Neuren (NEU) – ASX Announcement **25 August 2025**

First site initiated for Neuren's Phelan-McDermid syndrome Phase 3 trial

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today announced initiation of the first investigational site in the United States for its Phase 3 clinical trial of NNZ-2591 in Phelan-McDermid syndrome (PMS), after receiving Institutional Review Board (IRB) approval. Other trial sites in the US are at various stages of the initiation process. This is the first ever Phase 3 trial in PMS, a serious neurodevelopmental disorder with no approved treatments.

The randomised, double-blind, placebo-controlled trial will assess treatment for 13 weeks in approximately 160 children aged 3-12 with PMS. All participants may be eligible to continue treatment with NNZ-2591 for 12 months in an open-label extension trial. The trial program is fully funded by Neuren's existing cash reserves. Neuren conducted an End of Phase 2 Type B meeting and a subsequent Type C meeting with the US Food and Drug Administration, at which alignment was reached on the design of the Phase 3 trial, including the primary efficacy endpoints.

About Phelan-McDermid syndrome

Phelan-McDermid syndrome (PMS) is 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 neurons in the brain. It is estimated that between 1 in 8,000 and 1 in 15,000 people have PMS. There are no medications, drugs, or therapies specifically for PMS, which has an overwhelming unmet medical need. PMS has severe quality of life impacts on those living with it, as well as on parents and siblings. The most common characteristics are moderate to severe developmental and intellectual impairment and developmental delay, delayed or absent speech, symptoms of autism, low muscle tone, motor delays, mild to severe epilepsy, behavioural problems and difficulties with socialization, activities of daily living and self-care. Further information about PMS is available at: www.pmsf.org and www.cureshank.org

About Neuren

Neuren is developing new drug therapies to treat multiple serious neurological disorders that emerge in early childhood and have no or limited approved treatment options. Recognising the urgent unmet need, programs have been granted "orphan drug" designation in the United States, which provides incentives to encourage the development of therapies for rare and serious diseases.

DAYBUE™ (trofinetide) is approved by the US Food and Drug Administration (FDA) and Health Canada for the treatment of Rett syndrome. Neuren has granted an exclusive worldwide licence to Acadia Pharmaceuticals Inc. for the development and commercialisation of trofinetide.

Neuren's second drug candidate, NNZ-2591, is in development for multiple neurodevelopmental disorders, with positive results achieved in Phase 2 clinical trials in Phelan-McDermid syndrome, Pitt Hopkins syndrome and Angelman syndrome.

Contact:
investorrelations@neurenpharma.com
Jon Pilcher, CEO: +61 438 422 271

ASX Listing Rules information
This announcement was authorized to be given to the ASX by the Board of Neuren Pharmaceuticals Limited, Suite 201, 697 Burke Road, Camberwell, VIC 3124

Forward-looking Statements
This 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.