Neuren Pharmaceuticals Ltd. (ASX:NEU) is pleased to announce that results from testing of NNZ-2566 and NNZ-2591 in a model of Fragile X Syndrome are being presented at the FRAXA (Fragile X Research Foundation) Investigators Meeting in Southbridge, Massachusetts on 30 September and 1 October 2013.

In summary, NNZ-2566 and NNZ-2591 were each shown to reverse the differences between normal (wild-type) mice and fmr1 knockout mice, normalising known Fragile X behavioural, anatomic and biochemical characteristics. The studies were conducted by the FRAXA – Drug Validation Initiative (DVI) led by Dr Patricia Cogram. The attached poster on the results with NNZ-2591 is being presented and Dr Cogram will discuss the scientific rationale for development of NNZ-2566 for Fragile X Syndrome during a plenary session.

Commenting on the presentations, Neuren Chief Science Officer Larry Glass said: “As we move toward initiation of the Phase II clinical trial of NNZ-2566 in Fragile X Syndrome later this year, the expanding scientific foundation continues to reinforce our confidence in the strategy. The positive results with NNZ-2591, also an analogue of a naturally occurring growth factor, are encouraging as well, providing further options for therapy development.”

About NNZ-2566
NNZ-2566 is a synthetic analogue of a naturally occurring neuropeptide derived from IGF-1, a growth factor produced by brain cells. In animal models, NNZ-2566 inhibits neuroinflammation and normalises the function of microglia with consequent improvements in molecular, cellular, anatomic and behavioural outcomes. NNZ-2566 is being developed both in intravenous and oral formulations for a range of acute and chronic conditions. The intravenous form of NNZ-2566 is presently in a Phase II clinical trial in patients with moderate to severe traumatic brain injury as well as a Phase II trial in Rett Syndrome. Both programs have received Fast Track designation from the US FDA. The company intends to implement a Phase II clinical trial in Fragile X Syndrome and an additional Phase II trial with the oral form of NNZ-2566 in patients with concussion or mild TBI.

About NNZ-2591
NNZ-2591 is a synthetic analogue of a naturally occurring neuropeptide, which has been shown to have neuroprotective and nootropic (memory enhancing) effects in multiple
animal models. NNZ-2591 has excellent oral bioavailability and is currently being assessed as a clinical candidate for the treatment of chronic neurological disorders. NNZ-2591 is protected by both composition of matter and therapeutic use patents, as well as a number of pending applications.

About Fragile X Syndrome
Fragile X syndrome is the most common inherited cause of intellectual disability and the most common known cause of autism. It affects 1 out of 4000 males and 1 out of 6-8000 females. Fragile X syndrome is due to a single gene defect on the X chromosome that impacts the FMRP protein, which is responsible for regulating the synapses of nerve cells. Clinically, Fragile X Syndrome is characterized by intellectual handicap, hyperactivity and attentional problems, autistic symptoms, anxiety, emotional lability and epilepsy. The epilepsy seen in Fragile X Syndrome is most commonly present in childhood, but then gradually improves towards adulthood. Physical features such as prominent ears and jaw, and hyper-extensibility of joints are frequently present but are not diagnostic. Generally, males are more severely affected than females. Currently, there are no medicines approved for the treatment of Fragile X Syndrome.

About Neuren
Neuren Pharmaceuticals Limited (Neuren) is a publicly listed biopharmaceutical company focusing on the development of new therapies for brain injury, neurodevelopmental and neurodegenerative disorders. The novel drugs target chronic conditions such as Rett Syndrome and Fragile X Syndrome as well as acute neurological injuries. Neuren presently has a clinical stage molecule, NNZ-2566, in two Phase 2 clinical trials as well as NNZ-2591 in pre-clinical development. Neuren operates in New Zealand, Australia and the United States.

Forward-looking Statements
This ASX-announcement contains forward-looking statements that are subject to risks and uncertainties. Such statements involve known and unknown risks and important factors that may cause the actual results, performance or achievements of Neuren to be materially different from the statements in this announcement.

For more information, please contact:

Larry Glass, CSO
lglass@neurenpharma.com
Tel: +1 301 941 1830

Dr Richard Treagus, Executive Chairman
rtreagus@neurenpharma.com
Tel: +61 417 520 509
The Impact of NNZ-2591 on the fmr1 Knockout Mouse Model of Fragile X Syndrome

Robert Deacon, Larry Glass, M. F. Snape, Rolf Biekefsoy and P. Cogam

1 Neuren Pharmaceuticals Ltd, Auckland, New Zealand; 2 Neuro-DVI Ltd, Santiago, Chile; 3Autism Therapeutics Ltd, London, UK; 4University of Chile, Santiago, Chile

Background

Fragile X syndrome is a neurodevelopmental disorder caused by mutation of the fragile X mental retardation 1 (fmr1) gene, and characterized by intellectual disability, social anxiety, attention-deficit hyperactivity disorder and abnormal physical characteristics such as macro-orchidism (enlarged testes). Mutant fmr1 knockout (KO) mice recapitulate this phenotype and represent a preclinical model for assessment of putative drug treatments.

The current study evaluated the potential of NNZ-2591 to reverse the Fragile X phenotype exhibited by fmr1 KO mice.

Drug Treatment

Fmr1 KO and wild-type mice (C57BL/6J background) were dosed with either vehicle or NNZ-2591 (30 mg/kg i.p.) 1/day, starting at 14 weeks of age, for 28 days. Various behavioral and anatomic outcomes were assessed following treatment.

Results

At baseline, fmr1 KO mice manifested numerous phenotypic changes compared with wild-type mice, including: decreased hyperactivity in the open-field (p < 0.001) and successive alley trials (p < 0.001); increased contextual-fear conditioned memory (p < 0.001); increased social sniffing (p < 0.001); decreased dendritic spine density and decreased phosphorylation of ERK and Akt (p < 0.001). Treatment with NNZ-2591 significantly ameliorated all of these aberrant features of the fmr1 KO mouse phenotype.

Conclusions

NNZ-2591 treatment for 28 days appears to normalize the phenotype of fmr1 KO mice. The efficacy of the drug was observed not only in behavioral studies but also in studies of dendrite morphology and ERK/Akt activation. Taken together, these data suggest that the novel small molecule, NNZ-2591, may represent a potentially important treatment for Fragile X syndrome. Further studies are ongoing to expand our understanding of the mechanism of action of NNZ-2591 in fmr1 KO mice.