



pharmaceuticals

Neuren Pharmaceuticals

Annual Shareholders' Meeting

May 2010

2009: A Watershed Year for Neuren

- **Prioritized focus on NNZ-2566 and Motiva™**
- **Reduced operating costs**
- **Obtained approval and Fast Track designation for NNZ-2566 IND**
- **Secured a further \$14 million in non-dilutive funding from U.S. Army (US\$18m total)**
- **Established subsidiary, Perseis Therapeutics, to develop oncology assets in partnership and with funding from the NZ Breast Cancer Research Trust**
- **Developed strategic relationship with Cato Research, a U.S. based global CRO**
- **Enhanced board of directors—Dr. John Holaday**
- **Secured new funding**

Positioned for Success

- **Strong clinical candidates in neurology**
 - Two drugs in Phase II clinical trials for CNS indications
 - Opportunities to leverage NNZ-2566 in niche indications
 - Chemo therapy induced ototoxicity and neuropathy
 - Non-convulsive seizures associated with brain lesions (cancer, stroke)
 - Perinatal asphyxia
 - Opportunities for Motiva™ in additional indications
 - Parkinson's disease, depression, traumatic brain injury
- **Highly promising cancer portfolio (Perseis Therapeutics)**
- **Pipeline backed by strong patent estate**
- **Experienced, dedicated staff**
- **Proven ability to execute on clinical trials**
- **Funded through 2011 by combination of equity, convertible debt and grants**

Focused pipeline with two dynamic clinical programs

■ **Motiva™ (nefiracetam)**

- Treatment for psychiatric and behavioral effects of stroke, TBI and other chronic CNS disorders
- Clinical efficacy data in multiple Phase II and III trials including Phase IIb under US IND
- Phase IIb trial to be initiated in Q2 2010
 - Apathy in post-stroke patients
 - Funded by grant from the National Health & Medical Research Council to the University of Western Australia (Sergio Starkstein, MD, PhD)

■ **NNZ-2566**

- Phase II INTREPID²⁵⁶⁶ trial initiated in May 2010 for traumatic brain injury
- Partnership with US Army since 2004
- New patent for non-convulsive seizures
- Four peer reviewed papers in 2009, numerous posters and abstracts
- Development largely funded by U.S. Army grants

NNZ-2566

■ **Composition**

- Synthetic analogue of IGF-1(1-3) – composition of matter and method of use patent issued: expires in 2023

■ **Multiple modes of action**

- Molecular: inhibits inflammatory cytokine and apoptotic gene expression
- Cellular: inhibits microglial activation and neutrophil infiltration
- Functional: inhibits post-injury seizures

■ **Improved pharmacokinetics and oral availability**

- Intravenous formulation for moderate to severe TBI
- Oral formulation for mild TBI

■ **Phase II INTREPID²⁵⁶⁶ trial initiated in May 2010**

- Phase Ib completed in Nov. 2007; drug safe and well tolerated
- IND opened Feb 2009; Fast Track designation granted June 2009

■ **Partnership with U.S. Army since 2004 ~ US\$18M**

- Mechanisms of action and pharmacology discovered by Army scientists

Major Concern with No Available Therapy

- **Large and growing problem**

- Traumatic brain injuries (TBIs) account for 1.7 million hospital visits and 52,000 deaths each year -- almost a third of injury-related fatalities in the U.S.
- Major cause of accidental death among young people
- Leading cause of mortality and disability among military personnel

- **Current treatment options**

- Very little can be done to reverse the initial brain damage caused by trauma
- Supportive care focuses on stabilizing patient and preventing secondary injuries

