Neuren (NEU) - ASX Announcement **28 August 2019**

Neuren advances pipeline for multiple neurodevelopmental disorders

H1 2019 business and financial highlights:

- **Cash reserves $17.3 million at 30 June 2019 (31 December 2018: $23.6 million)**
- **Trofinetide - on track to commence US Phase 3 trial for Rett syndrome in Q4 2019:**
  - **"LAVENDER" study treats 180 females with trofinetide or placebo for 12 weeks to evaluate efficacy and safety, followed by "LILAC" study in which patients will be eligible to continue treatment with trofinetide for 40 weeks to evaluate longer-term safety**
  - **Timeline of commencing Phase 3 in H2 2019 and potential NDA in 2021 has remained unchanged since announcement of Neuren/ACADIA partnership**
  - **Positive Phase 2 study results for trofinetide in pediatric Rett syndrome published in *Neurology®*, the medical journal of the American Academy of Neurology**
- **NNZ-2591 - material progress made for 3 debilitating childhood conditions with no approved therapy:**
  - **Positive results in separate mouse models of Phelan-McDermid, Angelman and Pitt Hopkins syndromes**
  - **3 applications for Orphan Drug designation submitted to FDA**
  - **Required manufacturing development and non-clinical studies progressing in preparation for clinical trials in 2020**
- **Torreya process for evaluation of potential partnerships and corporate transactions presently underway.**

Melbourne, Australia, 28 August 2019: Neuren Pharmaceuticals (ASX: NEU) today reported its half-year financial results for 2019. Cash reserves at 30 June 2019 were $17.3 million, compared with $23.6 million at 31 December 2018. During the 6 months to 30 June 2019, very significant progress was made in both the development of trofinetide for Rett syndrome and the development of NNZ-2591 for multiple neurodevelopmental disorders.

Trofinetide

In Rett syndrome, manufacturing of trofinetide has been a key element of the extensive preparation leading into the Phase 3 trial, implementing significant changes to the Phase 2 product supply arrangements and a substantial investment for manufacturing of both the drug substance and the finished drug product, packaging and distribution. Neuren's North American partner ACADIA remains on target to commence the Phase 3 trial in the 4th quarter of 2019, which means that the timeline ACADIA

published when the partnership was announced in August 2018 – commencing the trial in H2 2019 and subject to the results submitting a New Drug Application (NDA) in 2021 – has remained unchanged. Neuren has completed certain manufacturing activities and non-clinical studies, with ACADIA funding and executing the remaining development for trofinetide in North America.

There are two parts to ACADIA's Phase 3 program – treatment of approximately 180 females aged 5 to 20 with trofinetide or placebo for 12 weeks to evaluate efficacy and safety (the "LAVENDER" study), following which patients will be eligible to continue treatment with trofinetide for 40 weeks to provide longer-term safety data (the "LILAC" study). Neuren anticipates that patient enrolment will again benefit from strong support from the Rett community. In July 2019, ACADIA announced "LILAC-2" to follow LILAC, in which eligible patients who have completed LAVENDER and LILAC will be able to continue to receive trofinetide.

In March 2019 the results of Neuren's Phase 2 study of trofinetide in pediatric Rett syndrome were published in *Neurology®*, the highly regarded peer-reviewed medical journal of the American Academy of Neurology. The publication was also the basis for an editorial in the journal titled "Turning the tide on targeted treatments for neurodevelopmental disorders".

NNZ-2591

In February and May 2019, Neuren announced positive results for NNZ-2591 in separate mouse models of Phelan-McDermid syndrome, Angelman syndrome and Pitt Hopkins syndrome. These are three debilitating childhood neurodevelopmental disorders with no approved drug therapy. The cause of each disorder is a mutation or deletion in a different gene or chromosomal region, however they share an underlying impairment in the connections and signaling between brain cells. The aim of treatment with NNZ-2591 is to restore normal functional connectivity and signaling.

In July 2019, Neuren submitted applications for Orphan Drug designation to the US Food and Drug Administration (FDA) for each of Phelan-McDermid syndrome, Angelman syndrome and Pitt Hopkins syndrome. Orphan Drug designation is a special status that the FDA may grant to a drug to treat a rare disease or condition. Orphan Drug designation qualifies the sponsor of the drug for incentives including 7 years of marketing exclusivity, plus 6 additional months if approved for pediatric use, as well as waiver of the prescription drug user fee for a marketing application.

Neuren is currently undertaking the manufacturing development and non-clinical studies required before submitting an Investigational New Drug (IND) Application for NNZ-2591 in the United States, aiming to commence Phase 2 clinical trials in the second half of 2020 after completing a Phase 1 trial in Australia. The NNZ-2591 program is benefiting from the extensive experience gained by Neuren during the development of trofinetide for Rett syndrome and Fragile X syndrome.

Corporate review

In February 2019, the board appointed Torreya, a global investment bank specialising in life sciences, as Neuren's corporate advisor to evaluate all potential corporate transactions, for individual products,

defined territories, or Neuren's entire business. A formal process commenced in April and is presently underway, engaging with third parties in the US, Europe and Japan.

Financials summary:

	2019	2018
	$m	$m
Interest income and foreign exchange gain	0.3	0.3
Research & Development	(6.9)	(2.6)
Corporate & Administration	(1.0)	(1.3)
Loss in fair value of Lanstead settlements	(0.3)	(0.5)
Loss after tax	**(7.9)**	**(4.1)**
Cash flow from operations	(7.9)	(4.0)
Cash flow from financing	1.6	10.6
Cash at 31 December	**17.3**	**23.6**

The net loss after income tax for the six months ended 30 June 2019 was $7.9 million, compared with $4.1 million for the six months ended 30 June 2018. The increase of $3.8 million was due to an increase of $4.3 million in research and development costs, resulting from the completion of Neuren's manufacturing and non-clinical activities for the commencement of the Rett Syndrome Phase 3 trial, as well as expenditure to advance the manufacturing scale-up and non-clinical studies for NNZ-2591.

About Neuren

Neuren Pharmaceuticals Limited (Neuren) is a biopharmaceutical company developing new therapies for neurodevelopmental disorders with high unmet need, utilizing synthetic analogs of neurotrophic peptides that occur naturally in the brain. Neuren completed Phase 2 development of trofinetide for Rett syndrome and has completed a Phase 2 clinical trial in Fragile X syndrome. The programs in Rett syndrome and Fragile X syndrome have each received Fast Track designation by the US Food and Drug Administration and Orphan Drug designation in both the United States and the European Union. Neuren has granted an exclusive license to ACADIA Pharmaceuticals Inc. for the development and commercialization of trofinetide in North America, whilst retaining all rights outside North America. Neuren is advancing the development of its second drug candidate NNZ-2591 for Phelan-McDermid syndrome, Angelman syndrome and Pitt Hopkins syndrome.

Forward-looking Statements
This ASX-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.

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