Neuren (NEU) – ASX Announcement **23 December 2022**

Neuren submits IND and first patients complete Phase 2 trials

Highlights:

- **IND application for NNZ-2591 in Prader-Willi syndrome submitted to US FDA**
- **First subject in Angelman syndrome trial and first subject in Phelan-McDermid syndrome trial have completed 13 weeks treatment period, with good safety and tolerability profile:**
  - **Successful escalation up to the target dose in two stages following independent review of safety data**
  - **No serious adverse events and no dose modifications required**
  - **Most adverse events were mild and not considered related to study drug**
  - **No clinically relevant findings from safety lab tests, or cardiac tests**
- **Enrolment in the second age group approved in Phelan-McDermid trial following independent review of safety data in oldest age group**
- **Series of top-line results from trials anticipated from H2 2023, commencing with Phelan-McDermid**

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today announced the submission of an Investigational New Drug (IND) application for NNZ-2591 in Prader-Willi syndrome and provided an update on progress in its ongoing Phase 2 clinical trials for each of Phelan-McDermid, Angelman and Pitt Hopkins syndromes. Neuren's drug NNZ-2591 is being developed for these four serious neurological disorders that emerge in early childhood and for which there are no approved medicines.

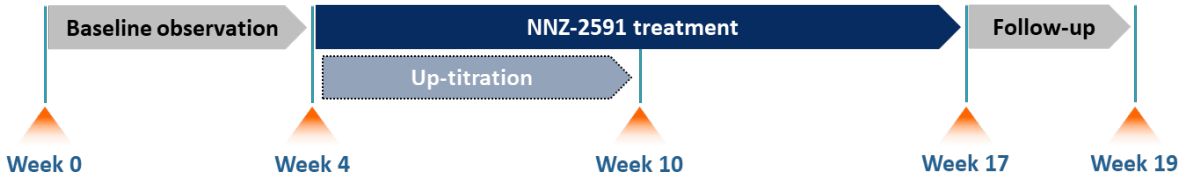
The new IND application was submitted to the US Food and Drug Administration (FDA) on 22 December for approval to proceed with a Phase 2 trial in Prader-Willi syndrome. Clinical trials are currently ongoing in each of the other three syndromes, which are the first trials of NNZ-2591 in children with each syndrome.

The open label Phase 2 trials are each enrolling up to 20 children to examine safety, tolerability, pharmacokinetics and efficacy over 13 weeks of treatment with NNZ-2591. All subjects receive NNZ-2591 as an oral liquid dose twice daily, with escalation in two stages up to the target dose during the first 6 weeks of treatment, subject to independent review of safety and tolerability data.

The trials are enrolling subjects in three age groups. Safety and tolerability data in the oldest age group must be independently reviewed before proceeding with dosing in the second age

group and then safety and tolerability data in the second age group must be independently reviewed before proceeding with dosing in the youngest age group.

The study begins with 4 weeks of observation to thoroughly examine baseline characteristics prior to treatment, against which safety and efficacy are assessed for each child. This is followed by the treatment period of 13 weeks. A follow-up assessment is made 2 weeks after the end of treatment.



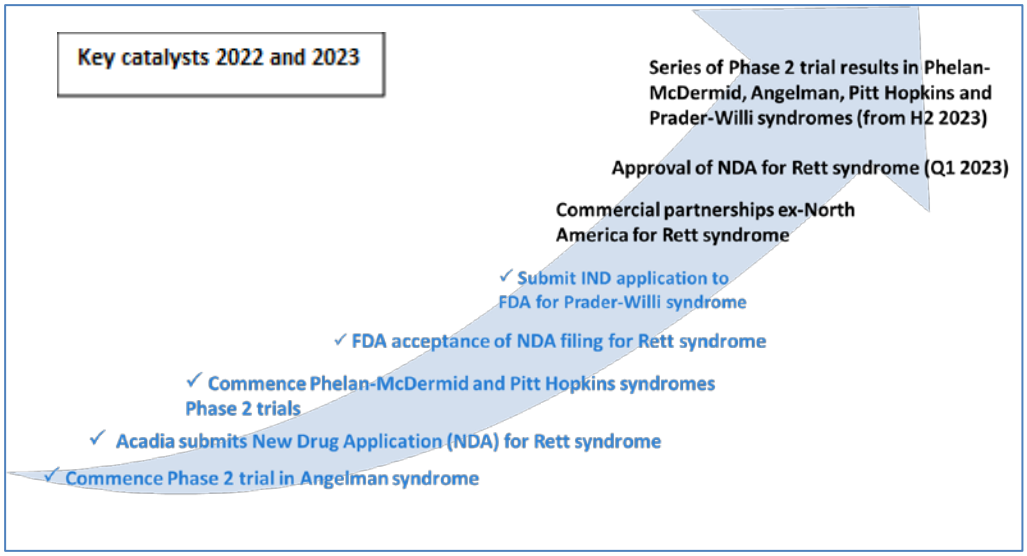
	Phelan-McDermid	Pitt Hopkins	Angelman
Subjects	Up to 20, aged 3 to 12	Up to 20, aged 3 to 17	Up to 20, aged 3 to 17
Number of sites	4 (US)	5 (US)	3 (Australia)
www.clinicaltrials.gov	NCT05025241	NCT05025332	NCT05011851

In the Phelan-McDermid syndrome trial and in the Angelman syndrome trial, the first subject in the oldest age group has now completed the treatment period of 13 weeks, with a good safety and tolerability profile. Each subject was successfully escalated up to the target dose following safety and tolerability reviews by an independent data and safety monitoring committee (DSMC). No serious adverse events were reported and no dose modifications were required. Most of the adverse events reported were mild and not considered to be related to study drug. There were no clinically relevant observations in safety laboratory measurements or cardiac tests.

In the Phelan-McDermid trial, enrolment in the second age group was approved following review by the DSMC of safety and tolerability data for subjects in the oldest age group.

The number of potential subjects identified for each trial exceeds the total requirement, however the restriction of enrolling subjects in three age groups sequentially commencing with the oldest is a constraint, delaying the start of the trial for younger subjects. Neuren is working closely with the patient communities and trial sites to accelerate enrolment after the holiday period in the first half of 2023 as younger age groups are activated.

The four trials will likely complete at different times, with a series of top-line results announcements now anticipated from H2 2023, commencing with Phelan-McDermid syndrome.



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.

A New Drug Application for the lead compound, trofinetide, to treat Rett syndrome is under Priority Review by the US Food and Drug Administration (FDA), with a PDUFA action date of 12 March 2023. 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 conducting 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.

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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.