



Neuren (NEU) - ASX Announcement

14 November 2016

Neuren completes enrolment into Phase 2 trial in pediatric Rett syndrome

Melbourne, Australia, 14 November 2016: Neuren Pharmaceuticals (ASX: NEU) today announced that enrolment into its Phase 2 clinical trial of trofinetide in pediatric Rett syndrome has been completed. The last subjects will conclude the trial in January 2017 and Neuren expects to receive top-line results in March 2017.

Neuren's trial is a randomized, double-blind, placebo-controlled Phase 2 clinical trial for girls aged 5 to 15 years with Rett syndrome. The trial is being conducted at 12 sites in the United States, led by clinicians experienced in the diagnosis and treatment of Rett syndrome. Neuren has received grant funding from Rettsyndrome.org towards the cost of the trial.

As previously announced, faster enrolment into the trial provided Neuren with the opportunity to expand the trial beyond the original target of 64 completing subjects, whilst still delivering top-line results in the first quarter of 2017. In total, 82 subjects have been randomized. 62 subjects were randomized into one of four treatment groups: 50mg/kg, 100mg/kg, 200mg/kg and placebo. A further 20 subjects have been randomized into one of two treatment groups: 200mg/kg and placebo. The total duration of a subject's participation in the trial, from screening through to follow-up, is eleven weeks. To date, 55 subjects have completed the trial and only one subject has withdrawn before completion.

The primary endpoint for the trial in this younger population is the safety and tolerability of trofinetide compared with placebo. In addition, a number of outcome measures have been included in the study design in order to provide valuable insights into the efficacy of trofinetide in younger subjects. The efficacy analysis will prioritize 5 core measures:

- The Motor Behavior Assessment Change Index, a subset of items from the Motor Behavior Assessment, in which the clinician rates the subject's current level of function.
- The Domain Specific Concerns Visual Analog Scale, in which the clinician assesses the severity of concerns identified for each subject on an individual basis.
- The Clinical Global Impression of Improvement (CGI-I), in which the clinician rates how much the subject's overall illness has improved or worsened, relative to baseline.
- The Caregiver Top 3 Concerns Visual Analog scale, in which the subject's caregiver assesses the severity of concerns identified for each subject on an individual basis.
- The Rett Syndrome Behavior Questionnaire, a rating scale in which the subject's caregiver rates the frequency of symptoms.



The analysis will examine mean change from baseline for each treatment group as well as the proportion of subjects from each treatment group that show improvements from baseline. The clinical importance of the observed changes in the 5 core efficacy measures and whether there is an overall pattern of benefit will be evaluated.

Other development programs

As previously reported, Neuren met with the US Food and Drug Administration (FDA) in May 2016 to discuss the further development of trofinetide for Fragile X syndrome. As agreed, Neuren is currently conducting analyses and planning an observational study to validate elements of its Fragile X Syndrome Rating Scale for use as an efficacy measure in pivotal clinical trials. Neuren plans to discuss the results of the analyses and the design of the observational study with the FDA in the first half of 2017.

In addition, Neuren is currently conducting a review of potential indications for trofinetide and NNZ-2591 across neurodevelopmental disorders, neurodegenerative diseases and acute brain injury. The review will identify priority indications to advance in the second half of 2017.

Neuren Executive Chairman Richard Treagus commented: "We are pleased to have been able to expand the pediatric clinical trial with the strong support of the Rett syndrome community. We look forward to receiving the top-line results in March 2017 and engaging with our clinical expert advisors and potential commercial partners to determine the optimum path to market for trofinetide in Rett syndrome and other indications."

About trofinetide

Trofinetide is a synthetic analogue of a naturally occurring neurotrophic peptide derived from IGF-1, a growth factor produced by brain cells. In animal models, trofinetide exhibits a wide range of important effects including inhibiting neuroinflammation, normalizing the role of microglia, correcting deficits in synaptic function and regulating oxidative stress response. Trofinetide is being developed both in intravenous and oral formulations for a range of acute and chronic conditions. The most advanced program is for Rett syndrome, supported by Rettsyndrome.org. Both the Rett syndrome and Fragile X syndrome programs have been granted Fast Track designation by the US Food and Drug Administration (FDA) and have orphan drug designation in both the United States and the European Union. Following marketing authorization, orphan drug designation provides a market exclusivity period of 7 years in the United States and 10 years in the European Union.

About Neuren

Neuren Pharmaceuticals Limited (Neuren) is a biopharmaceutical company developing new therapies for neurodevelopmental disorders, neurodegenerative diseases and acute brain injury. Neuren presently



has a clinical stage molecule, trofinetide in Phase 2 clinical trials as well as NNZ-2591 in pre-clinical development.

Forward-looking Statements

This ASX-announcement contains forward-looking statements that are subject to risks and uncertainties. Such statements involve known and unknown risks and important factors that may cause the actual results, performance or achievements of Neuren to be materially different from the statements in this announcement.

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