Neuren's third lead drug candidate, NNZ-2591, proves effective at reversing memory loss

Key points:

- Neuren's oral drug candidate NNZ-2591 has successfully reversed experimental memory loss, a common outcome associated with dementia and with many Parkinson's disease patients
- This improvement was seen in both ordinary (non-aged) animals with induced memory loss and older (aged) animals, the latter indicated the reversal of aged related memory loss as well
- Previous preclinical data for oral NNZ-2591 has shown improvement in the motor effects associated with Parkinson's
- NNZ-2591 now has preclinical evidence that it reverses both the motor effect and the memory loss effect associated with Parkinson's disease
- There is currently only one drug approved for Parkinson disease dementia but none approved that treats both the motor and the dementia effects
- Neuren intends to accelerate development of NNZ-2591 as a clinical candidate for treatment of Parkinson's disease dementia

Monday, 16 October 2006: Neuren Pharmaceuticals Ltd (ASX: NEU) today announced that its third lead candidate from its diketopiperazine (DKP) family, NNZ-2591, has reported positive preclinical effects of improved learning and memory after oral dosing. Memory was improved to pre-injury levels (100%), a statistically significant effect ($p<0.03$).

The results suggest that NNZ-2591 has the capacity to improve learning and memory processes after short-term treatment. The new data extends the potential application of NNZ-2591 as a treatment for dementias such as those associated with over 50% of Parkinson's disease patients. This is a much less competitive market when compared to the many drug therapies that are available for the treatment of the loss of motor skills associated with the Parkinson's disease.

Improvements were observed as early as two days after initial treatment and were observed throughout the four day study. NNZ-2591 was administered as an oral dose to the animals in each test, further supporting the development of this drug as an oral treatment for chronic disorders.

In addition results for NNZ-2591 in aged animals showed an improvement in aged related memory loss, often associated with the early stages of Alzheimer's disease and dementia. In the aged model, besides the improvement in recognition and memory, histology (analysis of brain cells) also showed an improvement in the connections between neurons (synaptic improvement). This indicates the potentially wide applicability of NNZ-2591 across a range of conditions.

Previous studies have shown that NNZ-2591 is effective at improving the motor skills impairment seen in an experimental model of Parkinson's disease and also showed that the drug produced a long-term benefit in this model of the disease, rather than just temporary symptomatic relief.

A drug capable of reducing the loss of motor skills and dementia symptoms directly meets the important needs of late-stage Parkinson's disease patients.

Neuren intends to accelerate development of NNZ-2591 as a clinical candidate for treatment of Parkinson's disease dementia. Further studies will assess the breadth of effect of NNZ-2591 on learning and memory processes to fully evaluate its potential for the treatment of other dementias, including Alzheimer's disease.

Mr David Clarke, CEO of Neuren said: "These are very promising preclinical results for NNZ-2591. A treatment for Alzheimer's and Parkinson's disease that improves memory would be very exciting. Importantly there is only one current drug on the market for Parkinson's dementia, and none that can address both the motor effects and the dementia effects. We will now put NZ-2591 through our clinical development path."

Appendix

The study was conducted in 55 rats using a learning and memory test called the Morris Water Maze. This test involves placing each animal in a pool of opaque (tinted) water in which a small platform is hidden just beneath the surface. The rats must swim to the platform in order to reach 'safe ground'. With subsequent tests, rats find the platform quicker as they learn where it is, and recall this information. Scopolamine causes the animals to take much longer to learn and recall where the platform is, as it induces a cognitive impairment. They therefore take longer to reach the platform.

Orally administered NNZ-2591 was given after the injected scopolamine had been given. 12 rats were controls, 16 received NNZ-2591 but not scopolamine, 12 received scopolamine plus vehicle (water) and 15 received scopolamine plus NNZ-2591 dissolved in water. Scopolamine significantly impaired memory (time to platform approximately 208% of control on day 4) and while NNZ-2591 had no effect in rats that were not treated with scopolamine, NNZ-2591 significantly reversed the cognitive impairment induced by scopolamine (time to platform 98% of control) and animals that received both scopolamine and NNZ-2591 found the platform in very similar times to those that were not treated (controls with normal memory performance).

Time taken to find platform (seconds) on the 4th day after treatment (mean plus standard error of mean)

	Number	Mean time to platform (seconds)	SEM
Saline/water (control)	12	8.8	1.1
Saline/NZ2591	16	11.0	1.2
Scopolamine/water	12	18.2	2.3
Scoplomaine/NZ2591	15	8.6	2.0

(SEM= standard error of the mean)

The scopolamine only group is different to all other groups by analysis of variance ($p<0.03$).

Other measures such as the time taken to enter the quadrant in which the platform is hidden showed similar conclusions

About Parkinson's and Alzheimer's diseases

Parkinson's disease is a progressive, degenerative neurological condition that affects the control of body movements. Market estimates of treatment costs are in the range of US$2.4 billion. In addition over 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 with Parkinson's being diagnosed before the age of 50 years.

Parkinson's disease dementia is characterised by cognitive slowing, attention deficit, and executive, visuospatial, and memory impairments. Dementia associated with Parkinson's disease is accompanied by a reduced quality of life for both patients and caregivers and by rapid functional and motor decline.

Overall the most common form of dementia among older people is Alzheimer's disease (AD), which involves the parts of the brain that control thought, memory, and language.

The disease usually begins after age 60, and the risk of developing AD goes up with age. While younger people may also get AD, it is much less common. About 5 percent of men and women aged 65 to 74 have AD, and nearly half of those aged 85 and older may have the disease. It is important to note, however, that AD is not a normal part of aging.

There are presently 4-5 million AD patients in the US alone with an estimated 15 million worldwide. The market for AD therapy is expected to exceed US$3 billion by 2009.

Statistics

- More than 162,000 Australians have a diagnosis of dementia, with perhaps as many again in the early stages of dementia
- Australians over the age of 65 have a one in 15 chance of developing AD
- Among people aged 80 to 84 the rate is one in nine
- Among those aged over 85 it is one in four
- The disease affects mostly people in their 70s and 80s, but can appear in people who are in their 40s or younger

How is Parkinson's and Alzheimer's disease currently treated?
No current treatment can stop Parkinson's disease or Alzheimer's disease. However, for some people in the early and middle stages of the disease, drugs may help prevent some symptoms from becoming worse for a limited time. Rivastigmine is a drug for the treatment of mild-to-moderate Alzheimer's disease and is the only drug currently approved for treatment of Parkinson's disease dementia.

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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