufficiency as determined by an estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m2, based on creatinine, at Screening. If the laboratory determines that the creatinine level is less than the lower limit of assay validation or detection, then the lowest limit cutoff value will be used to estimate eGFR.
- Severe hepatic insufficiency as determined by alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 3 × upper limit of normal (ULN) or total bilirubin > 1.5 × ULN at Screening Visit 1, unless the subject has a previously known history of Gilbert's syndrome and a fractionated bilirubin that shows conjugated bilirubin < 35% of total bilirubin.
- Mutations in another CLN gene.
- Mutation in another gene associated with inherited retinal disease.
- Contraindications to intraocular surgery (eg, severe coagulopathy).
- Positive urine pregnancy test at Screening (applying only to females of childbearing potential).
- Any other condition that would not allow the potential participant to complete follow-up examinations during the study or, in the opinion of the investigator, makes the potential

participant unsuitable for the study.

- The participant had a positive polymerase chain reaction (PCR) viral test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV2 PCR) within the last 4 weeks before signing the informed consent form (ICF) or has persistent coronavirus disease (COVID-19) symptoms regardless of when the last SARS-CoV2 PCR viral test was performed or when the infection occurred.

Ages Eligible for Study

12 Months to 84 Months (Child)

Sexes Eligible for Study

All

Accepts Healthy Volunteers

No

Study Plan

This section provides details of the study plan, including how the study is designed and what the study is measuring.

How is the study designed?

Design Details

Primary Purpose : Treatment
Allocation : Non-Randomized
Interventional Model : Sequential Assignment
Masking : Single (Outcomes Assessor)
Masking Description: In order to minimize the effect of potential bias, wherever possible, endpoints will be measured or interpreted by masked evaluators.

Arms and Interventions

Participant Group/Arm	Intervention/Treatment
Experimental: Cohort 1: Main Treatment Arm 2×10^10 GC/eye	Genetic: TTX-381 • One time subretinal dose in study eye • Other Names: ◦ Gene Therapy (AAV9.CB7.hCLN2)
Experimental: Cohort 2: Main Treatment Arm 6×10^10 GC/eye	Genetic: TTX-381 • One time subretinal dose in study eye • Other Names: ◦ Gene Therapy (AAV9.CB7.hCLN2)
Experimental: Expansion Cohort Expansion cohort, dose level 2×10^10 GC/eye as determined by Independent Data Monitoring Committee.	

What is the study measuring?

Primary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Ocular and overall AE and	To evaluate the safety and tolerability of TTX-381 through Day 360 in participants with	360 days

SAEs through Day 360	Neuronal Ceroid Lipofuscinosis Type 2 (CLN2) disease	

Secondary Outcome Measures

Outcome Measure	Measure Description	Time Frame
To evaluate the effect of TTX-381 on area of EZ loss	To evaluate the effect of TTX-381 on area of EZ loss as measured by SD-OCT	Day 180, Day 360
To evaluate the effect of TTX-381 on central subfield photoreceptor layer thickness	To evaluate the effect of TTX-381 on central subfield photoreceptor layer thickness as measured by SD-OCT	Day 180, Day 360
To measure TTX-381 transgene product (tripeptidyl peptidase 1 [TPP1]) in aqueous humor	To measure TTX-381 transgene product (tripeptidyl peptidase 1 [TPP1]) in aqueous humor	Day 90, Day 360
To evaluate shedding of TTX-381 in urine and tears	To evaluate shedding of TTX-381 in urine and tears	Day 360

Collaborators and Investigators

This is where you will find people and organizations involved with this study.

Sponsor

Tern Therapeutics, LLC

Study Record Dates

These dates track the progress of study record and summary results submissions to ClinicalTrials.gov. Study records and reported results are reviewed by the National Library of Medicine (NLM) to make sure they meet specific quality control standards before being posted on the public website.

Study Registration Dates

First Submitted
2023-03-17

First Submitted that Met QC Criteria
2023-03-17

First Posted
2023-03-30

Study Record Updates

Last Update Submitted that met QC Criteria
2025-02-11

Last Update Posted
2025-03-25

Last Verified
2025-02

More Information

Terms related to this study

Keywords Provided by Tern Therapeutics, LLC

CLN2
Batten Disease
Gene Therapy

Additional Relevant MeSH Terms

Heredodegenerative Disorders, Nervous System
Neurodegenerative Diseases
Nervous System Diseases
Genetic Diseases, Inborn
Lipidoses
Lipid Metabolism, Inborn Errors
Metabolism, Inborn Errors
Lipid Metabolism Disorders
Metabolic Diseases
Neuronal Ceroid-Lipofuscinoses

Plan for Individual Participant Data (IPD)

Plan to Share Individual Participant Data (IPD)?

No

Drug and device information, study documents, and helpful links

Studies a U.S. FDA-Regulated Drug Product

Yes

Studies a U.S. FDA-Regulated Device Product

No

Product Manufactured in and Exported from the U.S.

Yes