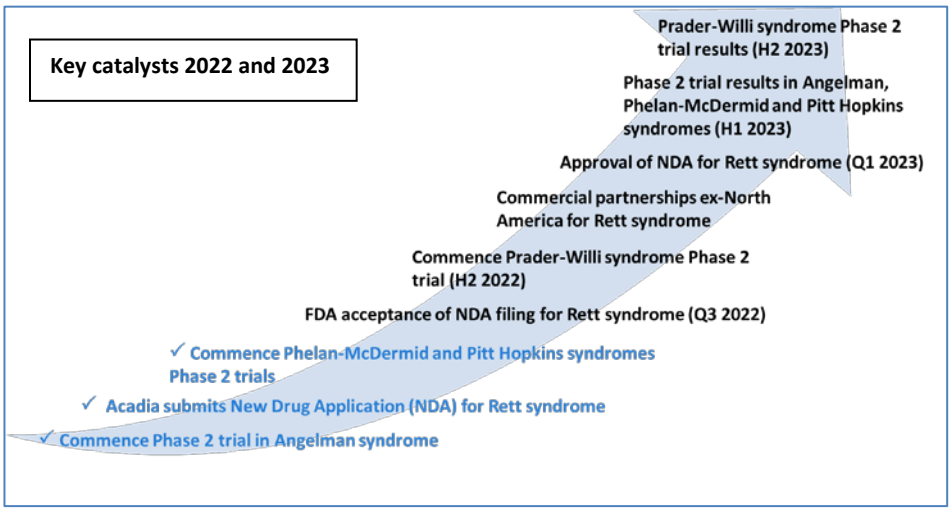
Neuren (NEU) - ASX Announcement **24 August 2022**

H1 2022 Interim Financial Report

Highlights:

- **Acadia submitted a New Drug Application (NDA) to the US Food and Drug Administration (FDA) for trofinetide for the treatment of Rett syndrome in adults and pediatric patients two years of age and older**
- **Subject to approval of the NDA, Neuren expects to receive revenue over 2022 and 2023 for Rett syndrome in the US alone of A$118 million plus double-digit percentage royalties on net sales**
- **Discussions continuing with potential partners for trofinetide ex-North America**
- **Three Investigational New Drug (IND) applications approved by FDA for NNZ-2591**
- **Phase 2 clinical trials commenced for NNZ-2591 in Angelman syndrome, Phelan-McDermid syndrome and Pitt Hopkins syndrome**
- **$31.1 million cash at 30 June 2022 – well funded to execute NNZ-2591 Phase 2 trials and foundational work for Phase 3 across all indications, notwithstanding the anticipated material cash flows from trofinetide**

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today filed its Interim Financial Report for H1 2022. Neuren CEO Jon Pilcher commented: "In 2022 so far we have remained on track along the series of catalysts in 2022 and 2023 that have the potential to transform the underlying value of Neuren's business."



Commentary on events since 1 January 2022 and outlook

Trofinetide for Rett syndrome

In July 2022, Neuren's US partner Acadia Pharmaceuticals (Nasdaq: ACAD) submitted a New Drug Application (NDA) to the US Food and Drug Administration (FDA) for trofinetide for the treatment of Rett syndrome in adults and pediatric patients two years of age and older.

The trofinetide program has Orphan Drug, Fast Track and Rare Pediatric Disease designations from the FDA. A NDA with Orphan Drug Designation is eligible for Priority Review in 6 months, compared with the standard review period of 10 months. The Review period commences when FDA formally accepts the NDA for review, which is due 60 days after its submission. Neuren therefore anticipates a decision on approval in March 2023, provided the NDA is accepted and receives Priority Review.

Acadia has exclusive rights to develop and commercialize trofinetide in North America. Under the terms of Neuren's agreement with Acadia, the development and commercialisation of trofinetide in North America is fully funded by Acadia and Neuren may receive potential milestone payments of up to US$455 million, plus 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 NDA for trofinetide.

If the NDA is approved by the FDA, Neuren expects to earn revenue over 2022 and 2023 for Rett syndrome in the US alone of A$118 million plus double-digit percentage royalties on net sales. The expected revenue in addition to the royalties comprises:

- A milestone payment in 2022 of US$10 million (A$14 million at assumed exchange rate of 0.70) following acceptance of the NDA for review by the FDA
- A milestone payment in 2023 of US$40 million (A$57 million), following the first commercial sale of trofinetide in the United States
- US$33 million (A$47 million) in 2023 as Neuren's one third share of the market value of a Priority Review Voucher, estimated as US$100 million.

