



Neuren (NEU) - ASX Announcement

26 April 2019

Neuren provides update on development of NNZ-2591 in neurodevelopmental disorders

Melbourne, Australia, 26 April 2019: Neuren Pharmaceuticals (ASX: NEU) today provided an update regarding its development plan for NNZ-2591 in neurodevelopmental disorders. NNZ-2591 recently demonstrated positive effects in the *Shank3* model of Phelan-McDermid syndrome (PMS), a genetic condition in which the most common characteristics are intellectual disability, delayed or absent speech, symptoms of autism, low muscle tone, motor delays, and epilepsy. There is no approved treatment specifically for PMS.

In parallel with investigating the effects of NNZ-2591 in neurodevelopmental disorders, Neuren is presently conducting non-clinical safety studies that are required before clinical trials may proceed. Neuren intends to fast-track the clinical development of NNZ-2591 by completing the non-clinical studies that will allow the initial Phase 2 trials to have a dosing duration of 3 months. In addition, manufacturing development studies are underway in order that Neuren may fully benefit from the technical and commercial advantages attributable to the properties of NNZ-2591.

The current development plan is targeting the following key near-term milestones:

- Submission for Orphan Drug designation in 2019
- Filing of an Investigational New Drug (“IND”) Application with the US Food and Drug Administration
- Commencement of Phase 2 clinical trials in the second half of 2020

The recent study in PMS compared normal mice (“wild type”) and mice with a disrupted *Shank3* gene (“knockout”). In the knockout mice, deficits in anxiety, repetitive behaviour, motor performance and social interaction were restored to the wild type state following treatment with NNZ-2591 for 3 weeks. Treated knockout mice also showed a 60% reduction in susceptibility to seizures. In addition, in the knockout mice the abnormal length of dendrite spines between brain cells, the excess pERK enzyme that interferes with the *Shank3* gene functioning and a depressed level of IGF-1 were all normalised after treatment with NNZ-2591.

Neuren Executive Chairman Dr Richard Treagus commented: “As this development work progresses we are increasingly optimistic about the prospects and potential for NNZ-2591. The recent results in the model of PMS were very promising and we look forward to working with physicians and families as we continue to expand Neuren’s novel drug pipeline into neurodevelopmental indications with a high unmet need.”

About Neuren and NNZ-2591

Neuren Pharmaceuticals Limited (Neuren) is a biopharmaceutical company developing new therapies for neurodevelopmental and neurodegenerative disorders and brain injury. Neuren completed Phase 2 development of its lead drug candidate trofinetide for Rett syndrome and has completed a Phase 2



clinical trial in Fragile X syndrome. The programs in Rett syndrome and Fragile X syndrome have each been granted Fast Track designation by the US Food and Drug Administration and Orphan Drug designation in both the United States and the European Union. Neuren has granted an exclusive license to ACADIA Pharmaceuticals Inc. for the development and commercialization of trofinetide in North America, whilst retaining all rights to trofinetide outside North America.

Neuren is advancing the development of its second drug candidate NNZ-2591, a synthetic analog of the neurotrophic peptide, cyclic glycine proline (cGP), which occurs naturally in the brain. NNZ-2591 has demonstrated efficacy in pre-clinical models of Parkinson's disease, stroke, traumatic brain injury, peripheral neuropathy, Fragile X syndrome, Phelan-McDermid syndrome, memory impairment and multiple sclerosis. The use of NNZ-2591 to treat Phelan-McDermid syndrome is covered by issued patents in the United States to 2034.

About Phelan-McDermid syndrome

Phelan-McDermid syndrome (PMS) is a rare genetic condition caused by a deletion or other change in the 22q13 region of chromosome 22, which includes the *SHANK3* gene, or a mutation of the gene. PMS is also known as 22q13 deletion syndrome. The *SHANK3* gene codes for the shank3 protein, which supports the structure of synapses between nerve cells in the brain.

The most common characteristics of PMS are intellectual disability, delayed or absent speech, symptoms of autism (approximately 75% are diagnosed with autism spectrum disorder), low muscle tone, motor delays, and epilepsy. There is currently no cure or treatment specifically for PMS. It is estimated that 1% of people with autism have PMS, which implies that between 1 in 8,000 and 1 in 15,000 people have PMS. This may be an underestimate since not all patients with PMS have autism.

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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.