- **Secondary injuries**

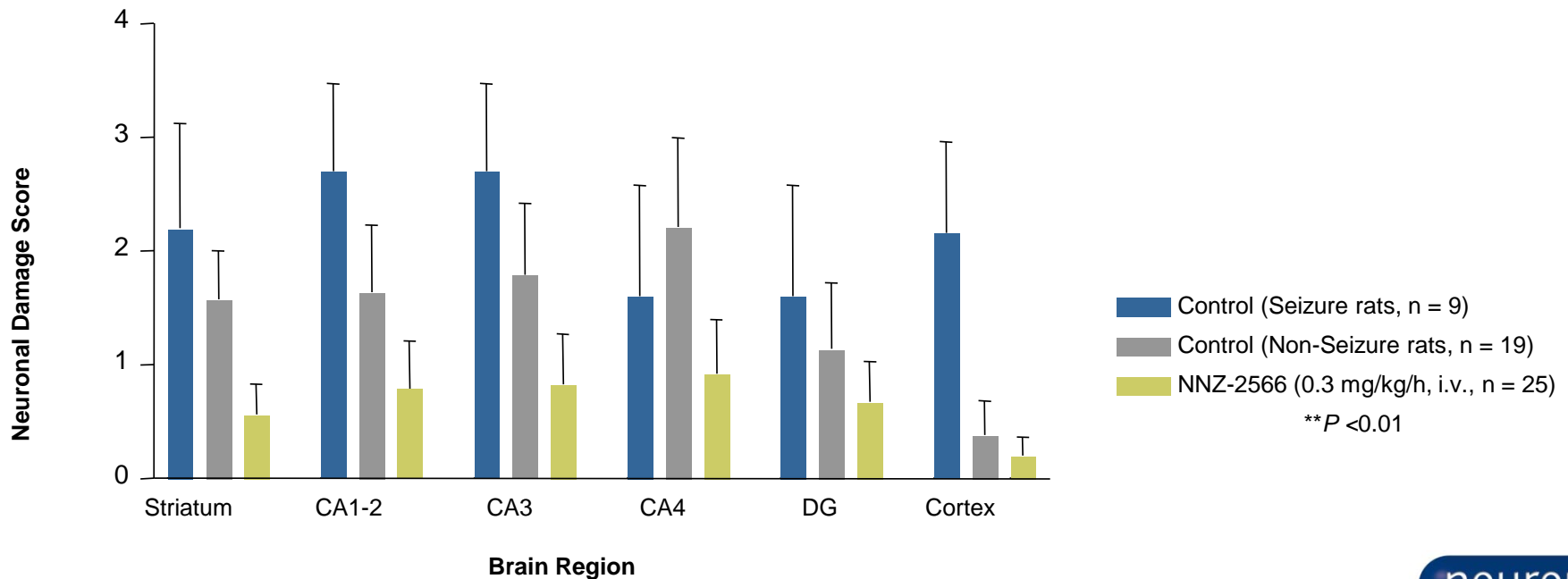
- Up to 80% of cell death results from processes caused by the primary injury

- **Provides clear development path**

- Time of injury known
- Time to admission in trauma center and possible treatment relatively short
- Standard, widely-used assessments provide validated endpoints

Non-convulsive Seizures (NCS): Secondary Injuries

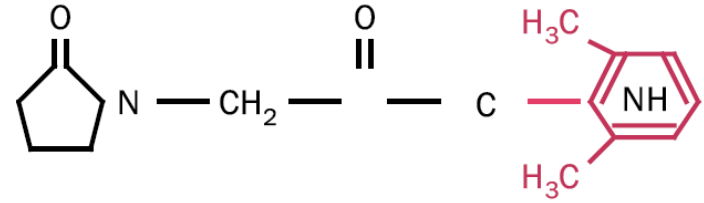
- **NCS are associated with significantly worse outcomes in TBI patients**
 - Frequently lead to spreading cortical depression, status epilepticus and death
 - Not effectively prevented or treated with anti-epileptic drugs
- **Dual strategy: prevent onset and stop or reduce frequency after onset**



