Transition Therapeutics Reports Findings from Bipolar Disorder Phase 2 Study

TORONTO, ON, November 4th, 2014 – Transition Therapeutics Inc. ("Transition" or the "Company") (NASDAQ: TTHI, TSX: TTH) today announced findings from a Phase 2 study of neuropsychiatric drug candidate, ELND005, as an adjunctive maintenance treatment for bipolar disorder type I patients (BPD). Transition's wholly-owned subsidiary, Transition Therapeutics Ireland Limited ("TTIL") terminated the bipolar disorder Phase 2 study on April 7, 2014 for business reasons, so that development resources were fully focused on the completion of the current on-going Phase 2 study of ELND005 in agitation and aggression associated with Alzheimer's disease. TTIL has completed a review of the data from this bipolar disorder Phase 2 study.

Overall, ELND005 had an acceptable safety and tolerability profile in the study, and showed numerical differences in the number of mood event recurrences favoring ELND005.

Safety, Pharmacodynamic & Pharmacokinetic Findings

The study enrolled 309 subjects with BPD into the open label phase of the clinical study. Approximately 50% of the subjects had a treatment emergent adverse event (TEAE) during this 16-week phase of the study. The most common TEAE with an incidence > or = 5% were: depression (6.8%) and nasopharyngitis (6.1%). Other than two mood events (1 depression, 1 mania), there were no serious adverse events that were considered drug related in the open phase.

Of the 309 subjects, a total of 129 were entered into the randomized phase of the study, with 64 and 65 subjects in the ELND005 and placebo groups, respectively. During the randomized phase, the incidences of TEAE in the ELND005 and placebo groups were approximately 47% and 45%; while discontinuation due to TEAE occurred in 3% of ELND005 group and 11% of placebo group. The most common TEAE in the ELND005 group, with incidence > or =5%, and double the placebo rates, were nasopharyngitis and headache (each 6.3%). There were no drug-related serious adverse events in the controlled phase.

At the time of study discontinuation, only 36 of the 129 patients had been in the randomized phase for 24 weeks or longer, the period when most mood recurrences are expected to occur. There were a total of 11 events of mood recurrence in the randomized phase, 3 occurred in the ELND005 group and 8 in the placebo group.

The pharmacokinetic profile of the 500mg BID ELND005 dose in the study was consistent with expected exposures based on modeling and simulation activities. Observed plasma levels showed that ELND005 achieved targeted exposures and effects on pharmacodynamic measures, namely reduction of brain myo-inositol levels (assessed by magnetic resonance spectroscopy imaging in a subset of patients).

Study Design

Bipolar disorder type 1 subjects entering the study had not experienced a mood episode for more than 90 days prior to their screening visit. All subjects were receiving maintenance doses of either lamitrogine or valproic acid entering the study and continued that regimen for the duration of the study.

There were two phases to the clinical study; an initial "open-label phase" where all subjects received 500mg of ELND005 orally twice daily for 4 months, followed by a "randomization phase" where subjects were randomized 1:1 to either continue to receive twice daily oral 500mg doses of ELND005 or placebo for an additional period up to twelve months. During the open-label phase, subjects were discontinued from anti-depressant and anti-psychotic medications. In the randomization phase, subjects continued to receive lamitrogine or valproic acid in addition to study drug and remained in the randomized phase until the occurrence of a mood episode or the completion of the 12 months of the randomized phase.

Recurrence of mood episodes during the randomized phase was the key efficacy evaluation of the study.

At the time of study termination, there were 129 bipolar disorder type 1 patients in the randomized phase, (64 in the ELND005 group, 65 in the placebo group). The patient's mean duration in the randomized phase for both groups was approximately three months.

About ELND005

ELND005 is an orally bioavailable small molecule that is being investigated for multiple neuropsychiatric indications on the basis of its proposed dual mechanism of action, which includes β-amyloid anti-aggregation and regulation of brain myo-inositol levels. An extensive clinical program of Phase 1 and Phase 2 studies has been completed with ELND005 to support clinical development, including the published Phase 2 study ELND005-AD201 in Alzheimer's disease ("AD"). ELND005 is also being studied as a potential treatment of agitation and aggression in Alzheimer's disease (Study ELND005-AG201), and as a therapy for those with Down syndrome (Study ELND005-DS-201). ELND005 has received fast track designation from the psychiatry division of the United States Food and Drug Administration for its potential as a treatment of Neuropsychiatric Symptoms (including Agitation) in AD.

About Transition

Transition is a biopharmaceutical development company, advancing novel therapeutics for CNS and metabolic disease indications. The Company's wholly-owned subsidiary, Transition Therapeutics Ireland Limited is developing CNS drug candidate ELND005 for the treatment of Alzheimer's disease and Down syndrome. Transition's lead metabolic drug candidate is TT401 (LY2944876) for the treatment of type 2 diabetes and accompanying obesity. The Company's shares are listed on the NASDAQ under the symbol "TTHI" and the Toronto Stock Exchange under the symbol "TTH". For additional information about the Company, please visit www.transitiontherapeutics.com.

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