

## **Neuren Pharmaceuticals**

Market Update October 2005



# 1 Corporate Overview



#### **Corporate Snapshot**

Neuren is a biotech development company targeting neuroprotection, metabolism and cancer

Neuren's lead products protect against brain damage

Glypromate® has been accelerated into Phase-3 clinical trials following a productive meeting with FDA

ASX code:	NEU
Share price:	\$0.75 (as at 13 October 2005)
Market cap:	\$75m
Cash:	\$9.1m (as at 1 October 2005)
Shares on issue:	100.0m (of which 62.5m are in escrow)
	20.5m options

#### Register

Neuronz Ltd:	12.4%
NZ Seed Fund Management Ltd:	11.4%
Macquarie Bank Tech Funds:	9.6%
Pfizer Inc:	8.1%
K One W One:	6.7%
Top Twenty:	74.5%

#### Share Price Performance Since IPO



Repairing brain damage from aging and injury



### Value Proposition: Why Invest in Neuren?

- News flow over next 6 12 months should lead to a significant re-rating in stock
  - Glypromate® enters Phase-3 trials in CY2006: Only a very small number of Australian Biotechs are testing Phase-3 products
  - NNZ-2566 currently being tested by the US in the US Department of Defence with extremely encouraging results : Enters clinic in early CY2006
- Breadth and quality of product portfolio
  - Offers <u>choice</u>: Strategic flexibility re- development (large portfolio) and commercialisation of product portfolio (out-license or fund affordable Phase-3).Potentially first in Market.
  - Attracted world class partners: Pfizer, US Department of Defence and Metabolic
- Addresses a large and growing market with unmet needs
  - Neuroprotection is a multi-billion dollar market (traumatic brain injury; stroke; Parkinson's disease, Alzheimer's disease; Multiple Sclerosis)
- Extensive international experience in drug development & commercialisation
  - 100+ years of clinical development in over 50 countries
  - Strong US focus and Big Pharma commercialisation experience



#### **Recent Events:**

- Initiated Phase 2a trial with Glypromate®
- Accelerated Glypromate® to Phase 3 following productive meeting with FDA: Expected to enter Phase 3 in CY2006
- NNZ-2566 (follow up compound to Glypromate®) delivered positive results in testing with WRAIR: Expected to enter Phase 1 in early CY2006
- Expanded contract with WRAIR
- Executed collaboration with Metabolic

#### **Recent Accolades:**

- BRW Top Ten Stocks under \$1.00: Only biotech selected
- Awarded NZ 2005 Biotechnology of the Company of the Year
- Rates best IPO in last 12-months (eG Capital, PwC)
  - Issue price: \$0.40; Current price: \$0.75



# 2 Product Development



### Lead Products are Key Value Drivers

	<ul> <li>Naturally occurring compound that protects against neuronal damage</li> <li>Many medical conditions result from damage to nervous tissue in the brain</li> </ul>
Glypromate®	<ul> <li>Key Features: Exhibited potent neuroprotective activity; Small enough to cross blood-brain barrier, long therapeutic window (11 hours)</li> </ul>
	Accelerated the clinical development plan: Phase 3 in CY2006

	<ul> <li>Modified version of Glypromate<sup>®</sup> which exhibit potent neuroprotective activity and is orally bioavailable</li> </ul>
NNZ-2566	<ul> <li>Currently being tested by the US Department of Defence (WRAIR) with extremely encouraging results</li> </ul>
	<ul> <li>Key Features: Oral bioavailability means it could be used to treat chronic indications (Parkinsons, Alzheimers, MS etc) and long therapeutic window (11+ hours)</li> </ul>
	Enter the clinic early CY2006



