

Neuren reports progress in its NNZ-2566 clinical trial programs

Highlights:

- **Phase 2 trial in Fragile X Syndrome has commenced in the US**
- **36 subjects enrolled in Phase 2 trial in Rett Syndrome and the planned higher dose group has commenced**
- **131 subjects recruited in Phase 2 trial in Traumatic Brain Injury (“Intrepid”)**
- **Preparations for Phase 2 trial in Concussion on track, with start scheduled for H1 2014**
- **New patent covering use of NNZ-2566 to treat cognitive and memory disorders issued in the US, with expiry in 2026**

Melbourne, Australia, 28 January 2014: Neuren Pharmaceuticals (ASX: NEU) today provided an update of progress in its Phase 2 trials of NNZ-2566 in four separate neurological disorders. All four conditions represent significant underserved markets, with no approved drug therapies currently available for patients.

Neuren Executive Chairman Richard Treagus commented “Neuren’s clinical trials are proceeding to plan and we remain on schedule and fully funded through to completion. We look forward to an exciting year as we begin reporting the first trial results and make ongoing progress towards realising the value of NNZ-2566 for patients and shareholders.”

Fragile X Syndrome

Neuren’s Phase 2 double-blind, placebo-controlled clinical trial of NNZ-2566 in Fragile X Syndrome has commenced, led by the Rush University Medical Center in Chicago. 60 male subjects are required to complete the trial, with subjects enrolling at 6 sites in the United States. Enrolment is expected to be completed by the end of 2014, with top-line results announced in the first half of 2015. The trial is designed to assess the safety, tolerability and efficacy of NNZ-2566 in treating symptoms of Fragile X Syndrome.

The US Food and Drug Administration (FDA) has granted orphan drug designation to NNZ-2566 for treatment of Fragile X 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 seven years of marketing exclusivity following approval as well as various development incentives including waiver of the prescription drug user fee for a marketing application. Neuren has also received Fast Track designation from the FDA, which is designed to expedite the development and review of important new medicines.

Rett Syndrome

Neuren initiated a Phase 2 double-blind, placebo-controlled clinical trial of NNZ-2566 in Rett Syndrome in April 2013. The trial is designed to assess the safety, tolerability and efficacy of NNZ-2566 in treating symptoms of Rett Syndrome. 48 female subjects are required to complete the trial and two dose-levels of NNZ-2566 are being tested. The first group of subjects has received the lower dose or placebo. The independent Data and Safety Monitoring Committee reviewed data from that group and gave approval for the trial to proceed to a second group of subjects who will receive the higher dose or placebo. The first subjects in the higher dose group have now commenced treatment. In total, 36 subjects have been enrolled in the trial and 22 patients have completed the entire trial. Enrolment is expected to be completed in the first half of 2014, with top-line results announced in the second half of 2014.

Neuren's Rett Syndrome program has received Fast Track designation from the FDA. Neuren also intends to seek orphan drug designation from the FDA after completing the current clinical trial.

Moderate to Severe Traumatic Brain Injury ("Intrepid")

131 subjects have now been enrolled in Neuren's Phase 2 clinical trial of the intravenous dosage form of NNZ-2566 in moderate to severe Traumatic Brain Injury (TBI). The INTREPID⁻²⁵⁶⁶ trial is being conducted as a collaboration between Neuren and the US Army, which is reimbursing the majority of direct costs associated with the trial through a grant. TBI is a leading cause of death and disability in both civilian and military populations. Neuren's TBI program has received Fast Track designation from the FDA.

The Intrepid trial aims to enrol 260 subjects. Two factors are expected to accelerate the rate of subject enrolment. Firstly, Neuren is currently in the process of increasing the number of US trauma centres participating in the trial and secondly two large clinical studies that were directly competing for subjects at some of the trial sites have recently completed enrolment. Intrepid enrolment is forecast to be completed by the end of 2014 with top-line results reported in the first half of 2015.

