Neuren Announces Results in Fragile X Model with NNZ-2591

Australia, 29 July 2013: Neuren Pharmaceuticals Limited (ASX:NEU) is pleased to announce positive results from a validated animal model using Neuren's second drug molecule, **NNZ-2591**.

The Fragile X Drug Validation Initiative (FX-DVI), an independent research institute supported by the Fragile X Alliance (FRAXA), has completed a study using NNZ-2591 in a mouse model of Fragile X Syndrome (fmr1 knockout mouse model). This experiment replicated the study with Neuren's lead drug molecule, NNZ-2566, the results of which were announced in November 2012.

Notably, this most recent study used a dose of NNZ-2591 approximately one-third that of NNZ-2566. The study protocol evaluated the treatment effect of NNZ-2591 compared with a control, and incorporated the following objective measures: (i) growth and development of dendritic spines (connections between brain cells); (ii) behavioural characteristics and (iii) brain biochemistry following treatment.

In summary, NNZ-2591 was shown to reverse the differences between normal (wild-type) mice and *fmr1* knockout mice, normalising known Fragile X neuronal, behavioural and biochemical characteristics.

The study confirmed a statistically significant ($p<0.005$), dose-dependent effect on reduction of excess dendritic spines, a hallmark component of Fragile X Syndrome.

Treatment with NNZ-2591 also significantly reduced both ERK phosphorylation ($p<0.05$) and Akt phosphorylation ($p<0.05$) in the brains of the *fmr1* knockout mice when compared to *fmr1* knockout mice treated with the control. Excessive phosphorylation (activation) of ERK and Akt is believed to contribute to the dysfunction in neuronal signalling observed in Fragile X Syndrome.

There were statistically significant differences (ranging from $p<0.0001$ and $p<0.005$) between *fmr1* knockout mice treated with NNZ-2591 versus those treated with placebo on all the behavioural measures related to anxiety, short term memory, long term memory, hyperactivity, learning, species typical behaviours and social interaction.

Commenting on the results, Larry Glass, Neuren's CEO, said: "We are truly excited with the outcome of this study. These results in a well-accepted model of Fragile X Syndrome are compelling and reinforce our belief that NNZ-2591 is a valuable compound with significant promise as a therapeutic for chronic neurological conditions. That both NNZ-2566 and NNZ-2591 exhibit significant benefits in this model suggests a "class effect" which has not previously been reported, in which two synthetic analogues of naturally occurring neuropeptides show therapeutic potential in the same condition."

The Company intends to formally present the results from the study at the FRAXA Investigators Meeting in Boston at the end of September.

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.

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.

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 currently has operations in New Zealand, Australia and the United States.

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