Transposon Announces TPN-101 Selected for Inclusion in the Phase 2/3 HEALEY ALS Platform Trial, Building on the Success of Phase 2 Study in *C9orf72*-related ALS

In the Phase 2 Study of TPN-101 in patients with C9orf72-related ALS, TPN-101 showed clinical benefits on key clinical outcome measures, including slow vital capacity and the ALSFRS-R

TPN-101 also had lowering effects on key biomarkers of neurodegeneration and neuroinflammation, including NfL and IL-6

Initiation of the TPN-101 regimen in the HEALEY ALS Platform Trial is expected in Q4 2025

SAN DIEGO, CA, May 28, 2025 – Transposon Therapeutics, a biotechnology company focused on developing novel, orally administered therapies for the treatment of neurodegenerative and aging-related diseases, including amyotrophic lateral sclerosis (ALS) and Alzheimer's disease, today announced that TPN-101 has been selected for inclusion in the Phase 2/3 HEALEY ALS Platform Trial. TPN-101, a potent nucleoside reverse transcriptase inhibitor that specifically inhibits the LINE-1 reverse transcriptase, is being developed for people with ALS, progressive supranuclear palsy (PSP), and Alzheimer's disease.

The HEALEY ALS Platform Trial is a multicenter, double-blind, placebo-controlled, adaptive trial for ALS that incorporates an innovative design to allow for the efficient evaluation of multiple products simultaneously and ongoing adaptation based on emerging data. The trial is being conducted at the Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital (MGH) and in partnership with the Northeast ALS Consortium (NEALS). Investigators expect to initiate the TPN-101 regimen in the study in the fourth quarter of 2025.

In the recently completed Phase 2 clinical trial of TPN-101 in patients with *C9orf72*-related ALS and/or frontotemporal dementia (FTD), in which the ALS population is further enriched for increased LINE-1 expression, TPN-101 treatment reduced the rate of decline of slow vital capacity in the ALS group by 50% compared to placebo after 24 weeks. Treatment with TPN-101 also showed a slowing of ALS disease progression as measured by the ALS Functional Rating Scale - Revised (ALSFRS-R). Additionally, TPN-101 was associated with reductions in key biomarkers of neurodegeneration and neuroinflammation, including neurofilament light chain (NfL), neurofilament heavy chain (NfH), and interleukin 6 (IL-6), compared with placebo. These results provide proof-of-concept for TPN-101 in all forms of ALS associated with TDP-43 pathology.

"We look forward to collaborating with the Transposon team to develop their regimen for investigating TPN-101 in people with ALS," said Merit Cudkowicz, M.D., principal investigator and sponsor of the HEALEY ALS Platform Trial, director of the Sean M. Healey & AMG Center for ALS, and executive director of the Neuroscience Institute at Mass General Brigham. "We are grateful to our patient advisory committee and all the people who participate in the Platform Trial to help discover new treatments for ALS."

"We appreciate the endorsement of the HEALEY Therapy Evaluation Committee for inclusion of TPN-101 into the platform trial based on its novel target and Phase 2 clinical data, and look forward to working with the HEALEY group to advance the development of TPN-101 in ALS," said Andrew Satlin, M.D., chief medical officer at Transposon. "TPN-101 is the first LINE-1 nucleoside reverse transcriptase inhibitor to show promise for the treatment of a range of neurodegenerative disorders for which few, if any, effective treatments are available."

Further information about the HEALEY ALS Platform Trial can be found at HEALEY ALS Platform Trial.

About TPN-101

TPN-101 specifically inhibits the LINE-1 reverse transcriptase that promotes LINE-1 replication. LINE-1 elements are a class of retrotransposable elements that in humans are uniquely capable of replicating and moving to new locations within the genome. When this process becomes dysregulated, LINE-1 reverse transcriptase drives overproduction of LINE-1 cDNA, triggering innate immune responses that contribute to neurodegenerative, neuroinflammatory, and aging-related disease pathology.

About the Phase 2 Study in C9orf72-related ALS/FTD

The Phase 2 study in patients with *C9orf72*-related ALS/FTD was a multi-center, randomized, double-blind, placebo-controlled parallel-group, two-arm study with an open-label treatment period. Participants (n=42) were randomized 3:2 to receive daily doses of 400 mg of TPN-101 or placebo. The study included a six-week screening period, a 24-week double-blind treatment period, a 24-week open-label treatment period, and a follow-up visit four weeks post-treatment. Further information on the study can be accessed at ClinicalTrials.gov.

About Transposon

Transposon Therapeutics, Inc. is a clinical-stage biopharmaceutical company focused on developing transformational therapies for the treatment of neurodegenerative and aging-related diseases, including ALS, PSP and Alzheimer's disease. The company's lead clinical compound, TPN-101, is first-in-class to address LINE-1 reverse transcriptase for treating neurodegenerative and autoimmune diseases. The company also has a discovery platform supporting a deep pipeline of novel therapies to address additional indications.

Contact:
Rick Orr
Transposon Therapeutics, Inc.
(858) 535-4821
rorr@transposonrx.com