Neuren reports successful NNZ-2566 Phase 1b safety trial results

Key points

- **Neuren successfully completes all cohorts of the Phase 1b study for NNZ-2566 to enable mild-moderate and severe Traumatic Brain Injury (TBI) trials to proceed**
- **NNZ-2566 development on track for Phase 2 mild-moderate and severe TBI trials to be conducted under a US IND**
- **World-leading TBI research institutes identified to participate in the Phase 2 trials**

Wednesday, 7 November 2007: Neuren Pharmaceuticals Ltd (ASX: NEU) has successfully completed its final high dose Phase 1b safety and tolerability trial for its second lead candidate, NNZ-2566, which is being developed to treat traumatic brain injury (TBI).

The completion of the Phase 1b trial will now enable Neuren to proceed with two Phase 2 trials, one in severe TBI and one in mild-to-moderate TBI. The trials, due to start in mid 2008, are planned to be conducted in the United States and New Zealand in collaboration with the US Army.

The results from the Phase 1b study were referred to the independent Data Safety Monitoring Committee (DSMC) for review. The DSMC confirmed the safety profile of NNZ-2566 for the fourth and final cohort which involved the maximum dose of 20 mg/kg bolus followed by a 6mg/kg/hour infusion over 72 hours. This dose provides a significant safety margin over the doses planned for future trials and will enable Neuren to proceed into Phase 2.

Planning is now well under way for two 2008 Phase 2 trials in patients with TBI. The Phase 2 mild-moderate and severe TBI trials will be conducted under a US IND which will enable Neuren to obtain early regulatory input into the final outcome measures for its major efficacy trials and will pave the way for a fast-track approval status for the drug. It will also enable access to world-leading experts in TBI (civilian and military) and very high recruiting US sites, which will expedite the study timelines.

Dr Parmjot Bains, Chief Operating Officer of Neuren, stated: “The completion of our Phase 1b clinical trial is a significant milestone for the company and represents a major step toward the potential development of a viable treatment option for traumatic brain injury. Moving forward into Phase 2 trials under a US IND will greatly help to accelerate development on the path to possible drug approval.”

Five world-leading investigators and research sites in the US have been identified for the trials (University of Rochester, University of Miami, US Army Institute of Surgical

Research; Inova Fairfax Hospital, University of California at Los Angeles) and three sites in New Zealand (Department of Neurosurgery, Auckland Hospital; Department of Emergency Medicine, Middlemore Hospital; Van Der Veer Institute, Christchurch Hospital).

The Phase 1b trial involved 28 healthy volunteers in four groups who received one of four escalating doses of a bolus (a large single dose) plus infusion of NNZ-2566 at the Royal Melbourne Hospital in Melbourne, Australia. Five volunteers in each of the four cohort groups received either 20mg/kg bolus of NNZ-2566 followed by a 1mg/kg/hr infusion for 12 hours, 3mg/kg/hr infusion for 24 hours, 3mg/kg/hr infusion for 48 hours or a 6mg/kg/hr infusion for 72 hours respectively. The remaining two in each group received placebo.

Clinical Appendix

The following additional information is provided in accordance with the Code of Best Practice for ASX Reporting by Life Science Companies.

Trial Title: A Phase 1b, single ascending dose, safety and pharmacokinetic study of NNZ-2566 in healthy volunteers.

Objectives: The unblinded trial aims to establish the safety of NNZ-2566 in humans. Data will also be obtained to understand the distribution of NNZ-2566 in the body to allow for the establishment of safe dosing levels for future trials. Proposed future trials will aim to test both the efficacy and safety of NNZ-2566 in patients with mild-to-moderate and severe traumatic brain injury (TBI).

Investigators:
Clinical Investigator: Dr Peter Hodsman
Project Manager: Dr Kathleen Durbin, Neuren Pharmaceuticals

Primary Objective: To establish safety, tolerability and pharmacokinetic action of NNZ-2566 in humans.

Secondary Objective: To understand the distribution of NNZ-2566 in the body to allow for the establishment of safe dosing levels for future trials.

Method: Four cohorts, each comprising seven healthy male volunteers. Starting from a very low dose the health and safety of each volunteer will be thoroughly checked before further higher dose levels are administered to other volunteers.

- **Cohort 1:** Five volunteers receive 20 mg/kg of NNZ-2566, via 10-min infusion, followed by 1 mg/kg/hr of NNZ-2566 for 12 hours. The remaining two receive placebo.
- **Cohort 2:** Five volunteers receive 20 mg/kg, 10-min infusion, followed by 3 mg/kg/hr for 24 hours. The remaining two receive placebo.
- **Cohort 3**: Five volunteers receive 20 mg/kg of NNZ-2566, via 10-min infusion, followed by 3 mg/kg/hr of NNZ-2566 for 48 hours. The remaining two receive placebo.
- **Cohort 4**: Five volunteers receive 20 mg/kg of NNZ-2566, via 10-min infusion, followed by 6 mg/kg/hr of NNZ-2566 for 72 hours. The remaining two receive placebo.

Trial Endpoints: The results of Cohorts 1-4 were submitted to the DSMC for review of safety, tolerability and pharmacokinetic action of NNZ-2566. The DSMC reviewed the final cohort and were satisfied that there were no major concerns regarding the safety of NNZ-2566.

About NNZ-2566

NNZ-2566 is a novel molecule that has a profile suitable for both intravenous infusion and chronic oral delivery. It has been shown to be protective in numerous in vitro and in vivo models of brain injury, and is currently in development to treat traumatic brain injury. Since 2004, NNZ-2566 has been developed in collaboration with the US Army's Walter Reed Army Institute of Research under a Cooperative Research and Development Agreement which includes Clinical Protocol development and regulatory filings.

About Neuren Pharmaceuticals

Neuren Pharmaceuticals (ASX: NEU) is a biopharmaceutical company developing novel therapeutics in the fields of brain injury and diseases and metabolic disorders. The Neuren portfolio consists of eight product families, targeting markets with large unmet needs and limited competition. Neuren has four lead candidates, Glypromate®, Motiva™, NNZ-2566 and NNZ-2591 targeting a range of acute and chronic neurological conditions. Neuren has commercial and development partnerships, including with the US Army Walter Reed Army Institute of Research, Metabolic Pharmaceuticals, UCLA Medical Center and the National Trauma Research Institute in Melbourne.

For more information, please visit Neuren's website at www.neurenpharma.com

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