

Positive preclinical results show fat reduction capability for Neuren's compound NNZ-3006

Key points

- Neuren's new compound NNZ-3006 has shown the effects of reducing fat mass and improving body composition in an animal model
- NNZ-3006 is particularly applicable to obesity, metabolic syndrome and adult growth hormone deficiency
- NNZ-3006 does not show any of the side effects often associated with conventional growth hormone treatment and which have precluded its use in these markets
- Conventional growth hormone market size is estimated at US\$2.4 billion and is mainly used in paediatric growth conditions
- Patents filed on unique profile of NNZ-3006 action and uses in approved and new indications
- Neuren will now actively evaluate partnership options for clinical development and marketing

Wednesday 27 September 2006: Neuren Pharmaceuticals (ASX: NEU) announced that its new variant growth hormone (GH) molecule, NNZ-3006, has shown the ability to reduce fat deposits in an animal model, but none of GH's unwanted side effects that include increased risk of diabetes and fluid retention.

Neuren's GH portfolio has historically arisen on the back of extensive research and consultation with Pharmacia, and more lately Pfizer, as well as Neuren's own related scientific endeavours in the field. Neuren has selected and patented unique technologies such as NNZ-3006 that have properties lending themselves to competitive market positioning.

NNZ-3006 is a novel, naturally-occurring variant of the human GH and is expected to be applicable to a wide range of conditions for which GH is already approved and may also have new uses related to obesity and fat metabolism.

The research work is partially funded by a grant from the Foundation for Research Science and Technology.

If the action profile is confirmed in human clinical trials, NNZ-3006 could significantly increase the therapeutic uses of GH in approved and new indications and capture significant market share due to the improved properties of this form of the hormone. Global sales of GH are estimated at US\$2.4 billion and growing at approximately 20% per annum.

The only product approved for use in humans is a recombinant form of the GH made by the pituitary gland. However unacceptable side effects limit the use of this product, particularly in adults. The profile of action of NNZ-3006 differs from that of other forms of GH found in the placenta or the pituitary gland.

Neuren will now actively explore potential partnerships for clinical development, marketing and sales.

Professor Peter Gluckman, Neuren's Chief Scientific Officer said: "This discovery creates considerable potential not only for growth hormone treatment of patients who were previously excluded from such therapy because of the issue of side effects, but also for growth hormone treatment of a wider range of indications."

Neuren is also researching the action of GH in certain cancers.

Appendix

Growth hormone (GH), which is produced by the anterior pituitary gland, is the primary regulator of postnatal growth and metabolism. Treatment of children and adults with GH-deficiency is often associated with unwanted side effects such as impaired insulin sensitivity, an enhanced susceptibility for the development of type 2 diabetes and increased water retention, most notably in GH treated adults. GH is naturally produced in a number of different forms with the 22kDa form pituitary isoform (GH-N or GH-“normal”) the basis for current treatment paradigms. The placenta produces two forms of placental GH, the dominant form which has a molecular weight of 22KDa (GH-V 22K) and an alternate form (NNZ-3006).

Neuren has tested the placental NNZ-3006 in vivo, in multiple independent rat trials and has shown NNZ-3006 to have significant functional advantages over other forms of growth hormone (see table 1 below).

NNZ-3006 does not impair insulin sensitivity associated with other forms of GH and the diabetogenic effects accompanying normal GH therapy are abolished with NNZ-3006. This removes the possibility of inducing type 2 diabetes. The effect on plasma IGF-1 levels was much less suggesting that NNZ-3006 will be of particular use in adults where the metabolic rather than IGF-1 inducing actions of GH are therapeutically desirable. Conventional GH treatment of adults results in the unwanted side-effect of fluid retention. However, in vitro and in vivo studies with the NNZ-3006 show that this placental GH variant is devoid of any lactogenic/fluid retentive activity.

NNZ-3006 reduces fat mass as effectively as the GH-N 22k and so can prevent and also reduce childhood and adult obesity without exacerbating insulin resistance. Limited evidence from Neuren trials indicates that NNZ-3006 actually improves insulin sensitivity.

	Total body fat (%)	Fat:lean ratio	Leptin (ng/ml)	Hematocrit (%)	Insulin (ng/ml)	IGF-I (ng/ml)
<i>Comparisons</i>						
Saline vs 22k GH-N	p<0.005	p<0.0005	p<0.05	p<0.05	p<0.005	p<0.05
Saline vs NNZ-3006	p<0.005	p<0.005	p<0.05	NS	NS	NS
22k GH-N vs NNZ-3006	NS	NS	NS	NS	p<0.005	p<0.005

Endocrine measures, blood hematocrit (a low measure reflects increased plasma volume or fluid retention) and body composition analysis following 7 days treatment with either saline, 22k GH-N or NNZ-3006. NS = not significantly different, n=6-8 per treatment group. Data were analysed using two-way factorial ANOVA with diet and treatment as factors.

NNZ-3006 and the 22k GH-N were equipotent in reducing fat mass (with a concomitant reduction in plasma leptin concentrations) and improving fat:lean ratios. Fasting plasma insulin was significantly increased in high fat fed animals and further significantly increased in animals treated with the 22k GH-N. The 22k GH-N mediated increases in plasma insulin were not observed in the NNZ-3006 treated animals where insulin concentrations were not different from those of saline controls. Plasma IGF-I concentrations were significantly increased with 22k GH-N treatment but were not significantly different between NNZ-3006 treated animals and saline controls.

About Neuren Pharmaceuticals

Neuren Pharmaceuticals (ASX: NEU) is a biotechnology 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 the clinic in development 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 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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