Neuren selects new compound targeted for the oral treatment of Parkinson's and related neurological diseases

Key points:

- NNZ-2591 has shown preclinical efficacy in animal models of Parkinson's disease
- NNZ-2591 showed long term beneficial effects in Parkinson's disease, in addition to short term symptomatic relief
- NNZ-2591 was shown to be orally neuroprotective and safe in animals at over 15 times the effective dose
- NNZ-2591 is a member of a new class of Neuren compounds and has been selected for development through to human clinical trials

Wednesday 2 August 2006: Neuren Pharmaceuticals (ASX: NEU) announces a new lead candidate, NNZ-2591, from its diketopiperazine (DKP) family, which has shown efficacy in a preclinical model of Parkinson's disease (PD) and in other animal models of brain injury. This is now Neuren's third lead candidate, after Glypromate® and NNZ-2566, which are both currently in human trials.

Importantly in the Parkinson's disease model, NNZ-2591 was administered after onset of Parkinsonian symptoms and the beneficial effect in the behavioural tests remained for weeks after the cessation of drug treatment. This suggests the compound produced a long-term benefit in this model of the disease, rather than just temporary symptomatic relief.

NNZ-2591 did not show any liability for drug-drug interactions or any safety concerns following wide screening. The compound did not display any adverse or unwanted pharmacological effects when orally administered to rats at doses over 15 times higher than the effective dose for neuroprotection. In addition, in an experimental model of stroke, NNZ-2591 has also been shown to reduce brain damage when given orally, an important feature for chronic neurodegenerative diseases where treatment is usually prolonged.

These observations have lead to the selection of oral NNZ-2591 as a lead candidate to treat chronic neurological disorders, such as Parkinson's disease and other neurological diseases, such as Alzheimer's disease. NNZ-2591 is now in manufacturing scale-up as a precursor to formal toxicology.

Dr Mike Bickerdike, Head of Preclinical Development, said: "This is a new molecule from our research pipeline and its progression to lead candidate status broadens Neuren's development portfolio. Along with the oral NNZ-2566 program announced recently, we're now able to target chronic conditions, such as Parkinson's disease and Alzheimer's disease, with two lead candidates, oral NNZ-2566 and now oral NNZ-2591."

NNZ-2591 is distinct from Neuren's other compounds, Glypromate® and NNZ-2566, coming from a different chemical class, and displaying distinct pharmaceutical and pharmacological properties. Glypromate® and NNZ-2566 are currently in human clinical trials for acute brain injury, specifically, cognitive impairment and traumatic brain injury respectively.

Mr David Clarke, CEO, said, "This is an exciting step for the Company. NNZ-2591 has all the right characteristics for a very promising candidate and has gone through a rigorous selection process over the last 12 months. NNZ-2591 will now follow the Company's well-tested drug development programme used for Glypromate® and NNZ-2566, both candidates that are currently in human trials. NNZ-2591 however will be targeting a new area of brain disease, with new potential markets."

Parkinson's disease is a progressive, degenerative neurological condition that affects the control of body movements. In addition, up 50% of Parkinson's patients go on to develop some form of dementia. It is estimated that approximately 1-2 people per 1,000 have Parkinson's, with the incidence increasing to one in 100 over the age of 60. In Australia there are approximately 40,000 people with Parkinson's, with one in seven people being diagnosed with Parkinson's before the age of 50 years. Alzheimer's disease has a reported 4.5 million cases a year in the US and an estimated market worth of US$2.5 billion.

The majority of work to date on NNZ-2591 has been funded by a New Enterprise Research Fund grant from the Foundation for Research Science and Technology in New Zealand.

Appendix:

Parkinson's disease data

Rats were assessed for their capacity to employ both forelimbs when walked laterally along a metre length. The onset of Parkinsonism on one side of the brain at week 0 resulted in poor use of one limb at week 2 (resulting in the low percent L/R steps measure shown in the table). One week of daily intraperitoneal treatment with saline (control) did not result in improved use of the affected limb. One week daily treatment with 0.2, 1 or 5 mg/kg NNZ-2591 (week 2 to 3; 35 animals in total) did, however, result in a statistically significant improvement in affected limb use. This effect was maintained throughout the experiment, for at least 8 weeks following cessation of treatment (represented by study week 11). The effect of 5 mg/kg NNZ-2591 is shown in the table below. Similar results have been obtained with NNZ-2591 in this model of Parkinson's disease when the drug is administered directly into the rat brain (20 ng/rat).

	Study Week	Percent L/R steps Control-treated (n=9)	Percent L/R Steps NNZ-2591-treated (n=8)
Pre-Parkinson's onset	0	95 %	94 %
Post-Parkinson's development	2	13 %	16 %
Post-Treatment	7	8 %	46 %
Post-Treatment	9	17 %	44 %
Post-Treatment	11	18 %	50 %
Statistical Significance of Drug			$p < 0.001$

Neuroprotective efficacy of oral NNZ-2591 treatment, administered to rats 3 hours after middle-cerebral artery occlusion, employed as an experimental rat model of focal ischemic stroke.

	Infarct Size	Percent Protection	Statistical Significance
Saline control (n=12)	88 mm^2	-	-
NNZ-2591 3 mg/kg (n=11)	60 mm^2	32 %	N.S.
NNZ-2591 30 mg/kg (n=11)	26 mm^2	70 %	$p < 0.01$

Pre-clinical safety data details

NNZ-2591 has shown no liability for drug-drug interactions. This has been ascertained by screening for inhibition of human cytochrome P450 liver enzymes responsible for the metabolism of most prescribed drugs.

NNZ-2591 has revealed no safety concerns following a wide ligand binding screen at over 70 receptors and enzymes. This data supports the view that NNZ-2591 should be devoid of unwanted pharmacological side effects known to result from interaction with these sites.

NNZ-2591 displays no adverse effects or unwanted pharmacological effects when orally administered to rats at doses more than 15 times higher than the effective dose for neuroprotection.

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 several commercial and development partnerships, including with 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

Contact details

Company	**Media and investor relations**
David Clarke CEO T: 1800 259 181 (Australia) T: +64 9 367 7167 ext 82308 (NZ) M: +64 21 988 052	Rebecca Piercy Buchan Consulting T: +61 2 9237 2800 M: +61 422 916 422