#### **Discovery Pipeline Offers Excellent Potential**

Diketopiperazines (DKPs)	<ul> <li>Small molecules that are both neuroprotectant and stimulate neurite growth for neurodegenerative diseases</li> <li>Most advanced compound, NNZ-2591, is currently being tested in animals</li> </ul>
Growth Hormones (GH)	<ul> <li>Growth hormone program is focused on finding molecules for the treatment of cancer (promote or inhibit growth in certain tumour types)</li> <li>Collaborations with Pfizer and Metabolic Pharmaceuticals</li> </ul>
Neural Regeneration Peptides (NRPs)	<ul> <li>Peptides that stimulate neuronal regeneration and may have application for stem cell based therapies</li> </ul>
Liggins Institute	<ul> <li>Under an agreement with the Liggins Institute (University of Auckland) Neuren has an automatic right-to-own any intellectual property generated in the fields of neuroprotection, growth and metabolism</li> </ul>



#### **Development Pipeline**



#### Glypromate®

- NNZ-2566 (acute/sub-acute)
- NNZ-2566 (oral)
- DKP's
- MC's
- NRP's
- GH Antagonists
- GH Variants

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#### **CNS Product Portfolio**

- 6 Compound Families
- Lead compound in Phase II and entering Phase III in CY2006

#### **Growth Hormone Portfolio**

 Collaborations with Pfizer and Metabolic

Extensive development portfolio offering several means of delivering value



# 3 Glypromate® and Clinical Development



### **Glypromate® - Lead compound**

- Molecule derived from the IGF-1 growth factor, but with distinct properties
- Naturally occurring
- Exceptional neuroprotection characteristics





#### **Glypromate® and the FDA**

- Pre-investigational new drug meeting with the US FDA
- Poised to commence Phase 3 clinical trial in 2006 (originally planned for 2008) directly from Phase 2a
- 400-500 patient multi site trial
- Approximate cost <AUD\$10 million
- Completion within 18 months

#### **Commercial Benefits**

- Significant cost savings for Neuren
- Positions Neuren as one of very few ASX-listed companies poised to enter Phase 3
- Potential for Neuren to self-fund Phase 3 trial and take drug to market
- Reduces time to market for the drug
- Increases potential to out-license and generate nearer term revenue



#### **Clinical Strategy**





### **Key Short-Term Milestones (CY2005)**

Glypromate®		
Completion of Phase 2a trial	Q4 CY2005	

NNZ-2566		
In-vivo efficacy results	Q3 CY2005	
Oral development results	Q4 CY2005	
Pre-clinical toxicology completed	Q4 CY2005	



### **Key Medium-Term Milestones (CY2006)**

Glypromate®		NNZ-2566		Other Compounds	
Results of Phase 2a Trial	Q1 CY2006	Third-stage contract with US Dep't of Defence	Q1 CY2006	NRP in vivo programme completes	Q3 CY2006
Commence Phase 3 Trial	Q3 CY2006	Commence Phase 1 Trial	Q1 CY2006	DKP's – Lead candidate selection	Q2 CY2006
Major value driver – One of only a very small group of Australian companies to enter Phase 3		Phase 1 results	Q2/3 CY2006		
		Oral – Chronic models complete	Q2 CY 2006		
		Commencement of Phase 2a	Q4 CY2006		



## Why Do Drugs Fail?

- Why do drugs fail?
  - Safety
  - Manufacturing The reason that 2/3 of drugs fail
  - Toxicology \_
  - Efficacy

Neuren's Glypromate®and 2566 Development Program has effectively mitigated against these development risks

- The Glypromate® Development Program:
  - Look at competitive space and why other drugs have failed
  - Identify all likely challenges and risks early
  - Plan and eliminate as many as possible
  - Ensure science and clinical development programs are conducted correctly
  - Work closely with FDA : Glypromate® is potentially "first in market" (i.e. no drug comparison thereby reducing efficacy development risks)

