



## **Transition Therapeutics Announces Results from Phase 1 AME & Renal Clearance Clinical Studies of Neuropsychiatric Drug Candidate ELND005**

**TORONTO, ON, March 26<sup>th</sup>, 2015 – Transition Therapeutics Inc.** (“Transition” or the “Company”) (NASDAQ: TTHI, TSX:TTH) today announced results from two phase 1 clinical studies of neuropsychiatric drug candidate ELND005. These studies, an absorption-metabolism-excretion (“AME”) study and a renal clearance study, are specialized clinical pharmacology trials that are required by the United States Food and Drug Administration (“FDA”) for the approval of most drugs in development.

The AME study enrolled 8 subjects and the renal clearance study enrolled 42 subjects. In both studies, ELND005 showed good safety and tolerability. The key result of the AME study was that ELND005 showed good oral bioavailability as there was nearly 100% absorption. ELND005 showed no evidence of hepatic or intermediary metabolism and the study demonstrated that the main excretion route of ELND005 is via the kidney. These AME properties of good oral bioavailability, low protein binding, and lack of CYP metabolism are usually associated with consistent plasma levels and with a reduced risk of drug-drug interactions. The AME profile of ELND005 is well suited for an Alzheimer’s disease patient population that is commonly administered multiple concomitant medications, many of which are metabolized by the liver.

The renal clearance study evaluated the pharmacokinetic profile of ELND005 in subjects with various degrees of renal impairment. In this study, ELND005 showed minimal protein binding in plasma regardless of renal function. Across the 5 study arms, subjects with worse renal function had increased plasma drug exposure compared to those with normal renal function. The study provided important guidance for the minimum creatinine clearance needed to allow patient participation in studies with a fixed dose regimen of ELND005. This minimum creatinine clearance is consistent with the threshold used as exclusion criterion in the ongoing study of ELND005 in Agitation and Aggression of AD (ELND005-AG201, the HarmonyAD Study).

“The informative results from these studies together with the thorough QT study results reported last November, showing no QTc prolongation, are supportive of the suitability of ELND005 in the elderly AD population. These studies are part of a comprehensive package of data being compiled by our wholly owned subsidiary, Transition Therapeutics Ireland Limited, to advance ELND005 toward regulatory approval,” said Dr. Tony Cruz, Chairman and Chief Executive Officer of Transition.

### **About the ELND005 AME and Renal Clearance Studies**

#### *AME Study Design*

This study was designed to assess the absorption, metabolism, and excretion of a radio labeled ELND005 molecule (“<sup>14</sup>C-ELND005”) following a single oral administration in healthy male subjects. All subjects received a single oral dose of 1000 mg (approximately 100  $\mu$ Ci) <sup>14</sup>C-ELND005. All subjects were enrolled and evaluated concurrently.

## *Renal Clearance Study Design*

This study was designed to evaluate the pharmacokinetics, safety, and pharmacodynamic profiles of ELND005 following a single 1000 mg dose to healthy matched control subjects and subjects with varying degrees of renal impairment (mild to severe) and following 2 single 1000 mg doses in end stage renal disease (“ESRD”) subjects.

### **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  $\beta$ -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. ELND005 is being studied as a potential treatment of agitation and aggression in Alzheimer’s disease and as a therapy for those with Down syndrome. 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 and Aggression) 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](http://www.transitiontherapeutics.com).

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