



Neuren (NEU) - ASX Announcement

17 May 2019

NNZ-2591 demonstrates positive effects in Pitt Hopkins syndrome pre-clinical model

Melbourne, Australia, 17 May 2019: Neuren Pharmaceuticals (ASX: NEU) today announced that treatment with its drug candidate NNZ-2591 has normalized all deficits in a pre-clinical model of the neurodevelopmental disorder Pitt Hopkins syndrome (PTHS). Neuren anticipates that PTHS meets the criteria for Orphan Drug designation. There is currently no treatment specifically for PTHS.

NNZ-2591 was tested in the *tcf4* mutation mouse model, which exhibits features of PTHS in humans, comparing normal mice and mice with a disrupted *tcf4* gene. In the mice with a disrupted gene, treatment with NNZ-2591 for 6 weeks normalized the deficits in all the tests of hyperactivity, daily living, learning and memory, sociability, motor performance and stereotypy. All positive confirmatory measures were statistically significant.

PTHS is a neurodevelopmental condition affecting both males and females, caused by the loss of one copy or a mutation of the *TCF4* gene on chromosome 18. The incidence of PTHS is not known, however it has been estimated potentially as high as 1 in 11,000 people.

Characteristics of Pitt Hopkins syndrome (PTHS) are developmental delay with moderate-to-severe intellectual disability and behavioral differences, hyperventilation and/or breath-holding while awake, seizures, gastrointestinal issues, lack of speech, sleep disturbance, stereotypic hand movements and distinctive facial features. Some individuals with PTHS are diagnosed with autism.

About Neuren and NNZ-2591

Neuren Pharmaceuticals Limited (Neuren) is a biopharmaceutical company developing new therapies for neurodevelopmental disorders with high unmet need. Neuren has 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, Angelman syndrome, Pitt Hopkins syndrome, memory impairment and multiple sclerosis.



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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.