Neuren (NEU) - ASX Announcement **18 February 2019**

NNZ-2591 demonstrates positive effects in Phelan-McDermid syndrome pre-clinical model

Melbourne, Australia, 18 February 2019: Neuren Pharmaceuticals (ASX: NEU) today announced that its drug candidate NNZ-2591 has demonstrated positive effects in a pre-clinical model of Phelan-McDermid syndrome (PMS). PMS is a rare 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 currently no treatment specifically for PMS. Neuren anticipates that PMS meets the criteria for Orphan Drug designation.

NNZ-2591 was tested in the *SHANK3* knockout mouse model by GeN.DDi Limited, an international contract research organization that provides CNS drug development and validation services for the pharmaceutical industry. As well as causing PMS, disruption of the *SHANK3* gene is thought to be associated with a large number of cases of autism spectrum disorder.

The study 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, the abnormal length of dendrite spines between brain cells, the excess activated ERK protein (pERK) and the depressed level of IGF-1 in the knockout mice were all normalised after treatment with NNZ-2591.

Neuren is investigating the effects of NNZ-2591 in models of other neurodevelopmental disorders including autism. In parallel with completing studies in these models, Neuren is proceeding as planned with the standard characterisation and non-clinical safety studies that are required before filing an Investigational New Drug application (IND) with the FDA and commencing clinical trials.

Neuren Executive Chairman Dr Richard Treagus commented: "These results are highly encouraging, both for the potential to address the unmet need in Phelan-McDermid syndrome and reinforcement of our view that NNZ-2591 could have broad utility in neurodevelopmental and autism spectrum disorders."

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.

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 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, 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.

Contact:

Dr Richard Treagus, Executive Chairman: rtreagus@neurenpharma.com; +61 417 520 509

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.