



pharmaceuticals

ASX code: NEU



metabolic

ASX code: MBP

ASX Announcement

NRP drug effective in animal models of motor neuron disease and peripheral neuropathy

- *Neural Regeneration Peptides (NRPs)* are a class of peptides which potentially protect and regenerate nervous system tissue
- Possible lead compound identified - *NNZ-4945*
- Results from animal studies indicate that *NRP* candidate *NNZ-4945* has potential to treat motor neuron disease and peripheral neuropathy
- Next steps are to repeat and expand the motor neuron disease animal studies, begin some early standard preclinical safety and pharmacokinetic evaluations on *NNZ-4945* and learn more about the mechanism of action

Melbourne, 15 October 2007. Neuren Pharmaceuticals Limited (“Neuren”) and Metabolic Pharmaceuticals Limited (“Metabolic”) today announced new animal data from their joint research programme to develop *Neural Regeneration Peptides (NRPs)* as a novel treatment for neuropathic and neurodegenerative conditions. *NRPs* are a class of human derived peptides that display a broad range of biological effects important for the protection and regeneration of nervous system tissue. A possible lead drug candidate with the desired physical characteristics has now been identified from preclinical tests. In rodent studies, drug candidate *NNZ-4945* has been shown to prolong the life of mice in a model of motor neuron disease and also to reduce functional impairment in a model of peripheral neuropathy.

NNZ-4945 tested on mice with motor neuron disease

Motor neuron disease (MND), also known as amyotrophic lateral sclerosis (ALS), is a progressive neurodegenerative disease that attacks motor neurons in the brain and spinal cord. Motor neurons are the cells that control skeletal muscle activities such as speaking, walking, swallowing and breathing. When motor neurons can no longer send impulses to the muscles due to MND, the muscles begin to waste away causing increased muscle weakness, and eventually makes it impossible for the brain to control muscles or signal them to move. The life expectancy for patients diagnosed with MND is typically 2-5 years, with the disease proving fatal within 14 months of diagnosis in 50 percent of patients. New treatments are needed for MND as the only available prescription is *riluzole*, a drug that extends life expectancy by only three months.

NRP compound *NNZ-4945* was tested in a mouse model of MND by a US-based laboratory and demonstrated promising efficacy. The longevity of mice with MND was significantly reduced by the progressive loss of motor neurons, with the animals succumbing to the disease 38 days after the first observation of MND symptoms (disease onset). Mice treated daily with doses of *NNZ-4945*, from the day of disease onset, lived significantly longer than mice treated with a placebo, with an average lifespan of 52 days from disease onset, representing a 37 percent increase in life expectancy.

NNZ-4945 tested on mice with peripheral neuropathy

Peripheral neuropathy is a relatively common and disabling condition characterised by nerve damage due to diseases such as diabetes, or as a result of drug treatments, such as chemotherapy. Peripheral neuropathy affects as many as 20 million people in the US alone, with at least 60 percent of all diabetic patients suffering neuropathic symptoms. Currently the approved drugs for the treatment of peripheral neuropathy, which have combined sales in excess of US\$2 billion a year, provide only symptomatic relief for pain and do not treat or prevent the underlying disease process. Health care costs associated with this condition are estimated to exceed US\$11 billion a year.

In studies of peripheral neuropathy, very low doses of NNZ-4945 administered to rats significantly reduces the development of a neuropathic impairment that is evident in a test of motor function in non-drug treated controls. NNZ-4945 has been shown in other *in-vitro* tests to prevent neuronal cells from dying as a result of various stress conditions, suggesting that the compound prevents neuropathic impairments by protecting the sensory nerves that are impaired in the neuropathy model.

Dr Mike Bickerdike, Head of Preclinical Development for Neuren, said, "the efficacy data generated with NNZ-4945 in these two disease models is an exciting development, particularly given the urgent need for new therapies to treat these conditions".

Next steps in development

Neuren and Metabolic agreed to jointly develop the *NRP* project in March 2005 with all intellectual property and commercial outcomes to be equally shared. Prior to initiating formal preclinical studies, the next steps in this collaboration include expanding the protocols in the mouse models, and learning more about the mechanism of action of the compound. The objective of future preclinical studies will be to investigate the safety and pharmacokinetics of a *NRP* lead compound as a prelude to clinical trials. Batches of the lead compound are expected to be manufactured in quantities sufficient for preclinical testing in 2008.

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About Neuren

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 two lead candidates, Glypromate®, Motiva™, NNZ-2566, and NNZ-2591 targeting a range of acute and chronic neurological conditions. Neuren has commercial and development partnerships, including 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.

About Metabolic

Metabolic Pharmaceuticals Limited (**ASX**: MBP, **NASDAQ OTC**: MBLPY) is a Melbourne based, ASX listed biotechnology company with 300 million shares on issue. Metabolic's focus is to take drug candidates through research, formal preclinical and clinical development. The Company's lead project is the development of a platform for the oral delivery of existing injectable peptide drugs. This platform has the potential to generate multiple internal projects as well as a variety of licensing opportunities. For more information, please visit Metabolic's website at www.metabolic.com.au.

Inherent Risks of Investment in Biotechnology Companies

There are many inherent risks associated with the development of pharmaceutical products to a marketable stage. The lengthy clinical trial process is designed to assess the safety and efficacy of a drug prior to commercialisation and a significant proportion of drugs fail one or both of these criteria. Other risks include uncertainty of patent protection and proprietary rights, whether patent applications and issued patents will offer adequate protection to enable product development, the obtaining of necessary drug regulatory authority approvals and difficulties caused by the rapid advancements in technology. Companies such as Neuren and Metabolic are dependent on the success of their research projects and on the ability to attract funding to support these activities. Investment in research and development projects cannot be assessed on the same fundamentals as trading and manufacturing enterprises. Thus investment in companies specialising in drug development must be regarded as highly speculative. Neuren and Metabolic strongly recommend that professional investment advice be sought prior to such investments.

Forward-looking statement

Certain statements in this ASX Announcement may contain forward-looking statements regarding Company business and the therapeutic and commercial potential of its technologies and products in development. Any statement describing Company goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those risks or uncertainties inherent in the process of developing technology and in the process of discovering, developing and commercialising drugs that can be proven to be safe and effective for use as human therapeutics, and in the endeavor of building a business around such products and services. Neuren and Metabolic undertake no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise. Actual results could differ materially from those discussed in this ASX Announcement.

Appendix

Scientific data – efficacy of NNZ-4945 in a model of motor neuron disease

	Treatment Start	Day of Mortality
Vehicle Control	91.9	129.9
NNZ-4945 (0.04 mg/kg)	92.9	144.9 *

Study Design: SOD1^{G93A} transgenic mutant mice develop motor neurone disease at approximately day 90 of life. Each mouse was treated daily from the day of onset of disease symptoms with either vehicle control (n=8) or NNZ-4945 at the dose shown (n=7). The mortality of the mice was recorded. NNZ-4945 treated mice lived significantly longer than the control-treated counterparts, * p < 0.05.