
# Investor Presentation

## May 2013

# Forward Looking Statement

This presentation contains forward looking statements that involve risks and uncertainties. Although we believe that the expectations reflected in the forward looking statements are reasonable at this time, Neuren can give no assurance that these expectations will prove to be correct. Actual results could differ materially from those anticipated. Reasons may include risks associated with drug development and manufacture, risks inherent in the regulatory processes, delays in clinical trials, risks associated with patent protection, future capital needs or other general risks or factors.

# Agenda

- Company snapshot
- Investment thesis
- Scientific foundation
- Intellectual property
- Strategy
- Clinical trials
  - TBI trial
  - Rett Syndrome trial
  - Fragile X Syndrome trial
  - Concussion trial
- Shareholding and financial position
- Expected news flow

# Company Snapshot

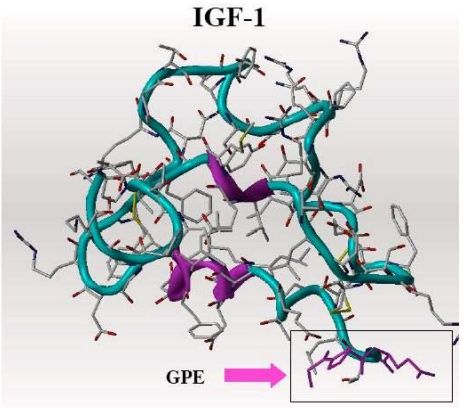
- Origins
  - Created in 2004 by merger of two companies formed around University of Auckland IP
  - Listed on the ASX in February 2005
- Leadership
  - Richard Treagus, Executive Chairman
  - Larry Glass, CEO & Managing Director
  - Joe Horrigan, VP for Clinical Development & Medical Affairs
  - CFO – Melbourne-based as of Q3-2013
- Key strategic relationships
  - US Army Medical Research & Materiel Command
  - International Rett Syndrome Foundation
  - Fragile X Drug Validation Initiative
- Operations
  - Finance and  shareholder relations relocating to Melbourne
  - Clinical development consolidating in the US

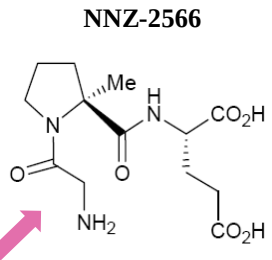
# Investment Thesis

- Lead clinical stage molecule has unique biology directly applicable to many key CNS conditions
- ~US$26m in non-dilutive funding from the US Army supports two clinical trials, funded development of the oral form of NNZ-2566
- Strong patent portfolio: composition of matter, formulation, methods of use
- Clinical trials in four distinct therapeutic areas provide multiple opportunities for success
- Rare, orphan, under-served conditions accorded regulatory flexibility with faster path to approval
- Development costs for rare/orphan conditions are lower – fewer trials, fewer subjects per trial
- Cost to progress from preclinical efficacy to clinical proof of concept is modest – significant increase in value with clinical proof of concept
- Execution further enhanced by organizational restructuring
- Capacity to wait for optimum timing on partnerships increases shareholder value

# Scientific Foundation

- IGF-1 is one of the primary growth factors in the CNS
- Glypromate is a key part of the brain's response to injury and stress
- **NNZ-2566 is a synthetic analogue of Glypromate**




- Addresses pathology underlying acute and chronic CNS conditions and disorders – not just targeting symptoms
  - Inflammation
  - Microglial function
  - Synaptic plasticity (inter-neuronal communication)
  - Neuronal loss due to apoptosis (programmed cell death)
  - Abnormal electrical activity (e.g., seizures)
- One molecule potentially treats a wide range of poorly treated CNS conditions at the cellular and molecular level

# Intellectual Property

- Robust patent estate
- No royalty burden on lead molecules
- NNZ-2566 and other GPE analogues
  - 7 issued patents covering composition, oral formulation and methods of use
  - 7 pending applications covering composition, oral formulations and methods of use
  - Broad method of use claims (TBI, stroke, non-convulsive seizures, autism spectrum disorders, cognition, Parkinson's, Alzheimer's, Huntington's, neurodegeneration, neuropathy, MS, diabetes)
  - Remaining patent life between 9 and 15 years
  - Additional market exclusivity may be available via Orphan and Pediatric Drug designations
- NNZ-2591 and other bicyclic analogues
  - 3 issued patents covering composition, formulation and methods of use
  - 3 pending applications covering composition, formulation and methods of use
  - Broad method of use claims (neurodegeneration, Parkinson's, neuropathy, cognition)
  - Remaining patent life between 11 and 15 years