Leading Edge TBI Program

- **Dose-dependent efficacy in all brain injury models**
 - Penetrating and concussive TBI, NCS, 2 focal stroke and 1 global HI model
 - Models with hemorrhagic, hypoxic, ischemic, reperfusion components
 - Therapeutic time window: up to 4 hrs in TBI; up to 7 hrs in stroke/HI models
- **Multiplicity of effects**
 - Neuroprotection, seizures, gene expression, cell regulation, functional recovery
- **Clinical trial design**
 - Stratification—2:1 (moderate : severe)
 - Randomization—2:1 (active : placebo)
 - Wide range of clinical and physiological endpoints (incl. EEG) supported by preclinical data
 - Neuropsychological endpoints are approvable and more sensitive than GOS-E
 - Dose-escalation—primarily safety but with dose-ranging component
- **Regulatory strategy**
 - No particular endpoint or pre-specified magnitude of effect required by FDA
 - One validated measure + one functional measure = approval
 - Approval possible with single pivotal trial

Motiva™ (nefiracetam) Overview



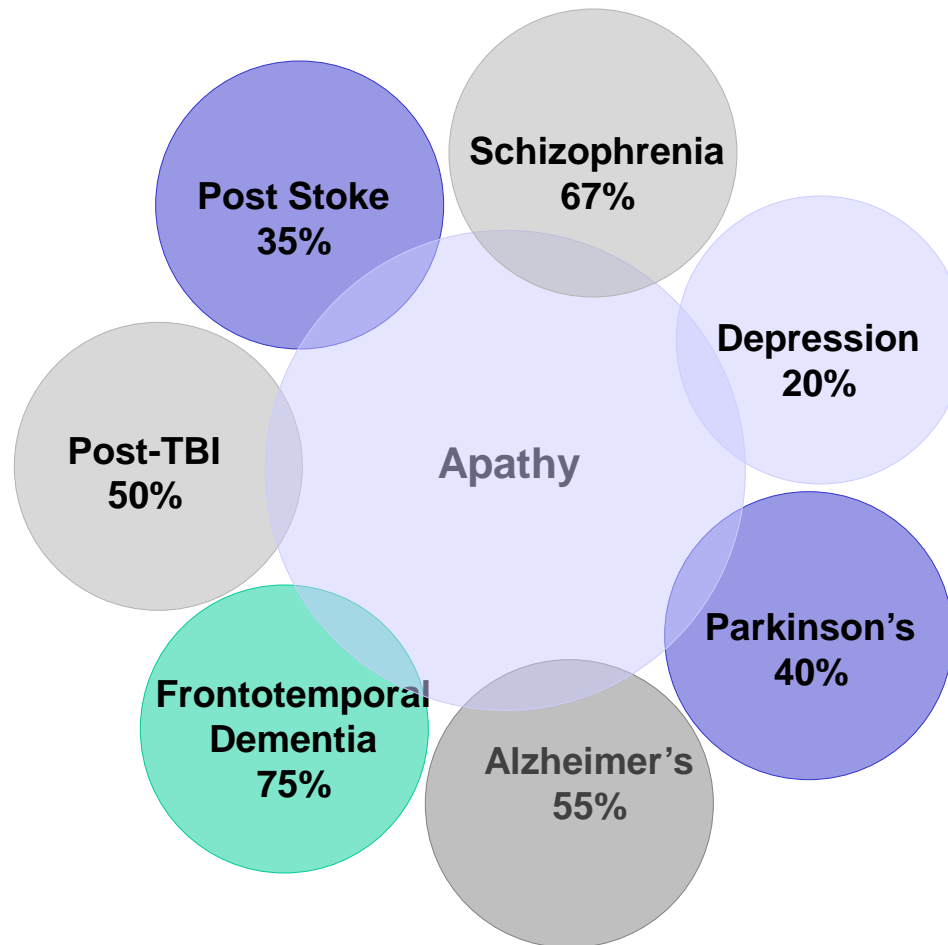
■ Origins

- Drug licensed from Daiichi by Hamilton Pharmaceuticals
- Belongs to well-known class of compounds (acetams)
- Well-characterized effects in neurobehavioural, cognition, epilepsy models
- Safety confirmed in 1,700+ patients in multiple clinical trials