Neuren understands and manages drug development risk



### Jain Report\* Criteria

#### Why have other neuroprotection drugs failed?

	Neuroprotection for Stroke (high hurdle)		
•	Poor Therapeutic Ratios**	1	
•	Cross BBB	$\overline{\checkmark}$	
•	Small Molecule	$\checkmark$	
•	Drug Administered 4 plus hours	$\checkmark$	
•	Safety Profile	$\checkmark$	
•	IV Administration	$\checkmark$	
•	Oral Bio availability desirable	√ (analogue)	
•	Water Soluble	$\checkmark$	
•	No anti-coagulant effect	$\checkmark$	
•	Combined with thrombolytic	ТВС	
•	Adequate animal models	$\checkmark$	
•	Ability to differentiate heterogeneous stroke population in Trial	<u>CABG</u>	
	*Jain Pharma Biotech Report, June 2002, p 98-99		
	**Dosage ratio: Efficacy/Toxicity		



# 4 Commercialisation and Market Metrics



## **Commercialisation Strategy**

- 1. Build World-Class Partnerships Early
  - Joint development (e.g. Pfizer, WRAIR, Metabolic Pharmaceuticals)
  - External verification (FDA IND)
- 2. Move Quickly into Clinical Trials
  - Acute CNS (CABG, TBI...) followed by chronic CNS diseases
- 3. Maintain Multiple Products and Parallel Development
  - Alzheimers, Parkinsons, Cancer

Effective commercialisation of portfolio and re-rating of stock:

- Drug co-development
- Out-licensing potential
- Contract revenue
- Lower cost, faster development of portfolio



### Large and Growing Market with Unmet Needs

Indication	Cases per Year (USA)	Market Size US\$	Effective Treatment
Neuroprotection			
Bypass Surgery	400,000	\$2.0b	Ν
Traumatic Brain Injury	1,000,000	\$1.0b	Ν
Stroke	800,000	\$3.5b	Ν
Parkinson's Disease	3,000,000	\$2.0b	Y/N
Alzheimer's Disease	4,500,000	\$2.5b	Y/N
Multiple Sclerosis	800,000	\$2.5b	Y/N



### **Limited Competition**

Acute Neuroprotection	No drug currently on the market		
	Trials ongoing for CABG (Medicure, Alexion, NIH)		
	Trials ongoing for stroke, TBI		
	<ul> <li>Neuren's products have superior profile</li> </ul>		
Chronic Neuroprotection and Neuroregeneration	<ul> <li>Limited effectiveness of current offerings</li> <li>Neuren's NP's animal model results</li> <li>Oral NNZ-2566 in development</li> </ul>		



# 5 Board and Senior Management



#### **Experienced Board with Direct Experience in Commercialising Drugs**

- Neuren's Board has extensive experience and expertise in drug development, regulatory approval and commercialisation
- Two of Neuren's Board have major multinational pharmaceutical experience with direct expertise in successfully taking drugs to global markets

Board of Directors		
Dr Robin Congreve (PHD)	Leading NZ international businessman	
<i>Chairman</i>	Partner in Oceania and Eastern Group	
David Clarke (ME, MBA)	Senior positions in healthcare, technology and finance	
<i>Executive Director, CEO</i>	Former CEO, South Auckland Health	
Dr Douglas Wilson, MB, ChB,	Former SVP, World Head Medical and Regulatory	
PHD	Affairs, Boehringer Inglehim	
<i>Non-Executive Director</i>	Participated in bringing 10 new drugs to market	
Dr Graeme Howie, PhD	Former Pfizer New York; Senior exec. Pharmacia	
Non-Executive Director	20+ years big pharma drug development expertise	
Tom Amos, B.Eng	Director, Macquarie Bank (Macquarie Technology	
Non-Executive Director	Ventures)	
Trevor Scott, FCA	Leading NZ businessman	
Non-Executive Director	Chair of Blis and PEBL	



