Neuren (NEU) – ASX Announcement **12 July 2022**

Neuren commences Phase 2 trial of NNZ-2591 in Angelman syndrome

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today announced that its Phase 2 clinical trial of NNZ-2591 in Angelman syndrome (AS) is open for enrolment. The first subjects are expected to enter the trial imminently at the Centre for Clinical Trials in Rare Neurodevelopmental Disorders at Children's Health Queensland Hospital.

The trial is being conducted at three hospitals in Brisbane, Melbourne and Sydney under an Investigational New Drug application (IND) with US Food and Drug Administration. Top-line results are anticipated for H1 2023.

Neuren CEO Jon Pilcher commented: "We are excited to commence this trial in Australia to assess the potential for NNZ-2591 to make a difference in Angelman syndrome, a seriously debilitating condition with no approved medicines. In the *ube3a* knockout mouse model of Angelman, treatment with NNZ-2591 normalized all the deficits, so we are now eager to observe the effects of treatment in children."

The open label Phase 2 trial (NCT05011851) will enrol a single group of up to 20 children aged 3 to 17 years with AS to examine safety, tolerability, pharmacokinetics and efficacy over 13 weeks of treatment with NNZ-2591. All subjects will receive NNZ-2591 as an oral liquid dose twice daily, with titration up to the target mg/kg dose during the first 6 weeks of treatment, subject to safety and tolerability. The treatment period is preceded by 4 weeks of observation to thoroughly examine the baseline characteristics prior to treatment, against which safety and efficacy will be assessed for each child. A follow-up assessment will be made 2 weeks after end of treatment.

The primary outcome measures are safety and tolerability, including the incidence, severity and frequency of adverse events, as well as measures of standard pharmacokinetic parameters. Secondary outcome measures include a range of exploratory efficacy measures completed by clinicians and caregivers.

The overall aim of the Phase 2 trial is to generate information to inform the design of a subsequent registration trial. In parallel with the Phase 2 trial, Neuren is also executing the foundational work to prepare for Phase 3 development across multiple indications.

There are currently no approved medicines for AS, which is characterized by severe developmental delay and learning disabilities that become noticeable by the age of 6 – 12 months. Children and adults with AS typically have balance issues, motor impairment and can

have debilitating seizures. Some individuals never walk, most do not speak and disruptive sleep also can be a serious challenge. Individuals have a normal life expectancy, but they require continuous care and are unable to live independently. AS is caused by a loss of function of the *UBE3A* gene on chromosome 15, with incidence estimated at between 1 in 12,000 and 1 in 24,000 people.

About Neuren

Neuren is developing two new drug therapies to treat multiple serious neurological disorders that emerge in early childhood, none of which have any approved medicines.

The lead compound, trofinetide, achieved positive results in a Phase 3 clinical trial for Rett syndrome and has also completed a Phase 2 clinical trial in Fragile X syndrome. Both programs have Fast Track designation from the US Food and Drug Administration (FDA). Neuren has granted an exclusive licence to Acadia Pharmaceuticals Inc. for the development and commercialisation of trofinetide in North America, while retaining all rights outside North America.

Neuren is initiating Phase 2 trials of its second drug candidate, NNZ-2591, for each of Phelan-McDermid syndrome, Angelman syndrome, Pitt Hopkins syndrome and Prader-Willi syndrome.

Recognising the urgent unmet need, all six 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.

Contact:

Jon Pilcher, CEO: jpilcher@neurenpharma.com; +61 438 422 271

ASX Listing Rules information

This announcement was authorized to be given to the ASX by the board of directors 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.