■ Confirmed clinical efficacy in trials in stroke patients

- Japan: 3 Phase IIa, 1 Phase Ib, 2 Phase III trials
- US/Canada: 1 Phase IIb trial (stroke patients with diagnosed depression)
 - Double-blind, placebo-controlled, 2 dose trial
 - 159 patients; 600 mg/day, 900 mg/day or placebo X 12 weeks
 - Primary endpoint: Hamilton Depression Scale (HAM-D)
 - Secondary endpoints: Apathy Scale, Symbol Digit Modality Test (SDMT), Burden Inventory (BI), other ADL and psychiatric tests
 - Statistically significant, time and dose-dependent effect on apathy (70 patients)
 - Repeated measures ANOVA for time (p=0.001)
 - Repeated measures ANOVA for time by treatment group (p=0.05)
 - Repeated measures ANOVA for time by 900 mg/day vs. placebo (p=0.01)
 - Dose-dependent effect on remission (75% reduction in apathy score) (p=0.031)

Apathy: Prevalence in Multiple Disorders



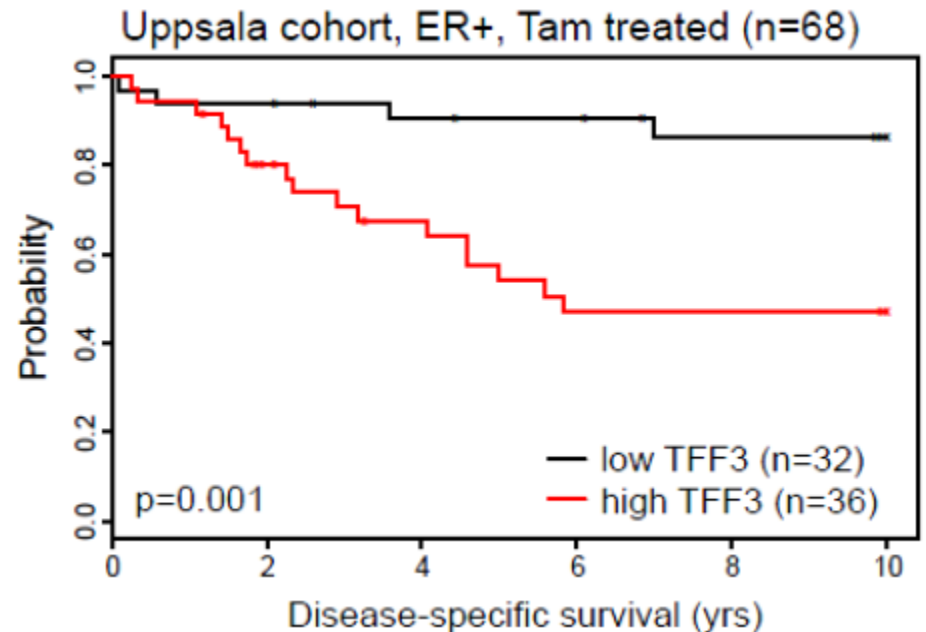
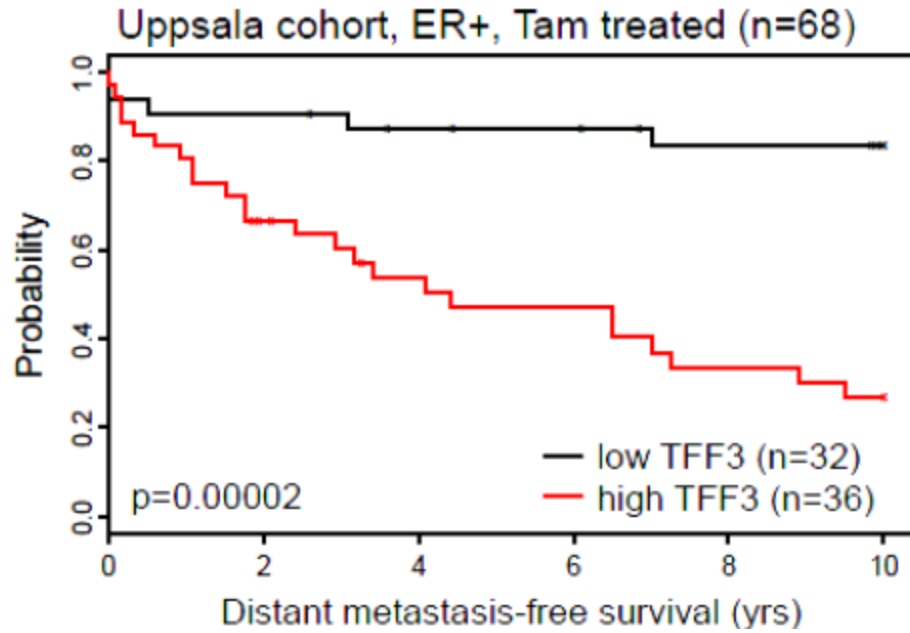
Drugs in Development for Apathy as Primary or Secondary Endpoint

