Neuren (NEU) – ASX announcement **28 June 2023**

Neuren opens first site in US for Prader-Willi syndrome Phase 2 trial

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today announced that the first site in the United States for its Phase 2 clinical trial of NNZ-2591 in Prader-Willi syndrome is now open.

Neuren CEO Jon Pilcher commented "The Neuren team is very excited to be working with the community to complete this important first study of NNZ-2591 in young children with Prader-Willi syndrome. We are eager to assess the potential impact of NNZ-2591, having observed highly encouraging effects in the pre-clinical model."

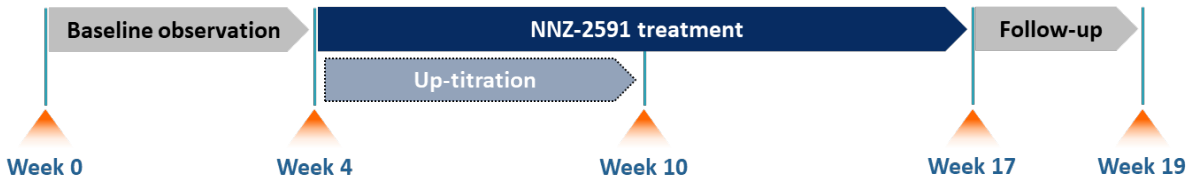
The overall aim of this first clinical trial in patients is to expedite the generation of data that will enable the subsequent trial to be designed as a registration trial. In parallel with conducting the Phase 2 trial, Neuren is executing the additional development work required to be ready for Phase 3 development.

Neuren is also conducting Phase 2 trials of NNZ-2591 in children with three other neurodevelopmental disorders – Phelan-McDermid, Pitt Hopkins and Angelman syndromes. All four programs have been granted Orphan Drug designation by the US Food and Drug Administration (FDA) and are being developed under Investigational New Drug (IND) applications. Each syndrome is a seriously debilitating disorder that emerges in early childhood and has no or limited approved treatment options.

About the Prader-Willi syndrome Phase 2 trial (NCT05879614)

The open label Phase 2 trial in up to 20 children aged 4 to 12 years at clinical sites in the United States is examining safety, tolerability, pharmacokinetics and efficacy over 13 weeks of treatment with NNZ-2591. The primary outcome measures are safety and tolerability, including the incidence, severity and frequency of adverse events, as well as measures of standard pharmacokinetic parameters. Secondary outcome measures include a range of efficacy measures, completed by clinicians and caregivers.

All subjects receive NNZ-2591 as an oral liquid dose twice daily, with two dose escalations up to the target dose during the first 6 weeks of treatment, subject to independent review of safety and tolerability data. The trial will enrol subjects in two age groups. Safety and tolerability data in the older age group must be independently reviewed before proceeding with dosing in the younger age group. The study begins with at least 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.



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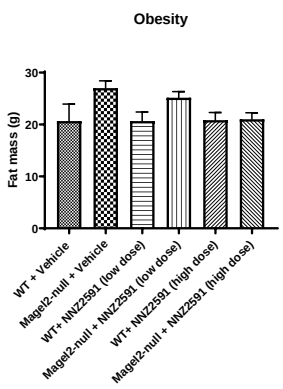
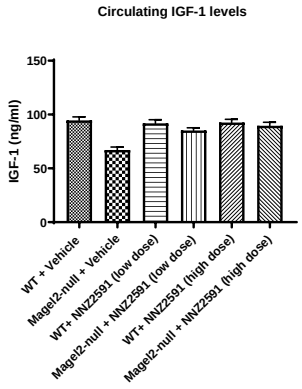
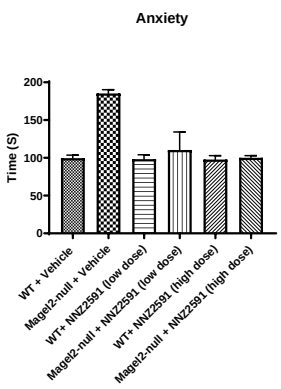
NNZ-2591 efficacy in mouse model of Prader-Willi syndrome

