

Further Validation of NNZ-2566 as a Traumatic Brain Injury Treatment

Key Points:

- Positive results in a new model of brain injury
- Multiple modes of action reinforce key potential benefits of drug in traumatic brain injury
- NNZ-2566 has shown the ability to completely block the onset of the second phase of brain seizures, which are associated with worse clinical outcomes
- Planning and preparations for Phase 2 trials underway

13 February 2007: Neuren Pharmaceuticals (ASX: NEU) today announced results that its traumatic brain injury (TBI) treatment compound, NNZ-2566, significantly reduces loss of brain function when administered in a closed head injury model. Closed head injury is a common TBI occurrence and results in injuries such as concussion and unconsciousness.

Previously announced findings with NNZ-2566 reported positive results in both brain injury and stroke models performed by the US Army's Walter Reed Army Institute of Research (WRAIR). Results from the recently completed study, performed by Cerebricon (Finland), provide further support for Neuren's strategy to initiate clinical trials in TBI patients (see Appendix 1 for a summary of the data).

Neuren has confirmed the safety and tolerability of NNZ-2566 in humans in a recently completed Phase 1a trial and is currently evaluating the compound's safety and tolerability in humans at longer infusions. Two Phase 2 trials - one in patients with moderate TBI and one in more severely brain injured patients - are planned for the second half of this year. The moderate TBI Phase 2 trial will be the first trial to start and will be carried out in Melbourne. The severe TBI trial will be undertaken in the US by the WRAIR.

Neuren has obtained consistent evidence of the drug's ability to improve outcomes by reducing loss of brain function in animal models. The data obtained from these trials has also revealed the compound's mode of action, or the specific biochemical interaction through which the compound produces its pharmacological effect. NNZ-2566 is shown to have multi-faceted action to significantly reduce both inflammation and apoptosis (cell death), protecting the neurons and their surrounding infrastructure. This is an important breakthrough for Neuren.

Following an acute brain injury, cells adjacent to the primary site of injury commonly experience delayed cell death and this secondary injury is responsible for a significant proportion of the eventual loss of brain function. Secondary cell loss is caused both by inflammation and by apoptosis. Damage occurs to both the neuronal cells and the supporting astrocyte cells. Multiple actions in different biological pathways for a single drug is increasingly recognised to improve the likelihood of efficacy in patients. The ability of a drug to protect both cell types has been identified as critical to its success.¹ Most acute CNS drug candidates do not do this. NNZ-2566 has been shown to protect both cell types. Understanding this mechanism of action is a key element in the clinical development and commercialisation of a compound.

¹ Gregory del Zoppo. Stroke and neurovascular protection. *New England Journal of Medicine* 354;6 (553-5), 2006

Neuren has previously reported that the ability of NNZ-2566 to reduce non-convulsive seizures is a key feature of the drug's actions. Non-convulsive or silent brain seizures occur frequently in TBI patients and are associated with worse clinical outcomes. In the US Army's model of non-convulsive seizures, these electrical abnormalities occur in two phases - one shortly after injury and a second 6-8 hours later. NNZ-2566 has shown the ability to completely block the second phase of seizures and to significantly reduce the first wave (see Appendix 2). This finding again reinforces the company's belief that NNZ-2566 can reduce secondary brain injury.

The market for TBI is estimated at US\$1 billion per annum. TBI is major source of death and disability and is associated with high socioeconomic costs. Currently no treatment for brain injury is available.

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 six product families, targeting markets with large unmet needs and limited competition. Neuren has three lead candidates, Glypromate® and NNZ-2566, presently in clinical trials to treat a range of acute neurological conditions, and NNZ-2591 in preclinical development for Parkinson's and other chronic 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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Facts about Traumatic Brain Injury

(from the Brain Injury Association of America)

What is a traumatic brain injury?

A traumatic brain injury (TBI) is defined as a blow or jolt to the head or a penetrating head injury that disrupts the function of the brain. Not all blows or jolts to the head result in a TBI. The severity of such an injury may range from "mild," i.e., a brief change in mental status or consciousness to "severe," i.e., an extended period of unconsciousness or amnesia after the injury. A TBI can result in short or long-term problems with independent function.

How many people have TBI?

Of the 1.4 million who sustain a TBI each year in the United States:

- 50,000 die;
- 235,000 are hospitalised; and
- 1.1 million are treated and released from an emergency department.

The number of people with TBI who are not seen in an emergency department or who receive no care is unknown.

What causes TBI?

The leading causes of TBI are:

- Falls (28%);
- Motor vehicle-traffic crashes (20%); and
- Assaults (11%).

Blasts are a leading cause of TBI for active duty military personnel in war zones.

Who is at highest risk for TBI?

