Neuren (NEU) – ASX announcement **25 August 2021**

H1 2021 Interim Report

Neuren on track for Phase 3 trial results in Q4 and three Phase 2 trials in H2

Highlights:

- **LAVENDER Phase 3 trial of trofinetide in Rett syndrome enrolment completed and on track for top-line results in Q4 2021**
- **Potential for Neuren to receive revenue over 2022 and 2023 for Rett syndrome in the US alone of A$111 million plus royalties on net sales**
- **$18.2 million cash at 30 June 2021:**
  - **US partner Acadia is fully funding the trofinetide Phase 3 program**
  - **Neuren is funded to achieve Phase 2 data in 2022 for NNZ-2591 in three indications**
- **Clear and constructive guidance received from pre-IND meetings with the FDA for Phase 2 clinical trials of NNZ-2591 in Phelan-McDermid, Angelman and Pitt Hopkins syndromes**
- **Phase 2 trials are all on track to commence in H2 2021, with top-line results in H2 2022**
- **Currently targeted markets for NNZ-2591, for which Neuren retains global rights, are estimated to be more than five times the Rett syndrome market**
- **Published analyst risk-adjusted valuations of Neuren pre-Phase 3 results are A$368 million to A$450 million - versus Neuren's current market capitalisation of A$250 million**

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today filed its Interim Report for H1 2021.

Neuren CEO Jon Pilcher commented: "Neuren has remained firmly on track to achieve before the end of 2021 the transforming milestones of commencing three Phase 2 trials of NNZ-2591 in Phelan-McDermid, Angelman and Pitt Hopkins syndromes, followed by the top-line results of the Rett syndrome pivotal Phase 3 trial. We are highly motivated to make a difference to the families impacted by these debilitating conditions, which will enable us to realise the near-term revenue opportunity in Rett syndrome and the large potential upside in value from global rights to NNZ-2591 in multiple indications."

Rett syndrome Phase 3 trial

Neuren's US partner for trofinetide, Acadia Pharmaceuticals (Nasdaq: ACAD), successfully completed enrolment in the LAVENDER Phase 3 trial of trofinetide in Rett syndrome, remaining on track for top-line results in Q4 2021. LAVENDER is a randomised, double-blind, placebo-controlled Phase 3 trial testing treatment of approximately 180 patients for 12 weeks with trofinetide or placebo.

Rett syndrome is a debilitating neurodevelopmental disorder estimated to affect between 1 in 10,000 and 1 in 15,000 females worldwide. A range of severe impairments emerge in infancy, affecting nearly every aspect of the child's life: their ability to speak, walk, eat, and even breathe. There are currently no medicines approved for Rett syndrome. The trofinetide program has Fast Track, Orphan Drug and Rare Pediatric Disease designations from the US Food and Drug Administration (FDA).

The development and commercialisation of trofinetide in North America is fully funded by Acadia and Neuren is eligible to receive potential milestone payments of up to US$455 million, plus tiered escalating double-digit percentage royalties on net sales of trofinetide in North America, plus one third of the market value of a Rare Pediatric Disease Priority Review Voucher if awarded by the FDA upon approval of a New Drug Application for trofinetide. In addition, Neuren has free and full access to all data for use in countries outside North America. Positive results from the Phase 3 trial should enable Neuren to commercialise trofinetide in Europe and Asia, as well as enabling a New Drug Application in the US.

Phase 2 trials in Phelan-McDermid, Angelman and Pitt Hopkins syndromes

Neuren conducted three pre-IND meetings with the FDA Office of Neuroscience to discuss the proposed Phase 2 clinical trials for NNZ-2591 in patients with each of Phelan-McDermid syndrome, Angelman syndrome and Pitt Hopkins syndrome. The clear and constructive guidance from the FDA enabled 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. In parallel with the IND applications, across all three disorders Neuren is completing the preparations for the trials with the patient communities, the clinical trial sites and CROs. Neuren aims to obtain top-line results from the trials in H2 2022.

The number of potential patients across the disorders currently targeted by NNZ-2591 is estimated to be more than five times the number of potential patients with Rett syndrome. Neuren retains full global rights to NNZ-2591.

Financials

Cash reserves at 30 June 2021 were $18.2 million, funding Neuren through to achieving Phase 2 data for NNZ-2591 in three indications while Acadia fully funds the trofinetide Phase 3 program.

The net loss after income tax for the half-year ended 30 June 2021 was $8.0 million, compared with $4.8 million for the half-year ended 30 June 2020, mainly due to an increase of $2.3 million in research and development costs. This expenditure related to the NNZ-2591 Phase 1 and Phase 2 clinical trials, manufacture of the drug for clinical trials and non-clinical studies. Net cash used in operating activities was $6.1 million (half-year to 30 June 2020: $5.1 million). The increase of $1.0 million was mainly in payments to other suppliers, due to the higher research and development expenditure.

If the results of the Rett syndrome Phase 3 trial are positive, a New Drug Application is approved by the FDA and trofinetide is launched in the US, Neuren would earn revenue over 2022 and 2023 for Rett syndrome in the US alone of A$111 million plus double-digit percentage royalties on net sales. This assumes a USD/AUD exchange rate of 0.75 and that Neuren receives US$33 million as its share of the market value of a Rare Pediatric Disease Priority Review Voucher awarded on approval of a New Drug Application. There is no cost associated with this revenue.

The currently published analysts' risk-adjusted discounted cash flow valuations of Neuren before the Phase 3 results range from A$368 million to A$450 million. Neuren's current market capitalisation of approximately A$250 million is between 56% and 68% of those valuations.

2021 milestones progress to date

- ✓ EU Orphan designations for Phelan-McDermid, Angelman, and Pitt Hopkins
- ✓ Successful Phase 1 trial results for NNZ-2591
- ✓ Prader-Willi syndrome added to NNZ-2591 pipeline
- ✓ Complete drug substance manufacturing for NNZ-2591 Phase 2
- ✓ Pre-IND meetings with FDA to agree NNZ-2591 Phase 2 plans
- ✓ Acadia completes enrolment in trofinetide Rett syndrome Phase 3
- **Submit NNZ-2591 INDs to FDA**
- **Commence NNZ-2591 Phase 2 trials**
- **Orphan designation for NNZ-2591 in Prader-Willi syndrome**
- **Trofinetide Rett syndrome Phase 3 top-line results**

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, 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 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 preparing 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 planning 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 development of therapies for rare and serious diseases.

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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.