February 27, 2025

Dear CLN2 Batten Community,

We are pleased to share updates on Tern Therapeutics' progress with our clinical trials for TTX-381 and TTX-181, which are investigational gene therapies being developed for the treatment of CLN2 Batten disease. These therapies aim to address both the vision loss and neurological symptoms.

Although we are a new company, we were part of the team that originally developed these CLN2 Batten programs, and we are deeply grateful to our former colleagues who helped carry this important work forward, allowing us to continue the progress.

We are excited to share key milestones and positive data from the clinical trials which were presented at the 21st Annual WORLD*Symposium*™ in San Diego, CA. For more information on this news, here is a link to the press release: Tern Therapeutics Advances Pipeline and Presents Positive Clinical Data for TTX-381 and TTX-181 Gene Therapies for CLN2 Batten Disease at 21st Annual WORLD*Symposium*™

Completion of Enrollment and Expansion for TTX-381 Trial: The Phase I/II clinical trial of TTX-381, which aims to treat vision loss associated with CLN2 Batten disease, has completed enrollment of Cohort 2, and selected the dose level for an expansion cohort. The trial is actively recruiting participants at Great Ormond Street Hospital in the United Kingdom.

Positive Clinical Data for TTX-381: Interim data from the trial show a favorable safety profile, increased TPP1 levels in treated eyes, and improvements in vision, with stabilization or improvement in the photoreceptor integrity of 100% of treated eyes. We have also observed promising functional vision outcomes.

Two-Year Data for TTX-181: A single patient study of TTX-181, which targets the neurological symptoms of CLN2 Batten disease, shows increases in TPP1 levels in the fluid surrounding the brain (cerebrospinal fluid, or CSF) through day 477 post-administration. This investigational gene therapy has also resulted in improvements in seizure control, stabilization of language and fine motor skills and allowed the patient to discontinue enzyme replacement therapy (ERT). Additional data at timepoints through 24 months post-administration are pending.

U.S. FDA Clearances: We are excited to announce that the U.S. Food and Drug Administration (FDA) has granted Investigational New Drug (IND) clearances for both TTX-381 and TTX-181, enabling us to continue developing these investigational gene therapies.

We remain committed to advancing both TTX-381 and TTX-181 through clinical trials, and we are encouraged by the progress made thus far. Our next steps include continuing to gather data to better understand the long-term effects of these therapies and working closely with regulatory agencies to bring these potential treatments to additional clinical trials.

We understand how important it is to have options for families living with CLN2 Batten disease, and we are focused on moving forward with urgency to provide meaningful therapies. We will continue to share updates with the Batten patient advocacy groups as they become available.

Thank you for your trust and partnership in this journey. Should you wish to contact us, please email patientadvocacy@terntx.com.

Warm regards,

Tern Therapeutics

Questions you may have about TTX-381 and TTX-181 for CLN2 Batten disease.

What is TTX-381 and what does it do?

TTX-381 is a one-time investigational gene therapy designed to deliver a working copy of the TPP1 gene directly to the retina, which is essential for maintaining vision in children with CLN2 Batten disease. It aims to slow or even stop vision loss that occurs despite other treatments.

How is TTX-381 administered?

TTX-381 is administered as a one-time injection directly into the eye (subretinal administration). The goal is to preserve or restore photoreceptor health and vision in affected individuals.

What have the results been so far for TTX-381?

Early results from the trial are encouraging. All treated eyes have shown improvements or stabilization of photoreceptor integrity, and preliminary data suggest that functional vision may be either maintained or improved. The therapy has been well tolerated, with no serious side effects.

What is TTX-181 and how is it different from TTX-381?

TTX-181 is another one-time gene therapy that targets the neurological aspects of CLN2 Batten disease and is designed to deliver a working copy of the TPP1 gene to the central nervous system (CNS). Unlike TTX-381, which focuses on vision loss, TTX-181 addresses the disease's effects on the brain.

How has TTX-181 performed in clinical trials?

The results from the one-patient, investigator-initiated study of TTX-181 have been positive. The therapy was well tolerated, and it showed benefits in terms of seizure control, developmental stabilization, and allowed the discontinuation of enzyme replacement therapy (ERT) in a five-year-old patient. We are continuing to monitor the patient’s progress for further data.

How will these therapies help children living with CLN2 Batten disease?

Both TTX-381 and TTX-181 hold the potential to address two of the most urgent aspects of CLN2 Batten disease—vision loss and neurological degeneration. By targeting these core issues, these therapies could improve quality of life and slow disease progression for children and adults with CLN2 Batten disease.

What is an Investigational New Drug (IND) clearance?

An IND application is submitted to the U.S. Food and Drug Administration (FDA) by a Sponsor of a clinical trial to ask for permission to start the trial. The FDA reviews the application, which includes discovery, research results, the proposed clinical trial design, and product manufacturing to determine if the FDA believes the clinical trial is safe to start in humans.