- Males are about 1.5 times as likely as females to sustain a TBI.
- The two age groups at highest risk for TBI are 0 to 4 year olds and 15 to 19 year olds.
- Certain military duties (e.g., paratrooper) increase the risk of sustaining a TBI.
- African Americans have the highest death rate from TBI.

What are the costs of TBI?

Direct medical costs and indirect costs such as lost productivity of TBI totalled an estimated US\$56.3 billion in the United States in 1995.

What are the long-term consequences of TBI?

The Centers for Disease Control and Prevention estimates that at least 5.3 million Americans currently have a long-term or lifelong need for help to perform activities of daily living as a result of a TBI. According to one study, about 40% of those hospitalised with a TBI had at least one unmet need for services one year after their injury. TBI can cause a wide range of functional changes affecting thinking, sensation, language, and/or emotions. It can also cause epilepsy and increase the risk for conditions such as Alzheimer's disease, Parkinson's disease, and other brain disorders that become more prevalent with age.

Appendix 1

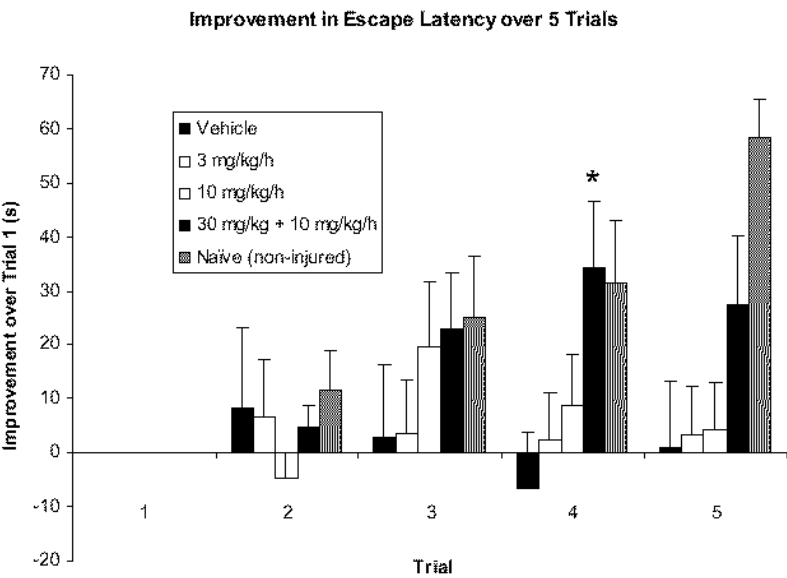
Cerebricon TBI Study Summary of Results

Study design: Non-penetrating controlled-cortical impact injury to rats
Drug given 1 hour post-TBI (bolus and/or infusion)
NNZ-2566 given i.v. for 24 hour infusion
Doses according to table below.

	Injury	i.v. Bolus	i.v. Infusion
Group 1	Naive	-	-
Group 2	TBI	-	Vehicle
Group 3	TBI	-	3 mg/kg/h
Group 4	TBI	-	10 mg/kg/h
Group 5	TBI	30 mg/kg	10 mg/kg/h

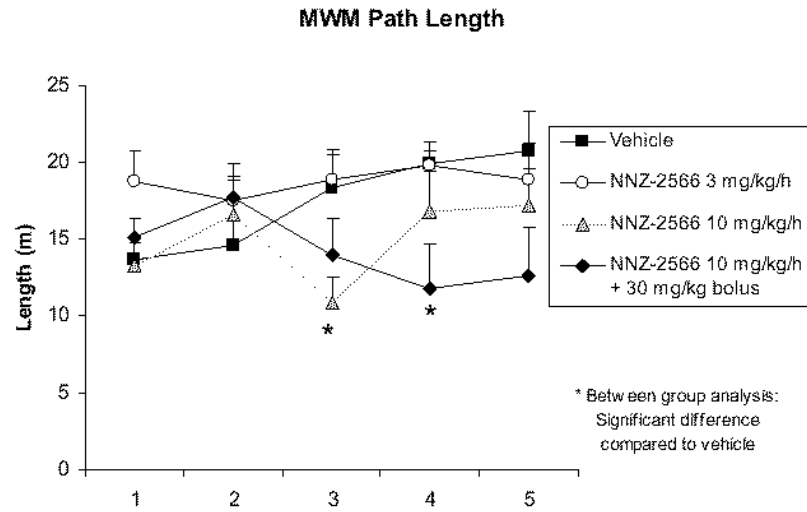
Results

(i) Significant improvement in escape latency in the Morris water maze with the highest dose.



Appendix 1

(ii) Significant improvement (reduction) in path length in the Morris water maze with the top two doses.



Appendix 2