Concussion

Preparations are continuing for a Phase 2 clinical trial of the oral dosage form of NNZ-2566 in concussion (mild traumatic brain injury). In collaboration with the US Army, the trial will be conducted in 132 subjects at Womack Army Medical Centre, Fort Bragg, North Carolina. The trial protocol is under review and arrangements with clinical service providers are being finalised. The trial will commence in the first half of 2014, complete enrolment in the first half of 2015 and report results in the second half of 2015.

New US patent for NNZ-2566

Neuren has received notice from the US Patent and Trademark Office that a new patent for NNZ-2566 will issue on 28 January 2014. Patent number 8637567, which will expire in December 2026, claims a method for treating a cognitive disorder or a memory disorder with NNZ-2566.

NNZ-2566 is now covered by 8 issued US patents covering the composition, oral formulation and methods of use, with additional patent applications pending. One patent covering oral formulations of NNZ-2566 has also now been granted in Japan.

All patents are owned by Neuren and no royalties are payable to third parties. Expiry dates of the patents range between 2022 and 2028.

Summary of expected clinical trial timelines

Study	Complete enrolment	Top-line results
Rett Syndrome	H1 2014	H2 2014
Fragile X Syndrome	H2 2014	H1 2015
Intrepid	H2 2014	H1 2015
Concussion	H1 2015	H2 2015

About Rett Syndrome

Rett Syndrome is a post-natal neurological disorder that occurs almost exclusively in females following apparently normal development for the first six months of life. Typically, between 6 to 18 months of age, patients experience a period of rapid decline with loss of purposeful hand use and spoken communication. Many patients have recurrent seizures. They experience a variety of motor problems including increased muscle tone (spasticity) and abnormal movements. These individuals are never able to provide for their own needs. It is a rare disorder and is believed to be second only to Down Syndrome as a genetically-determined cause of chronic neurological problems in females that include severe communication, motor disabilities and epilepsy. Rett Syndrome is caused by mutations on the X chromosome on a gene called MECP2. There are more than 200 different mutations found on the MECP2 gene. Rett Syndrome strikes all racial and ethnic groups and occurs worldwide in approximately 1 in every 10,000 live female births.

About Fragile X Syndrome

Fragile X syndrome is the most common inherited cause of intellectual disability and the most common known cause of autism. It affects 1 out of 4000 males and 1 out of 6-8000 females. Fragile X Syndrome is due to a single gene defect on the X chromosome that impacts the FMRP protein, which is responsible for regulating the synapses of nerve cells. Clinically, Fragile X Syndrome is characterized by intellectual handicap, hyperactivity and attentional problems, autistic symptoms, anxiety, emotional lability and epilepsy. Generally, males are more severely affected than females. Currently, there are no medicines approved for the treatment of Fragile X Syndrome.

About NNZ-2566

NNZ-2566 is a synthetic analogue of a naturally occurring neurotrophic peptide derived from IGF-1, a growth factor produced by brain cells. In animal models, NNZ-2566 exhibits a wide range of important effects including inhibiting neuroinflammation, normalising the role of microglia and correcting deficits in synaptic function. In the Fragile X model, these actions resulted in statistically significant improvement in all core anatomic and behavioural features of the disorder that were assessed. NNZ-2566 is being developed both in intravenous and oral formulations for a range of acute and chronic conditions. The intravenous form of NNZ-2566 is presently in a Phase II clinical trial in patients with moderate to severe traumatic brain injury. The oral form of NNZ-2566 is in Phase II trials in Rett Syndrome and Fragile X Syndrome. All three programs have received Fast Track designation from the US FDA and the Fragile X Syndrome program has also received Orphan Drug designation. Neuren intends to implement a Phase II clinical trial with the oral form of NNZ-2566 in patients with concussion (mild traumatic brain injury).

About Neuren

Neuren Pharmaceuticals Limited (Neuren) is a publicly listed biopharmaceutical company focusing on the development of new therapies for brain injury, neurodevelopmental and neurodegenerative disorders. The novel drugs target chronic conditions such as Rett Syndrome and Fragile X Syndrome as well as acute neurological injuries. Neuren presently has a clinical stage molecule, NNZ-2566 in two Phase 2 clinical trials as well as NNZ-2591 in pre-clinical development.

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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