## **Management and Scientists**

Management and Scientists		
Prof Peter Gluckman (MB, DSc, FRS)	Pediatrician, endocrinologist, Director of Liggins Institute	
cso	Former Dean, University of Auckland Medical School	
	World authority in neuroscience and endocrinology	
Dr Mike Bickerdike (Phd )	Formerly private UK biotech	
Managing Scientist	Clinical and Collaboration/JV experience (Roche)	
Lawrence Glass (BSc, MSc)	25+ years experience in biomedical research and product development	
СВО	Former CEO of a CRO that was a subsidiary of a NYSE public company	
Robyn Murdoch (MBA)	Extensive experience in Clinical Development	
СДО	Formerly Pfizer, Roche, Lilly	
Maggie Scott (MBA)	18 years experience in Clinical Trials	
Head Clinical Operations	Formerly Pfizer, Roche, Novartis, Lilly	
Rob Turnbull (Bcom, CA)	Corporate finance experience in Biotech	
CFO	Formerly with PriceWaterhouseCoopers	
Dr Kathryn Jones (PhD)	Neuroscientist with Masters in Commercial Law	
BD	Extensive IP and project management experience	



# 6 Conclusion



### **Investment Highlights**

- Stage of Development: Glypromate® enter Phase 3 in CY2006
  - FDA verification...Safety and need
  - Further CY2006 milestones focused on increasing investor value
- Breadth and quality of portfolio
  - World class partners: Pfizer, US Department of Defence, Metabolic
  - Not a one product company
- Extensive international experience in drug development and commercialisation
  - 100+ years of clinical development experience in 50+ countries
  - US Big Pharma focus
- Products address a large, growing market with unmet needs
  - Multi-billion dollar market with limited competition
- Favourably priced with significant investor upside





**Neuren Pharmaceuticals** 

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# Appendices



### **Neuren's Core CNS Biology**





### **Neuronal Regeneration Peptides**





- Promote neurite and axonal growth
- Promote neural stem cell proliferation, migration and differentiation
- Optimal Attributes for a Neural Recovery Drug



### **GH – Implication in Breast Cancer**

#### Without Growth Hormone



 Cells that do not express GH remain non aggressive and non invasive

#### With Growth Hormone



• Cells made to express GH become aggressive, proliferative and invasive



**Collaborations with WRAIR and Metabolic** 

US Army Stage 2 WRAIR	Metabolic Deal
<ul> <li>TBI Stage 1 results confirmed</li> <li>US Army confirmed 2nd Stage</li> <li>Move to Pre-Clinical <ul> <li>Share Costs</li> <li>Save 50%</li> </ul> </li> <li>"Goal advanced drug for brain injury"</li> <li>Stage 3 underway</li> </ul>	<ul> <li>Faster Development</li> <li>Less Costs <ul> <li>MBP 2:1</li> </ul> </li> <li>Government Grant A\$585,000</li> <li>Utilise MBP Peptide Chemistry Skills</li> </ul>



## **Executive Staff Experience**

#### Drugs to market in USA: 100+ years experience, Multiple IND's

- Atrovent for common cold, Atrovent nasal for allergic rhinitis, Combivent for COPD, Asasantin for TIAs, pameprexole for Parkinson's, Meloxicam as a NSAID for osteoarthritis, Spiriva for COPD, Nevirapine for HIV, Flomax for prostatic hypertophy, Telmisartan for hypertension, and Telmisartan/hydrochlorothiazide combo for hypertension, bolus thrombolytic for AMI, TPA for stroke
- Plus worked on drugs in Hepatitis C, various anti cancer drugs, anti adhesion molecules in stroke and burns, NMDA antagonists in stroke, thrombolytics in stroke, bolus thrombolytics for acute myocardial infarcts, drugs for Alzheimer's and depression, P38 MAP kinase inhibitors for Rheumatoid arthritis, drugs to inhibit nausea and vomiting after intense cytotoxic therapy for cancer, drugs for migraine, ICAM receptor inhibitors for rhinovirus induced common cold, Non-peptidic HIV protease inhibitors for HIV