Neuren (NEU) – ASX Announcement **14 April 2025**

Neuren confirms primary endpoints for Phase 3 trial of NNZ-2591 in PMS

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today announced that the primary endpoints for its planned single Phase 3 pivotal clinical trial of NNZ-2591 in Phelan-McDermid syndrome (PMS) have been confirmed at a productive Type C Meeting with the US Food and Drug Administration (FDA).

Neuren CEO Jon Pilcher commented: "We are very pleased with the outcome of another constructive discussion with the FDA and are now excited to be able to move forward as planned with the first ever Phase 3 trial in children with Phelan-McDermid syndrome."

The co-primary endpoints in the double-blind placebo-controlled study of treatment for 13 weeks will be the change from baseline in the Receptive Communication sub-domain of the Vineland Adaptive Behavior Scales, Third Edition (VABS-3 Receptive-Raw Score) and the overall score in the Phelan-McDermid Syndrome Assessment of Change (PMSA-C, previously referred to as CGI-I in Neuren's Phase 2 trial). Both measures were robustly positive with clinically meaningful improvement in Neuren's Phase 2 open-label clinical trial. 16 out of 18 children showed improvement measured by the VABS-3 Receptive-Raw Score, with mean improvement of 7.5 from a mean baseline of 29.0 (Wilcoxon signed rank test $p=0.0001$) and 16 out of 18 children showed improvement from baseline measured by the PMSA-C with a mean score of 2.4 (Wilcoxon signed rank test $p<0.0001$).

The endpoints pair the caregiver's assessment of change in one important symptom area with the clinician's assessment of change across multiple aspects of PMS. Communication is one of the most impactful health concerns in PMS reported by caregivers. Receptive communication, as measured by VABS-3 Receptive-Raw Score, is the ability to receive and understand non-verbal and verbal interactions which is a foundational skill for the development of learning, social interaction, and speech.

Alignment with FDA was previously reached on the other key features of the Phase 3 program at an End of Phase 2 Meeting. Neuren remains on-track to commence the Phase 3 trial mid-year 2025, subject to FDA review of the final version of the trial protocol. Further Information about the trial will be provided in due course. Neuren's financial strength means that no additional funding is required to execute the program.

About VABS-3 and PMSA-C

The Vineland Adaptive Behavior Scales, Third Edition (VABS-3) is an individually-administered measure of adaptive behavior – the things that people do to function in everyday life. It is widely used to assess individuals with intellectual, developmental, and other disabilities. Administered through a structured interview with the caregiver, the measure has five domains including Communication, which comprises three sub-domains: Receptive, Expressive and Written. The Receptive Communication sub-domain comprises 39 items which are rated 0, 1 or 2 with a higher score indicating higher functioning.

The Phelan-McDermid Syndrome Assessment of Change (PMSA-C) is a clinician-rated measure designed to assess the change in core symptoms associated with PMS. The PMSA-C is based on a PMS-anchored Clinical Global Impression Scale of Improvement (Guy, 1976; Berry-Kravis et al. 2022). The PMSA-C

captures the clinician's impression of the participant's change in symptom presentation compared with the baseline visit considering seven domains: Receptive Communication, Expressive Communication, Gross Motor Function, Fine Motor Function, Social Interaction, Attention/Awareness and Self-care. A change score of 3 and below represents improvement, with a lower score indicating greater improvement.

About Phelan-McDermid syndrome (PMS)

Phelan-McDermid syndrome 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 nerve cells 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, all programs have been granted "orphan drug" designation in the United States. Orphan drug designation provides incentives to encourage 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.