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*™

- *Completed enrollment of Cohort 2 and selected dose level for an expansion cohort in the Phase 1/2 clinical trial of TTX-381, a potential one-time AAV gene therapy for the treatment of vision loss associated with CLN2 Batten disease. The trial is active and recruiting participants at Great Ormond Street Hospital (GOSH) in the United Kingdom.*
- *US FDA granted IND clearances for both its lead program, TTX-381, as well as for TTX-181, a potential one-time AAV gene therapy for the CNS manifestations of CLN2 Batten disease.*
- *Interim data from the clinical trial evaluating subretinal administration of TTX-381 show a favorable safety profile, rapid and sustained dose-dependent increases in tripeptidyl peptidase 1 (TPP1) transgene expression, stabilization or improvement of photoreceptor integrity in 100% of treated eyes, and promising changes in functional vision.*
- *Two-year data from a single patient investigator-initiated study show that intracisternal TTX-181 was well-tolerated, achieved durable increases in TPP1 transgene expression that correlated with improvements in multiple clinically meaningful measures of efficacy, and allowed discontinuation of enzyme replacement therapy (ERT).*

WASHINGTON, DC, February 10, 2025 —Tern Therapeutics, LLC ("Tern"), a biotechnology company developing transformative one-time gene therapies for rare diseases, reported the achievement of key development milestones for its programs TTX-381 and TTX-181, as well as presented positive clinical data relating to the safety and efficacy of both programs on February 7, 2025 at the 21st Annual WORLD*Symposium*™ in San Diego, California. TTX-381 and TTX-181 are novel one-time gene therapy products being developed for the treatment of the ocular and central nervous system (CNS) manifestations of CLN2 disease, a form of Batten disease.

Interim clinical data (n=6) from the ongoing Phase 1/2 clinical study evaluating TTX-381 at GOSH were presented by Christina Ohnsman, M.D., Chief Medical Officer of Tern. Physician investigators from the Hospital de Clinicas in Porto Alegre, Brazil presented two-year follow-up data from a single-patient, investigator-initiated study of TTX-181 administered to a five-year-old child.

"We are encouraged and energized by the TTX-381 clinical data showing photoreceptor preservation in the treated eyes of 100% of participants. This demonstrates the potential of TTX-381 as a one-time gene therapy to address the urgent unmet medical need of rapidly progressive vision loss caused by CLN2 disease. We are excited to report continued progress in the TTX-381 clinical trial," said Ohnsman.

"Intracisternal TTX-181 has had a very positive impact on our patient's quality of life, with better seizure control, developmental stabilization, improved ability to communicate, and discontinuation of enzyme replacement therapy. However, some aspects of CLN2 that impact developmental skills were not addressed by TTX-181, especially vision loss," said Carolina Fischinger Moura de Souza, MD, PhD, principal investigator. Roberto Giugliani, MD, PhD, who presented the data at the conference, added, "These results support initiation of a clinical trial to further explore safety, efficacy, dose level, and optimal age of administration for TTX-181."

Program updates

Tern reported the completion of enrollment of Cohort 1 (n=3) and Cohort 2 (n=3) in the ongoing Phase 1/2 human clinical trial of TTX-381. Dose level 1 ($2x10^{10}$ genome copies (GC)/eye) has subsequently been selected for an expansion cohort, and the trial is ongoing at GOSH in the United Kingdom. Tern also announced that it has received clearances

from the United States Food and Drug Administration (FDA) for their Investigational New Drug (IND) applications for both TTX-381, its lead program, and TTX-181.

“We are thrilled with the progress we have made advancing our therapeutic pipeline. The opening of the INDs for TTX-381 and TTX-181 represents a significant expansion of Tern’s capabilities, as well as provides us with an increased ability to collaborate with the FDA on the continued development of these promising programs” said Alex Bailey, PhD, Chief Executive Office of Tern.

Interim Data from TTX-381 Phase 1/2 Clinical Trial

Safety and Tolerability

As of the data cut-off on December 6, 2024, TTX-381 has been well tolerated at Dose Level 1 ($2.0x10^{10}$ GC/eye; n=3) and Dose Level 2 ($6.0x10^{10}$ GC/eye; n=3) with no serious adverse events (SAEs) related to the drug or administration procedure. Time of post-administration follow-up includes a minimum of six months for all participants and one year for participants in Cohort 1.