# Strategy

- Build on the unique biology of NNZ-2566 to pursue multiple indications and commercial opportunities
- Expand therapeutic focus to include both **acute** and **chronic** conditions
- Criteria for selecting therapeutic targets
  - Significant unmet need with no approved drugs
  - Opportunity to be first in class; limited clinical-stage competition
  - Regulatory advantages – eligible for Fast Track, Orphan Disease, Breakthrough Therapy
  - Clear, accelerated pathway to approval
  - Strong support from advocacy groups and other stakeholders
  - Clinical endpoints tied directly to known biology and results in animal models at clinical doses
- Realising value
  - Eliciting a clinical signal
  - Advancing the CMC package
  - Strengthening the IP portfolio
  - Maintaining dialogue with potential partners

# Key Programmes

# TBI and concussion: rationale

- NNZ-2566 inhibits inflammatory cytokines, pathological microglial activation, apoptosis and necrosis
- NNZ-2566 improves functional recovery, preserves cognitive function, inhibits post-injury seizures
- > 1.5 million head injuries annually in the US alone; >75% are mild or concussion
- Leading cause of death and disability, especially in young people and the elderly
- Partnership and ~$26 million in non-dilutive funding by US Army
- Only late-stage competition is progesterone
- $4+ billion estimated global market potential

# TBI (*INTREPID-2566*)

- Phase II randomized (2:1), placebo-controlled, fixed dose escalation, safety and efficacy study
- 260 subjects, ages 16-75 with moderate to severe TBI (Glasgow Coma Scale 4-12)
- NNZ-2566 IV solution or placebo administered within 8 hours of injury as a 20 mg/kg bolus followed by 72 hours of infusion at 1, 3 or 6 mg/kg/hr (30, 30 and 200 subjects, respectively)
- Endpoints: safety, functional status at 1 and 3 months, cognitive and neuropsychological function at 1 and 3 months, non-convulsive seizures and biomarkers in the first 5 days
- 2 protocols: Legally Authorized Representative consent and Exception from Informed Consent
- Goal: 18 Level I and II US trauma centers with 10 under EFIC
- 109 subjects enrolled to date

# Concussion (TBI-003)

- Phase II randomized (1:1:1), placebo-controlled, fixed dose safety and efficacy study
- 132 subjects, 18-55 with mild TBI (Glasgow Coma Scale 13-15) and a pre-injury computerized neurocognitive assessment
- NNZ-2566 oral solution or placebo administered within 24 hours of injury at 35 or 70 mg/kg twice daily for 7 days
- Endpoints: safety, change from baseline cognitive function and time to return to pre-injury baseline cognitive function assessed at 1, 2, 4 and 8 weeks
- Sites: 2-3 US military training facilities
- Start date to be determined

# Neurodevelopmental disorders: rationale

- **Rett Syndrome**
  - NNZ-2566 increases dendritic length and branching
  - NNZ-2566 improves signal transmission between neurons and improves survival
  - Cause of profound disability and huge financial burdens for >50,000 patients and families
  - No other sponsor-led trials
  - $2+ billion estimated global market potential
- **Fragile X Syndrome**
  - NNZ-2566 normalizes activation of pathways controlling signal transmission between neurons
  - NNZ-2566 reverses core molecular, cellular, anatomic and behavioral deficits
  - Leading genetic cause of intellectual disability in >100,000 people worldwide
  - Significant big pharma interest and participation
  - $4+ billion estimated global market potential

# Rett Syndrome Phase II (RTT-001)

- Phase II randomized (2:1), placebo-controlled, dose escalation, safety and efficacy study
- Up to 60 (48 complete) female subjects ages 16-40 years with a diagnosis of Rett Syndrome
- Subjects stratified 1:1 based on mutation (correlates with severity)
- NNZ-2566 oral solution or placebo administered for 14 days following 3 days of dose titration up to 35 or 70 mg/kg b.i.d.
- Endpoints: safety, seizure activity, cardiac and respiratory irregularities, caregiver and clinician assessments of symptom severity and behaviour
- Sites: Rett Syndrome Centers at Baylor College of Medicine and University of Alabama
- 3 subjects enrolled to date

