



Neuren (NEU) - ASX Announcement

29 July 2015

## Neuren reports progress in orphan drug programs

### Highlights:

- **Orphan drug designation for trofinetide in both Rett syndrome and Fragile X syndrome recommended by European Medicines Agency**
- **Productive meeting with US Food and Drug Administration (FDA) on remaining development for Rett syndrome:**
  - **Neuren and FDA commit to reach agreement quickly on a primary efficacy endpoint for pivotal trials based on the Motor Behavior Assessment (MBA) used in Neuren's Phase 2 clinical trial**
  - **Neuren to propose to FDA a design for a single Phase 3 clinical trial to support a New Drug Application for Rett syndrome**
  - **Neuren to conduct a brief tolerability clinical trial in children and adolescents to test higher doses of trofinetide in a younger population and confirm dose levels for the Phase 3 trial**
- **Enrolment completed in Fragile X Phase 2 clinical trial; top-line results expected in December 2015**

**Melbourne, Australia, 29 July 2015:** Neuren Pharmaceuticals (ASX: NEU) today reported important progress in its development programs for trofinetide in Rett syndrome and Fragile X syndrome.

The Committee for Orphan Medicinal Products (COMP) of the European Medicines Agency (EMA) has recommended that Orphan designation be granted for trofinetide in both Rett syndrome and Fragile X syndrome. Neuren anticipates that the European Commission will provide formal confirmation of these designations in August 2015.

Orphan designation in the European Union (EU) enables sponsors to benefit from a number of incentives, including 10 years of market exclusivity once the medicine is on the market. During that exclusivity period, the EMA and the EU Member States shall not accept another application for a marketing authorisation, for the same therapeutic indication, in respect of a similar medicinal product. Neuren's programs for Rett syndrome and Fragile X syndrome have previously been granted Orphan Drug designation by the US Food and Drug Administration (FDA), which provides 7 years of market exclusivity in the United States.

Neuren recently attended a highly productive meeting with the FDA to discuss the remaining development requirements for trofinetide in Rett syndrome. The meeting provided meaningful guidance for Neuren in all areas of the development program. Importantly, this included guidance on



efficacy endpoints for pivotal clinical trials, the requirements for Phase 3 trials and the testing of trofinetide in subjects younger than age 16.

Neuren and the FDA committed to reach agreement quickly on the primary efficacy endpoint to be used in a pivotal trial for Rett syndrome, with Neuren to propose a subset of items from the clinician-completed Motor Behavior Assessment (MBA). The MBA was utilised by Neuren in its Phase 2 clinical trial and has been used to assess over 1,100 children, adolescents and adults with Rett syndrome enrolled in the Rett Natural History Study, a study sponsored by the National Institutes of Health.

Generally, two Phase 3 clinical trials are required to support approval of a New Drug Application in the United States. However, for rare diseases it may be acceptable to design a single Phase 3 trial to collect sufficient evidence of safety and efficacy. It was agreed that Neuren will submit a design proposal to the FDA for a single Phase 3 trial.

Neuren received encouragement to conduct a brief paediatric tolerability clinical trial in which higher doses of trofinetide will be tested in subjects below the age of 16. Neuren's Phase 2 trial tested adults and adolescents aged 16 years and older. The trial will enable Neuren to confirm the optimum dose levels for the Phase 3 trial, as well as generating useful information on the treatment of children and younger adolescents.

Preparations for the paediatric trial are underway. Neuren is currently well funded, with cash reserves at 30 June 2015 of \$17.7 million. The board will consider all strategic options for progressing the Phase 3 development as quickly and efficiently as possible.

"To date trofinetide has demonstrated an excellent safety and tolerability profile, with evidence of a pattern of clinical benefit across the broad phenotype of Rett syndrome, which is consistent with its normalising effects on brain biology", commented Neuren's Chief Science Officer, Larry Glass.

Neuren is also presently completing a Phase 2 clinical trial in the United States, collecting information on the safety, efficacy and pharmacokinetics of trofinetide in adults and adolescents with Fragile X syndrome. Enrolment of subjects has now been completed, with 72 subjects participating. The last subject is due to complete the trial at the end of September 2015. Neuren expects to release top-line results in December 2015.

"Following a productive and collaborative meeting with the FDA, we now have a pathway towards a New Drug Application for Rett syndrome", commented Neuren Executive Chairman, Richard Treagus. "We are also very pleased to have secured the important commercial incentive of Orphan designation in the European Union for both indications and we are on track to provide the top-line results from our Phase 2 trial in Fragile X before the end of the year".



### **About trofinetide (proposed INN)**

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 and correcting deficits in synaptic function. The intravenous form of trofinetide is presently in a Phase 2 clinical trial in patients with moderate to severe traumatic brain injury. The oral form of trofinetide is in Phase 2 development in Rett syndrome, Fragile X syndrome and mild traumatic brain injury (concussion). Three programs have received Fast Track designation from the US FDA and the Rett syndrome and Fragile X syndrome programs have also received Orphan Drug designation. In November 2014, Neuren announced top-line results from its Phase 2 clinical trial in Rett syndrome, which successfully demonstrated clinical benefit from treatment with trofinetide. The benefit observed in the trial encompassed many of the core symptoms of Rett syndrome and was observed in both clinician and caregiver assessments.

### **About Neuren**

Neuren Pharmaceuticals Limited (Neuren) is a biopharmaceutical company developing new therapies for brain injury, neurodevelopmental and neurodegenerative disorders. The novel drugs target chronic conditions as well as acute neurological injuries. 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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