Neuren (NEU) – ASX Announcement **1 June 2021**

Positive FDA meetings enable Neuren to proceed with INDs for three Phase 2 trials

Highlights:

- **Clear and constructive guidance received from pre-IND meetings with the FDA Office of Neuroscience for Phase 2 clinical trials of NNZ-2591 in Phelan-McDermid, Angelman and Pitt Hopkins syndromes**
- **Positive outcome is an important milestone that enables Neuren to proceed with IND applications for FDA clearance to start the trials**
- **Subject to IND clearance, trials to commence as planned in H2 2021, aiming for top-line results in H2 2022**
    - **Angelman syndrome trial will be conducted in Australia**
    - **Phelan-McDermid and Pitt Hopkins syndrome trials will be conducted in the United States**
    - **Each trial will study treatment of pediatric patients for 13 weeks**
- **All three syndromes are serious neurological disorders that emerge in early childhood and have no approved medicines**

Melbourne, Australia: Neuren Pharmaceuticals Limited (ASX: NEU) has received clear and constructive guidance from the FDA Office of Neuroscience in pre-IND meetings for Phase 2 clinical trials of NNZ-2591 in Phelan-McDermid, Angelman and Pitt Hopkins syndromes. All three syndromes are serious neurological disorders that emerge in early childhood and have no approved medicines.

The FDA guidance is an important milestone that enables Neuren to proceed with preparing Investigational New Drug (IND) applications for clearance to start the trials. Subject to that clearance, the trials will commence as planned in H2 2021. Neuren aims to obtain top-line results from the trials in H2 2022.

Neuren CEO Jon Pilcher commented: "Our positive dialogue with FDA was very helpful and with only minor modifications confirmed our plans for three disorders that have such urgent unmet need. NNZ-2591 has ideal attributes – a unique mechanism of action, consistent and compelling results in the model of each disorder, a clearly identified optimum dose and

proprietary manufacturing with high purity and yield. The final piece of the jigsaw is to demonstrate its impact in patients, so we are eager to expedite that data from these three Phase 2 trials."

The Angelman syndrome trial will be conducted in Australia, while the Phelan-McDermid and Pitt Hopkins syndrome trials will be conducted in the United States. Each trial will test treatment of between 10 and 20 pediatric patients for 13 weeks.

The primary objective will be to confirm safety and tolerability of dosing for 13 weeks in these pediatric patients. The secondary objective will be to assess efficacy by observing the extent of change in each patient from a well characterised baseline, using a range of efficacy measures. The overall aim is to generate the information that will enable the next stage to be the design of adequately powered pivotal registration trials with the optimum primary efficacy endpoints.

About the three disorders

Each syndrome is a highly debilitating neurodevelopmental disorder with no approved medicines. Symptoms emerge in early childhood and persist into adulthood, requiring lifelong care from clinicians and caregivers.

Phelan-McDermid syndrome is caused by a deletion or other change in the 22q13 region of chromosome 22, which includes the *SHANK3* gene. The most common characteristics 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.

Angelman syndrome is caused by a deletion or mutation in the *UBE3A* gene on chromosome 15. Characteristics are delayed development, intellectual disability, anxiety and hyperactivity, severe speech impairment, problems with movement and balance, seizures and sleep disorders.

Pitt Hopkins syndrome is caused by the loss of one copy or a mutation of the *TCF4* gene on chromosome 18. Characteristics 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 and distinctive facial features.

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 drug compound, trofinetide, is currently in a Phase 3 clinical trial for Rett syndrome with top-line results expected in Q4 2021 and has completed a Phase 2 clinical trial in Fragile X syndrome. Both programs have been granted Fast Track designation by 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 plans to initiate Phase 2 trials of its second drug candidate, NNZ-2591, for each of Phelan-McDermid syndrome, Angelman syndrome and Pitt Hopkins syndrome in H2 2021. Neuren is also preparing for a Phase 2 trial in Prader-Willi syndrome.

Because of the urgent unmet need, five programs have been granted "orphan drug" designation in both the United States and the European Union, a designation that provides incentives to encourage therapies for rare and serious diseases.

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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.

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