Neuren's additional ongoing revenue from potential sales has two components:

- Double digit percentage royalties on net sales of trofinetide in all indications. The annual net sales are recorded in tiers and an escalating percentage is applied to each successive tier.
- Payments of up to US$350 million (approximately A$500 million) on achievement of a series of 4 thresholds of total annual net sales for all indications.

No royalties or similar costs are payable by Neuren to third parties, which means that Neuren's revenue from Acadia will flow through to pre-tax profit.

Neuren retains all rights to trofinetide for all countries outside North America and has a fully paid-up, irrevocable licence for use in those countries to all data generated by Acadia. Rett syndrome is a devastating condition with no approved therapies and there is urgent unmet need around the world for a treatment. Neuren has received strong interest for potential commercial partnerships and discussions are continuing.

NNZ-2591 for multiple neurodevelopmental disorders

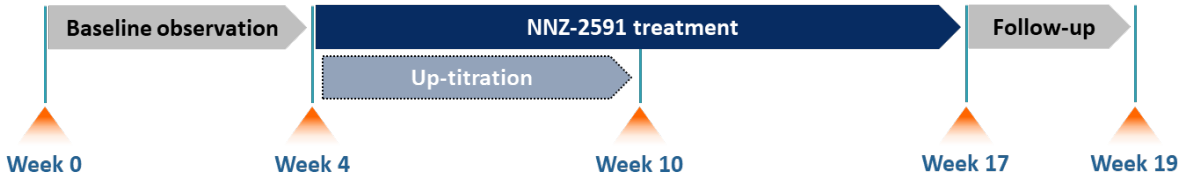
In July and August 2022, Neuren announced the commencement of its Phase 2 clinical trials of NNZ-2591 in each of Angelman syndrome (AS), Phelan-McDermid syndrome (PMS) and Pitt Hopkins syndrome (PTHS). The open label Phase 2 trials will each enrol a single group of up to 20 children to examine safety, 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.

Top-line results from all three trials are anticipated in H1 2023. Neuren is also planning a Phase 2 trial in a fourth disorder, Prader-Willi syndrome, with results targeted for H2 2023.

Neuren has Orphan Drug designation from the FDA for NNZ-2591 in all four syndromes, which are serious neurodevelopmental disorders with no approved medicines. The estimated number of potential patients being targeted across these four disorders is more than five times larger than Rett syndrome. Neuren retains all global rights to NNZ-2591.

The overall aim of these first trials in patients is to expedite the generation of data that will enable the subsequent trials to be designed as registration trials. Prioritising fast enrolment of subjects, the AS trial is being conducted in Australia, whilst the PMS and PTHS trials are being conducted in the US.

	PMS	PTHS	AS
Subjects	Up to 20, aged 3 to 12	Up to 20, aged 3 to 17	Up to 20, aged 3 to 17
Number of sites	4 (US)	5 (US)	3 (Australia)
www.clinicaltrials.gov	NCT05025241	NCT05025332	NCT05011851



In order to expedite the overall development plan, in parallel with conducting the Phase 2 trials Neuren is executing the additional development work required to be ready for Phase 3 development. This includes non-clinical toxicity studies to support longer clinical trials and commercial use of the product, as well as optimisation of the drug product and drug substance manufacturing arrangements.

Neuren is well funded from current cash reserves to execute the Phase 2 trials and Phase 3 preparation, notwithstanding the anticipated material cash flows from trofinetide.

Financials

The net loss after income tax for the half-year ended 30 June 2022 was $7.0 million, compared with $8.0 million for the half-year ended 30 June 2021. Research and development costs decreased by $2.4 million, with the higher expenditure in 2021 mainly due to the NNZ-2591 Phase 1 clinical trial and manufacture of the drug for clinical trials and non-clinical studies. This was partially offset by an increase in corporate and administrative costs of $0.8 million, due to appointment of new personnel and the timing of insurance premiums, and by an increase in share-based payments expense of $0.7 million following the issue of new share options in February 2022.

The net loss per share for the half-year to 30 June 2022 was $0.056 (half-year to 30 June 2021: $0.070) based on a weighted average number of shares outstanding of approximately 126 million (half-year to 30 June 2021: 114 million).

Cash reserves at 30 June 2022 were $31.1 million (31 December 2021: $36.8 million). Net cash used in operating activities was $5.8 million (half-year to 30 June 2021: $6.1 million).

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.