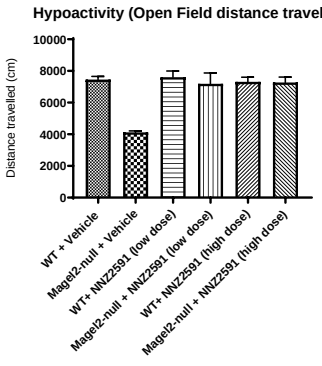
In the *Magel2*-null mouse model, which exhibits features of Prader-Willi syndrome in humans, wild type and *Magel2*-null mice were treated with placebo (vehicle) or NNZ-2591 for 6 weeks. Treatment with NNZ-2591 normalized fat mass, insulin levels, IGF-1 levels and all behavioural deficits in the *Magel2*-null mice and had no effect on the wild type mice:

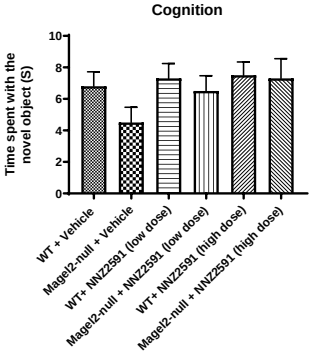


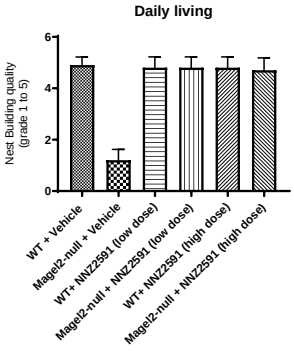


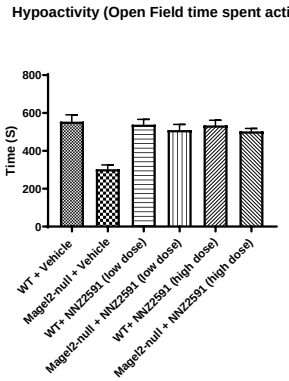


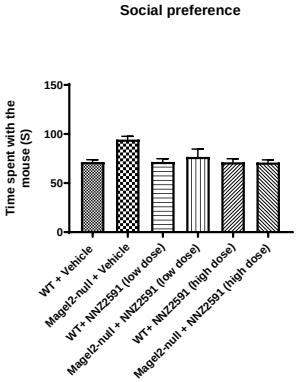
Insulin levels (pM)					
WT plus vehicle	*Magel2* -null plus vehicle	WT plus NNZ-2591 low dose	*Magel2* -null plus NNZ-2591 low dose	WT plus NNZ-2591 high dose	*Magel2* -null plus NNZ-2591 high dose
110	173	112	143	115	119

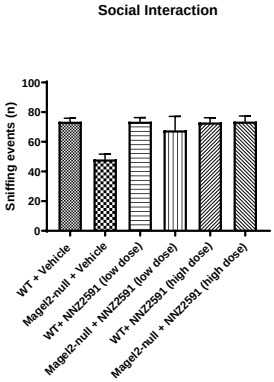












About Prader-Willi syndrome

Prader-Willi syndrome (PWS) is a highly debilitating neurodevelopmental disorder, caused by defects in the 15q11-q13 region of chromosome 15. The estimated incidence is 1 in 10,000 – 30,000 males and females across all races and ethnicities. PWS is associated with a constellation of symptoms that significantly negatively impact upon quality of life for affected individuals and their families.

Infants with PWS have very low muscle tone and suffer from feeding difficulties. An unregulated appetite and easy weight gain characterize the later stages of PWS, which can lead to morbid obesity. The range of other challenges for individuals with PWS can include intellectual and learning disabilities, growth hormone deficiency, sleep disturbances, speech difficulties, obsessive-compulsive symptoms, gastrointestinal complications, and difficulty controlling emotions.

Growth hormone deficiency is reported to occur in 40-100% of patients and dysregulation of the growth hormone-IGF-1 axis is considered to be universal, with sub-normal serum IGF-1 levels.

Further information about PWS is available at: www.pwsusa.org and www.fpwr.org

About Neuren

Neuren is developing new drug therapies to treat multiple serious neurological disorders that emerge in early childhood and have no or limited approved treatment options.

DAYBUE™ (trofinetide) is approved by the US Food and Drug Administration (FDA) for the treatment of Rett syndrome in adult and pediatric patients two years of age and older. 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 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.