Favourable Phase 2a pharmacokinetic and safety data for Glypromate® confirmed

Key points:

- **Release of detailed pharmacokinetic analysis of Glypromate®**
- **No difference in safety between treated and untreated groups in study**
- **Linear relationship between treatment groups enable good prediction of exposure following other doses, and supports safe profile**
- **Neuren on track to progress Glypromate® into Phase 3 clinical trial**

Tuesday, 22 August 2006: Neuren Pharmaceuticals (ASX: NEU) has today announced the detailed pharmacokinetics analysis of the Phase 2 clinical trial of its lead compound, Glypromate®, for the reduction of cognitive decline following cardiac surgery.

Cognitive impairment at discharge from cardiac surgery has been reported in up to 70% of patients and there is currently no treatment to alleviate or prevent this decline. Pharmacokinetic studies provide information about how the body deals with the drug after it is administered, such as the concentration the drug reaches in the blood and the amount of time the drug remains in the circulation.

Neuren's Phase 2a clinical trial investigated the safety, tolerability and pharmacokinetics of a 4-hour infusion of Glypromate® in 33 cardiac surgery patients. Twelve patients received 3.0 mg/kg/hr, 11 patients received 1.0 mg/kg/hr and 10 patients received placebo. The average age of patients was 69 years.

Patients infused at the lower dose achieved blood levels of Glypromate® of 960 ng/mL and those infused at the 3 fold higher dose had a maximal level of 3,508 ng/mL. The study therefore confirmed a linear relationship between dose and exposure, such that a 3-fold increase in dose corresponded to a 3-fold increase in exposure of the patient to the drug. This type of relationship is desirable because it enables clinicians to predict the exposure of the patient to different doses of the drug. Non-linear pharmacokinetics can lead to poor predictability of exposure to a particular dose.

At both doses, Glypromate® displayed an elimination half-life of 2 to 3 minutes, meaning that the concentration of Glypromate® in the blood halved every 2 to 3 minutes. This is in line with previous predictions. It also adds to the safety profile of the drug in that it departs the body rapidly after the time it is needed

The independent Data Safety Monitoring Committee (DSMC) had determined earlier that there were no major concerns regarding the safety of Glypromate®.

“The Phase 2a trial has shown Glypromate® to be as safe as the placebo and confirms the predicted pharmacokinetics” said Dr Doug Wilson, Chief Medical Officer of Neuren.

“These Phase 2a results reinforce our confidence to move forward into Phase 3 later this year. Neuren is in the final stages of selecting the key centres that will participate in its Phase 3 clinical trial, which will be conducted in the USA, Australia and New Zealand” Mr David Clarke, CEO of Neuren added.

The Phase 2a trial data is now being prepared for peer-reviewed publication.

Appendix

The following additional information is provided in accordance with the Code of Best Practice for Reporting by Life Science Companies:

A Randomized, Double-blind, Placebo-controlled study of Glypromate® in Patients undergoing Coronary Artery Bypass Graft Surgery

Protocol Abbreviated Name:	**S**tudying **N**eurons **U**sing **G**lypromate **(SNUG)**
Name of Investigational Agent:	**Glypromate®** (glycyl-L-prolyl-L-glutamate)
Study Centres:	4 centres in New Zealand, 1 in Australia
Phase of Development:	2a
Objectives:	**Primary:** To investigate the pharmacokinetics of Glypromate® in post-CABG patients **Secondary:** To monitor the safety profile of Glypromate® treatment compared to placebo in CABG patients.
Design:	Randomised, double-blind, placebo-controlled, parallel-group study
Proposed Sample Size:	
Stage 1:	Up to 12 patients randomised to open-label active treatment at 1 centre
Stage 2:	30 in total, randomized in a 1:1:1 treatment allocation
Inclusion criteria:	Patients 60 years of age or over undergoing non-urgent coronary artery bypass graft surgery with or without valve replacement/repair
Dose, method of administration:	
Stage 1:	Glypromate® given as a continuous 4-hour i.v. infusion administered at a dose of either 1 mg/kg/hr or 3 mg/kg/hr. The infusion commenced at the start of chest closure.
Stage 2:	Glypromate® or matched placebo given as a continuous 4-hour i.v. infusion, administered at a dose of either 1 mg/kg/hr *or,* 3 mg/kg/hr. The infusion commenced at the start of chest closure.
Reference therapy:	Placebo - normal saline for injection
Trial Standard	ICH GCP and all applicable local regulations
Actual recruitment:	
Stage 1:	2 open label patients were recruited. One patient received Glypromate 1 mg/kg/hr x 4 hours and one patient received Glypromate 3 mg/kg/hr x 4 hours.

Stage 2:

Ten (10) patients received placebo.
Ten (10) patients received Glypromate 1 mg/kg/hr x 4 hours.
Eleven (11) patients received Glypromate 3 mg/kg/hr x 4 hours. One additional patient was recruited as a replacement for a patient with an incomplete set of samples for pharmacokinetic analysis. All patients are included in the safety analysis.

Demographics:

Average Patient age was 69.7 yrs (60.9–93.1 yrs)
31 males and 2 females entered the study.

Primary Endpoint results:

Conclusions derived from complete data set

Parameter	1.0 mg/kg/hr (n=11)	3.0 mg/kg/hr (n=12)
Maximal concentration (C_{max}) (ng/mL)	958.9	3508.2
Time to maximal concentration (T_{max}) (hr)	1.5	0.54
Area under concentration time curve AUC_{0-t}	5567.4	14789.4
Terminal half life (min)	2.99	2.84
Clearance (L/hr/kg)	0.74	0.85
Volume of Distribution (L)	4.33	4.92
Normalised Volume of Distribution (L/kg)	0.0554	0.0577

Secondary Endpoint results:

All safety data was reviewed by an independent Data Safety Monitoring Committee. No drug-related adverse effects were noted.

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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