Study	Sponsor
Study of Rivastigmine to Treat Parkinsonian Apathy Without Dementia (CHoPA-I)	Novartis
Carbidopa/Levodopa/Entacapone Verses Immediate Release (IR) Carbidopa/Levodopa on Non-Motor Symptoms in Patients with Idiopathic Parkinson's Disease	Novartis
A comparison of Sertraline-Reboxetine Combination Therapy Versus Sertraline of Reboxetine Monotherapy in the treatment of major depression	Pfizer
Methylphenidate for Apathy in Alzheimer's Dementia	Dept of Veterans Affairs
Rasagiline and Apathy in Parkinson's Disease	L'Hospital de la Santa Creu I Sant Pau (Spain)
Apathy Associated with Alzheimer's Disease	Sunnybrook Health Sciences Center
Wellbutrin XP Effects on SSRI Induced Changes	Indiana University School of Medicine
Amantadine for the Treatment of Behavioral Disturbance in Frontotemporal Dementia (FTD)	Johns Hopkins University (NIH)
Acetylcholinesterase Inhibitors to Improve Cognitive Function and Overall Rehabilitation after a stroke	National Institute of mental Health
Antidepressant medication plus donepezil for treating Late-Life Depression	National Institution of Mental Health/ NIH

Perseis Therapeutics: Profile

- **Developing antibody therapeutics for the treatment of breast and other cancers**
 - Established April 2009 by Neuren Pharmaceuticals and the Breast Cancer Research Trust
 - Seed funding of NZ\$1.18M from Breast Cancer Research Trust
 - New Zealand Company
- **Three associated research programs aimed at targeting cancers (breast, prostate, colorectal and gastric cancer) with monoclonal antibodies**
 - Targets the Trefoil Factors (TFF-1 and TFF-3) and Growth Hormone found to play a significant role in the growth and spread of cancer
 - TFF-3 strongly associated with tamoxifen resistance in breast cancer
- **First major development milestone expected Q4 2010**
 - *in vivo* efficacy of antibodies to support selection of therapeutic candidates for further development or partnering discussions

TFF-3 role in breast cancer survival



Further Information

New Zealand

Level 2, 57 Wellington Street
Freemans Bay 1011, Auckland
New Zealand

+64 (9) 3700 200
1 800 259 181 (Australia Freephone)

USA

3 Bethesda Metro Center, Suite 700
Bethesda, Maryland 20814 USA

Larry Glass, CEO
+1 (301) 941 1830
lglass@neurenpharma.com