Neuren (NEU) – ASX Announcement **27 March 2025**

Neuren initiates development of NNZ-2591 to treat HIE in newborns

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) announced the initiation of development of NNZ-2591 to treat hypoxic-ischemic encephalopathy (HIE). HIE is a devastating type of brain injury caused when a baby's brain does not receive enough oxygen or blood flow before or shortly after birth. About two to three in every 1,000 births in high income countries and 10-30 per 1,000 births in low- and middle-income countries will be affected by HIE, which means that many thousands of babies and children experience HIE every year. It is one of the leading causes of neonatal death and neurodevelopmental disability worldwide.

HIE can lead to a range of symptoms in surviving children, including developmental delays, cognitive impairment, cerebral palsy, and seizures. Some children develop serious long-term complications that can affect them well into adulthood. Currently, the only approved treatment for HIE is temporary hypothermia (cooling the head or whole body to lower the baby's metabolic rate and give the brain some time to recover from the hypoxic event). Hypothermia provides a modest decrease in mortality and severe neurodevelopmental disability, however even with hypothermia, 40-45% of children who survive HIE have significant neurodevelopmental impairment at 2 years of age.

Based on its therapeutic properties and compelling data from preclinical models, Neuren believes that NNZ-2591 can potentially provide a highly differentiated form of treatment continuing beyond acute treatment in the neonatal intensive care unit to target both the acute effects and chronic impairments resulting from HIE.

Neuren anticipates that NNZ-2591 in HIE will qualify for Orphan Drug and Rare Pediatric disease designations from the US Food and Drug Administration (FDA). Leveraging the platform of clinical, non-clinical and manufacturing data that Neuren has built for NNZ-2591, a pre-IND meeting with the FDA is targeted in Q4 2025 before initiating a clinical trial in HIE patients.

Neuren Chief Science Officer Larry Glass commented: "We are very excited to announce HIE as a new indication for NNZ-2591. Neuren has a long heritage in brain injury, dating back to our inception at the University of Auckland and scientists at the University also played a major role in the development of hypothermia as the current standard of care for HIE. Neuren is now targeting a potential new paradigm in treatment to improve long-term outcomes for children and their families."

Brian Kalish MD, a neonatologist and neuroscientist in the Division of Newborn Medicine at Boston Children's Hospital and Harvard University and member of the Hope for HIE Scientific Advisory Board commented: "I am genuinely excited about Neuren's development program for NNZ-2591 in HIE. There is a tremendous need for therapeutics to address both acute and chronic consequences. NNZ-2591 has demonstrated an ability to target early effects of brain injury as well as longer term effects on brain development and neuroplasticity. Its role in restoring IGF-1 levels in the brain, which are significantly impacted by HIE, is very promising. I'm looking forward to working with Neuren to make this program successful."

Conflict of Interest Disclosure Statement: Dr. Brian Kalish is a member of Neuren Pharmaceuticals' scientific advisory board.

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.

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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.