Neuren (NEU) – ASX Announcement **27 November 2026**

Neuren updates on Pitt Hopkins syndrome Phase 3 development program

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today provided an update following its recent face-to-face Type B End of Phase 2 meeting with the US Food and Drug Administration (FDA) discussing a Phase 3 study to demonstrate efficacy and safety of NNZ-2591 in patients with Pitt Hopkins syndrome to potentially support a marketing application.

At the meeting Neuren proposed two options for a controlled study, designed to accommodate the rarity and specific characteristics of Pitt Hopkins syndrome after extensive consultation with, and support from, the Pitt Hopkins Research Foundation and expert advisors. In the official meeting minutes now received the FDA has reiterated that a double-blind, randomized, placebo-controlled study with an observer-reported functional primary endpoint, such as the Vineland-3, along with Neuren's Pitt Hopkins syndrome-specific CGI-I as a coprimary endpoint or key secondary endpoint is likely to provide the most interpretable data to support a future marketing application. Neuren had communicated that the sample size required for this design and primary endpoint is not executable in this population.

The recently launched FDA initiative of "A New Framework for Rare Disease Review" is highly relevant to Pitt Hopkins syndrome. Neuren is participating in the initiative process, having presented at the public meeting on 29 October 2026 and now completing a formal written submission due in December 2026. Neuren will assess the impact of the initiative and continue to work with the FDA to advance the program.

Neuren CEO Jon Pilcher commented: "The Neuren team is determined to find a solution to move forward with an executable study for the Pitt Hopkins community and we are encouraged that the FDA's Rare Disease Framework Initiative appears designed for programs with these characteristics. The urgent unmet need and the severe impact faced by the Pitt Hopkins syndrome community were well highlighted at the Externally-Led Patient-Focused Drug Development Meeting hosted on 13 November 2026 by the Pitt Hopkins Research Foundation and attended by FDA representatives. While we continue working towards commencing a Pitt Hopkins syndrome study, successful completion of the ongoing Phase 3 study in Phelan-McDermid syndrome remains Neuren's most important value-creating milestone. Enrolment is progressing well and we look forward to providing guidance in the New Year on the expected timing of top-line results."

The FDA whitepaper for the "A New Framework for Rare Disease Review" initiative can be viewed via the following link:

https://www.fda.gov/media/195694/download?attachment

The following two extracts from the whitepaper highlight the relevance of the initiative to the Pitt Hopkins program.

"THE SCIENTIFIC AND OPERATIONAL CHALLENGES OF RARE DISEASE DRUG DEVELOPMENT: Developing therapies for rare diseases presents challenges that are qualitatively different from those in common disease drug development. Patient populations are small, sometimes numbering in the

hundreds globally, and are often geographically dispersed, making clinical trial enrollment difficult and slow. Natural history data, which forms the evidentiary foundation for trial design and endpoint selection in common disease drug development, is frequently sparse or nonexistent for rare diseases. Biomarkers that could serve as surrogate endpoints may be non-validated or entirely absent. Disease heterogeneity — genetic, phenotypic, or both — can make it difficult to define a homogeneous study population or to interpret results across subgroups.

These constraints have direct implications for trial design. The evidentiary tools that are routine in common disease drug development (e.g., placebo-controlled trials, primary endpoints with validated surrogate measures or meaningful clinical endpoints) may simply not be available. Rare diseases require a regulatory approach based on attainable evidence, product type, and the needs of the patient population. While this approach is certainly utilized at the FDA on many occasions, it is important that all review divisions use this approach as a matter of course and communicate it transparently with sponsors.

Rare diseases demand a regulatory framework that accounts for the nuances of each particular disease and product application, takes patients' needs into account, and makes the best use of both internal and external expertise in regulatory decision making."

"STATEMENT OF PURPOSE:
The FDA will build an improved framework for rare disease drug development and regulatory review where advice and decision-making are consistently tailored to what evidence is reasonably attainable given the nature of the disease, its onset and progression, target population, patient needs, and the characterizations of the product under investigation, and clearly communicated throughout the development and review process. The FDA intends to implement and communicate these improvements as appropriate, including potentially via changes to regulations, guidance documents, and internal processes and resources, which in turn will increase efficiency and enhance consistency and predictability."

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About Neuren

Neuren Pharmaceuticals is developing new drug therapies to treat multiple serious neurological disorders caused by genetic abnormalities or brain injury, that have no or limited approved treatment options. Neuren's therapies target the critical role of Insulin-like growth factor 1 (IGF-1) in the brain, using orally administered analogs of naturally occurring peptides.

DAYBUE® (trofinetide) oral solution and DAYBUE STIX (trofinetide) powder are approved for the treatment of Rett syndrome by the US Food and Drug Administration (FDA). The oral solution is also approved by the European Medicines Agency, Health Canada and the Ministry of Health in Israel. Neuren has granted an exclusive worldwide license to Acadia Pharmaceuticals Inc. for the development and commercialisation of trofinetide.

Neuren's investigative drug candidate, NNZ-2591 (ercanetide), is in clinical development as an oral solution treatment for multiple neurodevelopmental disorders, including Phelan-McDermid syndrome, Pitt Hopkins syndrome and Angelman syndrome. Each of these programs has been granted "orphan drug" designation in the United States and the European Union as well as Fast Track and Rare Pediatric Disease designations from the FDA. NNZ-2591 has also been granted orphan drug designation for the treatment of hypoxic ischemic encephalopathy (HIE), a serious condition caused by brain injury before or shortly after birth.

Currently, Neuren is conducting a Phase 3, randomized, double-blind, placebo-controlled clinical trial ("Koala") evaluating the safety and efficacy of NNZ-2591 in children aged 3 to 12 years with Phelan-McDermid syndrome and a 52-week open-label extension study.

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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 1.01, 117 Camberwell Road, Hawthorn East, VIC 3123

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.