Neuren and US Army Continued Success in Traumatic Brain Injury program and now File Joint Patent

Key points:

- **US Army and Neuren make significant progress in joint Traumatic Brain Injury programme confirming NNZ-2566 as a "very promising candidate for brain trauma"**
- **In the latest experiment NNZ-2566 shows significant reductions in non-convulsive seizures following traumatic brain injury**
- **Non-convulsive seizures are a significant predictor of outcome in Traumatic Brain Injury, are easily and practically detected and provide an important additional clinical endpoint**
- **This new therapeutic target of non-convulsive seizures will be included in NNZ-2566 Traumatic Brain Injury Phase 2 trial. This will result in increased sensitivity, earlier detection of effects and lower cost of trials compared to traditional methods**
- **The US Army and Neuren have filed a joint patent for non-convulsive seizures and NNZ-2566**

Wednesday 26 April 2006: Neuren Pharmaceuticals (ASX: NEU) today announced that it has jointly filed a new patent with the US Army's Walter Reed Army Institute of Research (WRAIR) as a result of new experiments showing its compound, NNZ-2566, significantly reduces non-convulsive seizures following traumatic brain injury (TBI).

Non-convulsive seizures often occur soon after brain injury and are an important predictor of patient recovery. Non-convulsive seizures are significant both as readily detectable predictors of clinical outcome from TBI as well as being a target for therapeutic intervention.

Dr Frank Tortella, Chief of the Department of Applied Neurobiology at WRAIR and the Research Director for the Combat Casualty Care Research Program in Brain Trauma and Neuroprotection, said: "We are very encouraged by the results with Neuren's drug. NNZ-2566 is a very promising therapeutic candidate for brain trauma as evidenced by efficacy across several models of experimental brain injury, and by its effect on trauma-induced non-convulsive seizures."

"This clearly reinforces our perspective on the value and significance of non-convulsive seizures as a therapeutic target for drug intervention. Development of a safe, effective treatment for brain trauma that can be delivered after injury by those on the scene, including combat medics or civilian emergency medical personnel, without the need for extensive and time-consuming diagnostic workups is an extremely high priority for both our military and civilian medical communities," Dr Tortella added.

NNZ-2566 is being developed by Neuren and the WRAIR for acute neurological conditions and NNZ-2566 has recently begun a Phase 1 safety and tolerability trial. NNZ-2566 is also available in an oral form targeted towards chronic neurological conditions.

The benefit of Neuren's drug in preventing this phenomenon builds on the already significant evidence of the drug's effectiveness. It also means that Neuren will be able to

include electroencephalographic (EEG) effects as outcome measures in planned clinical trials. Use of EEG measurements will permit earlier detection of an effect in the Phase 2 trials as well as reducing the cost of the studies.

New techniques for measuring brain waves in patients are pointing to new ways of measuring damage during stroke and TBI and have shown these early changes are solid indicators of longer term outcome. The beneficial effects of NNZ-2566 in reducing seizures strongly suggest that the drug might have similar benefits in both TBI and stroke patients and the early assessment of these benefits by the new brain wave monitoring could provide an early signal of the drug's efficacy.

In experiments conducted by the WRAIR in an established animal model of non-convulsive seizures, administration of NNZ-2566 after brain injury resulted in a reduction in the incidence of seizures, total time in seizure, the average duration of seizures and an increase in the time between brain injury and onset of seizures (please see Appendix below).

Mr David Clarke, CEO of Neuren stated: "These findings, together with earlier positive results in the Army's traumatic brain injury model, support Neuren's confidence in the NNZ-2566 program and provide encouragement to progress this drug into Phase 2 human clinical trials as soon as practical. TBI is a critical indication that most clearly calls for a creative, aggressive approach both to drug development and patient treatment."

The preclinical research and development work is being conducted with the WRAIR under a Cooperative Research and Development Agreement. The Phase 2 study protocol is being jointly developed by Neuren, Army physicians and scientists involved in the TBI program.

Approximately 2 million people worldwide suffer a TBI each year. Of these, an estimated 1.5 million are seen in a hospital emergency room or admitted to a hospital. The market potential for an effective TBI drug has been estimated at US$1 billion. A drug that is also effective for acute treatment of ischemic and haemorrhagic stroke would potentially be applicable to an additional 3 million patients with an estimated market potential of US$4 billion worldwide.

Appendix:

The study was conducted in a rat model of brain injury-induced seizures using the validated and widely-used middle cerebral artery occlusion (MCAO) model. EEG activity was recorded continuously for 72 hours and analysed for incidence of seizures, mean duration of individual seizures, total time in seizure and latency, the time between injury and occurrence of the first seizure. (For a more complete description of methods, please see: Hartings JA et al. *Experimental Neurology* 179:139-149, 2003.)

The study involved 13 control animals that received vehicle only and 11 animals that received drug. The dosing regimen for animals receiving drug was a 3 mg/kg bolus followed immediately by a 12-hour infusion at 3 mg/kg/hr. Results are presented in the following table.

Non-convulsive Seizures

	Incidence	Total Time (sec)	Mean Time (sec)	Latency (min)
Vehicle	92%	1277	80.2	75.4
NNZ-2566	60%	555	48.7	208.7
Percent change	-35%	-56%	-39%	+133%

About Walter Reed Army Institute of Research
Walter Reed is the largest, most diverse, and oldest laboratory in the US Army Medical Research and Material Command. It conducts research on a range of military relevant issues, including naturally occurring infectious diseases, combat casualty care, operational health hazards, and medical defence against biological and chemical weapons. Walter Reed is the Department of Defense's lead agency for infectious disease research and a crucial source of research support for medical product development.

About Neuren Pharmaceuticals
Neuren Pharmaceuticals (ASX: NEU) is a biotechnology company developing novel therapeutics in the fields of neurotherapy and metabolic disorders. The Neuren portfolio consists of six product families, targeting markets with large unmet needs and limited competition. Neuren has two lead candidates, Glypromate® and NNZ-2566, targeting a range of acute and chronic neurological conditions. Neuren has commercial and development partnerships, including Pfizer, the US Army's Walter Reed Army Institute of Research and Metabolic Pharmaceuticals.

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

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