TPP1 Concentration in Aqueous Humor (AH)

In CLN2 Batten disease, TPP1 deficiency results in lysosomal accumulation of storage material and degeneration of nerve cells, particularly in the brain and retina. At baseline, all participants had either undetectable or trace concentrations of TPP1 in AH of both eyes. At day 90 following the administration of TTX-381, the treated eyes in 100% of participants (6/6) demonstrated dose-dependent increases in TPP1 expression compared with baseline, with 5 of 6 approximating or exceeding mean TPP1 concentrations of non-CLN2 eyes. Untreated eyes continued to have undetectable or trace concentrations of TPP1.

Anatomic Data from SD-OCT Imaging

Natural history data demonstrate that rapid photoreceptor degeneration in children with CLN2 is strikingly symmetrical in both eyes and first detectable in the ellipsoid zone (EZ). Areas with loss of the EZ as measured with SD-OCT directly correlate with areas of vision loss. Following administration of TTX-381, photoreceptor preservation as measured by stabilization or improvement in the area of EZ loss was observed in 6 of 6 participants, in contrast to progressive retinal degeneration in their untreated eyes. Differences in anatomic changes between treated and untreated eyes were observed as early as three months.

Functional Vision

Preliminary functional vision data suggest maintenance or improvement in visual skills in participants with the longest follow-up data available. These functional vision data, observed on a modified version of the Mullen Scales of Early Learning Visual Reception subscale, are consistent with stable to improved photoreceptor integrity observed on SD-OCT in treated eyes and with parental reports of maintained visual skills.

Data from TTX-181 Investigator-Initiated Study

Safety and Tolerability

As of the data cut-off on December 26, 2024, TTX-181 at a dose level of 1.25×10^{11} GC/gram of brain mass was well tolerated through two years post-administration with the patient experiencing no SAEs related to the drug or administration procedure.

TPP1 Concentration in cerebrospinal fluid (CSF)

TPP1 concentration was measured in CSF samples collected prior to administration of TTX-181 and at 12 timepoints through day 477 post-administration. Each sample was collected at least 19 days following infusion of ERT. Measurements showed a rapid and sustained 27- to 55-fold increase in CSF TPP1 compared with baseline through day 477 (last time point available). Additional data at timepoints through 24 months post-administration are pending.

Seizure Frequency, anti-epileptic medication use, and discontinuation of enzyme replacement therapy (ERT)

The monthly frequency of seizure events decreased by 90% after administration of TTX-181 in comparison with the frequency of seizures pre-administration and remained stable through two years. Two of four anti-epileptic medications were discontinued within six months. In addition, under the direction of the physician, intervals between ERT infusions

were lengthened following administration of TTX-181, until ERT was ultimately discontinued at 16 months post-administration of TTX-181.

Neurodevelopment Measures

Stabilization or a small increase in age equivalent fine motor, receptive and expressive language skills were observed at two years post-administration of TTX-181, as compared with baseline on the Mullen Scales of Early Learning. Gross motor skills declined over the two years on this measure.

About TTX-381 and TTX-181

TTX-381 is an investigational one-time AAV gene therapy designed to deliver a working copy of the TPP1 gene directly to the retina, potentially providing a durable source of TPP1 activity intended to maintain the health of the retina and address vision loss in people with CLN2 disease. Vision loss in children with CLN2 disease progresses to blindness, despite treatment with enzyme replacement therapy. There is currently no available treatment for the ocular manifestations of CLN2 disease.

TTX-181 is an investigational one-time AAV gene therapy designed to deliver a working copy of the *TPP1* gene directly to the central nervous system (CNS), potentially providing sustained levels of TPP1 intended to prevent worsening of neurological degeneration in people with CLN2 disease.

ABOUT TERN THERAPEUTICS

TERN THERAPEUTICS is a privately-held biotechnology company founded in 2023 with a new vision for speeding the development of transformative, one-time gene therapy medicines for rare diseases. Guided by a team of leading physicians, scientists, and business leaders and in collaboration with patient communities, we are driven to deliver transformative treatments with urgency to those living around the world with rare diseases. For more information about Tern, please visit **WWW.TERNTX.COM**.

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