# Fragile X Syndrome (FXS-001)

- Phase II randomized (1:1:1), placebo-controlled, fixed dose, cross-over, safety and efficacy study
- Up to 60 (48 complete) male subjects ages 16-40 years with a diagnosis of Fragile X Syndrome
- NNZ-2566 oral solution or placebo administered for 28 days at 35 or 70 mg/kg twice daily with cross-over to active for subjects initially receiving placebo
- Endpoints: safety, seizure activity, caregiver and clinician assessments of symptom severity and behavior
- Sites: Fragile X Syndrome clinical centers

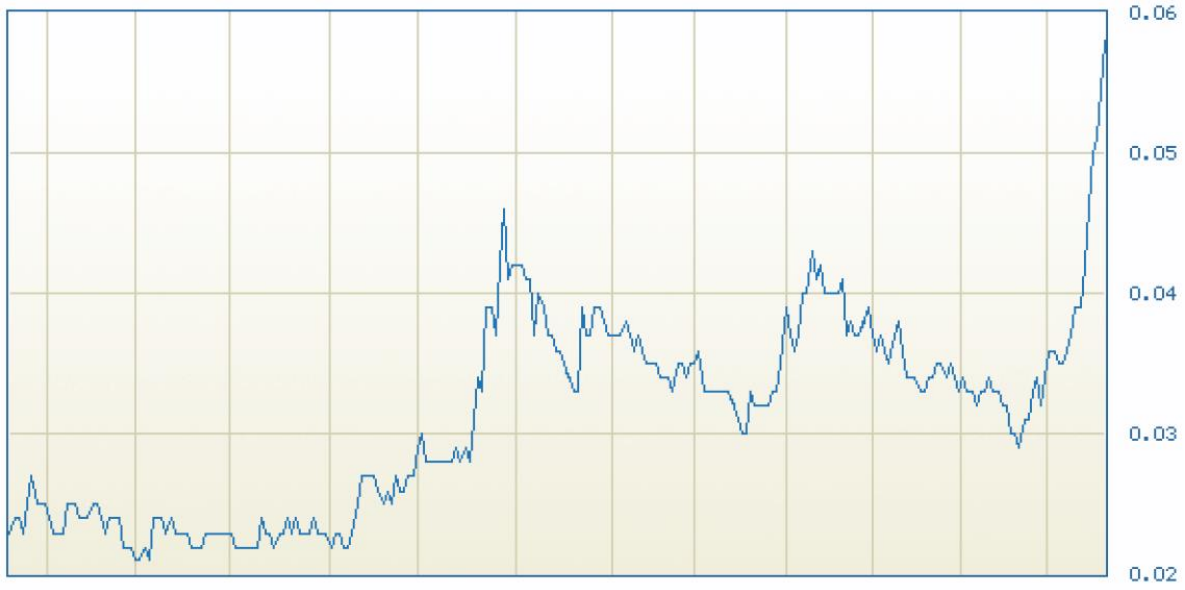
# NNZ-2591

- Lead preclinical molecule in cyclic dipeptide portfolio
- Synthetic analog of naturally occurring neurotrophic factor
- 100% orally bioavailable candidate for chronic, oral therapy
- Manufacturing development for preclinical R&D nearing completion
- US Army working on mechanism of action under Cooperative R&D Agreement
- Testing in Fragile X model underway at FraX-Drug Validation Initiative

# Shareholding and Financial Position

- Shares outstanding: 1.2b
- Options outstanding: 274m
- Closing price (20 May 2013): $0.058
- Market capitalization: $69m
- Current cash (30 April 2013): NZ$4.24m
- Top 20 shareholders: 57% (approximate)
- Institutions: 9%; directors: 6%; substantial: 20%; retail: 65%
- 52 week range:

  $0.021 – $0.074



# Expected News Flow

| | |
|---|---|
| • Initiate Fragile X Phase 2 | 2H-2013 |
| • Complete enrollment in Rett Phase 2 | 1H-2014 |
| • Top-line results for Rett Phase 2 | 2H-2014 |
| • Complete enrollment in Fragile X Phase 2 | 2H-2014 |
| • Complete enrollment in *INTREPID*$^{-2566}$ | 2H-2014 |
| • Top-line results for Fragile X Phase 2 | 1H-2015 |
| • Top-line results for *INTREPID*$^{-2566}$ | 1H-2015 |