



# Investor Presentation

31 July 2015

# Forward looking statements

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.

# Company snapshot

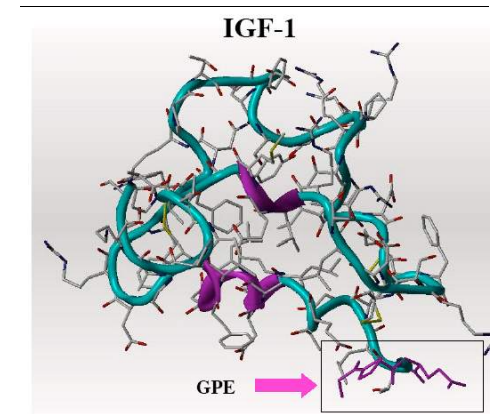
- ▣ Stock code ASX: NEU – market cap approximately A\$160 million
- ▣ Developing treatments for chronic and acute neurological conditions
  - Large markets with no therapies currently available
  - Orphan drug designation and potential for abbreviated regulatory pathways
- ▣ Lead drug candidate “trofinetide”
  - In development for Rett syndrome, Fragile X syndrome, Traumatic Brain Injury and Concussion
  - Excellent tolerability profile to date
  - Clinical evidence of a pattern of benefit across the broad phenotype of Rett syndrome
  - Benefit consistent with its normalising effects on brain biology
- ▣ Fully funded through to completion of Phase 2 trials in 4 different indications
  - Cash reserves A\$18 million at 30 June 2015
- ▣ Key strategic relationships
  - US Army Medical Research & Materiel Command
  - International Rett Syndrome Foundation (Rettsyndrome.org)
  - FRAXA and National Fragile X Foundation

# Strategy

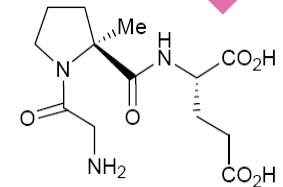
- ▣ Demonstrate the therapeutic benefit of **trofinetide** in human subjects in both acute and chronic conditions
- ▣ Potential to establish a “**gateway**” to autism and other neurodevelopmental disorders
- ▣ Criteria for selecting therapeutic targets
  - Significant unmet need and commercial opportunity with no approved drugs
  - Regulatory advantages – candidates for *Fast Track*, *Orphan Drug*, *Breakthrough Therapy*
  - Strong support from advocacy groups and other stakeholders
- ▣ Realising value
  - Generate clinical data with trofinetide in Phase 2 clinical trials
  - Define optimum pathway towards New Drug Application
  - Optimise manufacturing process for commercial product supply
  - Maintain dialogue with potential partners

# Scientific foundation

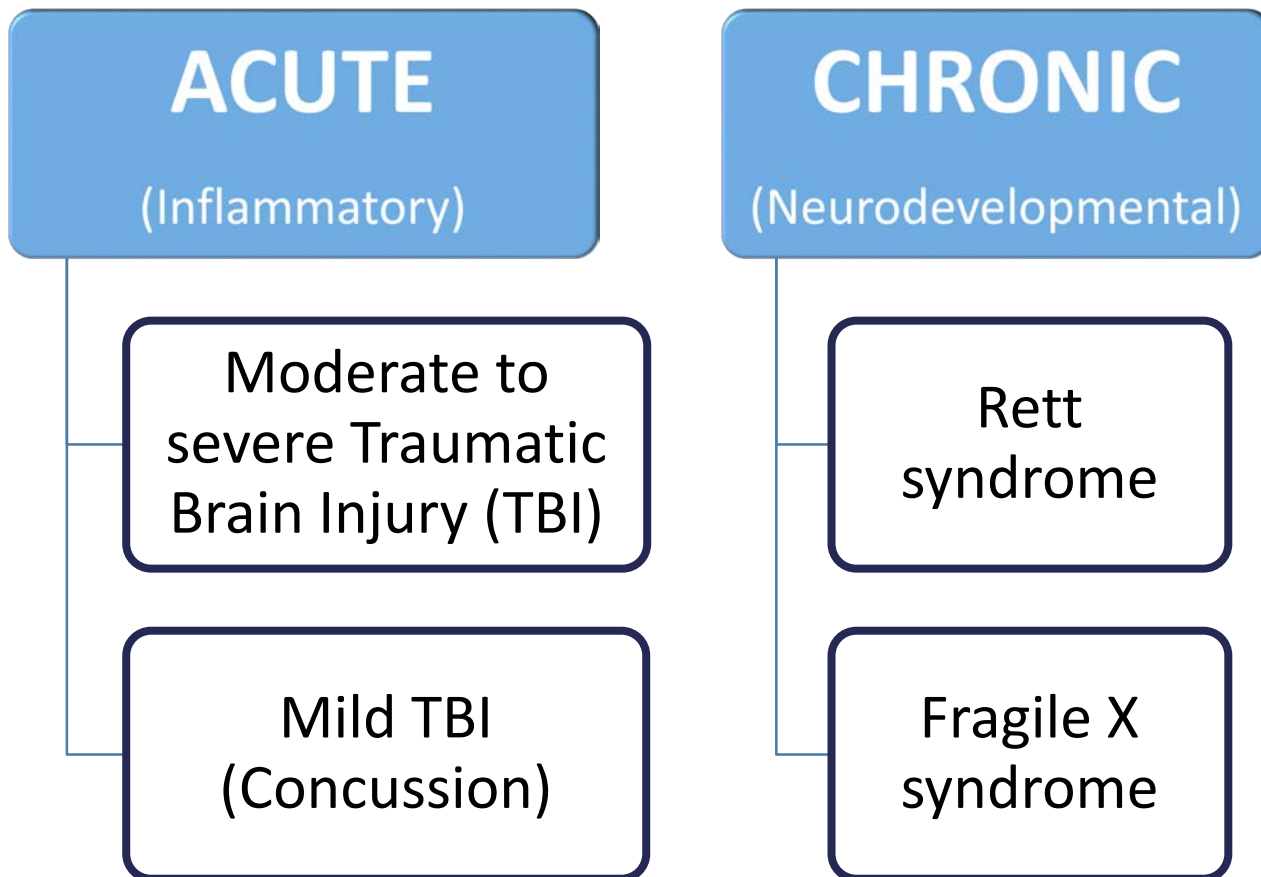
- ❑ **IGF-1** is a naturally occurring growth factor in the brain
- ❑ Glypromate (**GPE**) separates from IGF-1 in the brain
- ❑ IGF-1 and GPE maintain and restore equilibrium in the brain
- ❑ **Trofinetide** is a synthetic analogue of GPE with a longer half-life, better stability and suitability as an oral medication
- ❑ **Trofinetide** influences the processes in impaired development and injury of the brain
  - Inflammation
  - Microglial function
  - Synaptic plasticity (inter-neuronal communication)
- ❑ **NNZ-2591** is in the same class of peptides, with higher bioavailability and potential for a solid oral dosage form
- ❑ **Trofinetide** and **NNZ-2591** each potentially treats a wide range of neurological conditions



trofinetide

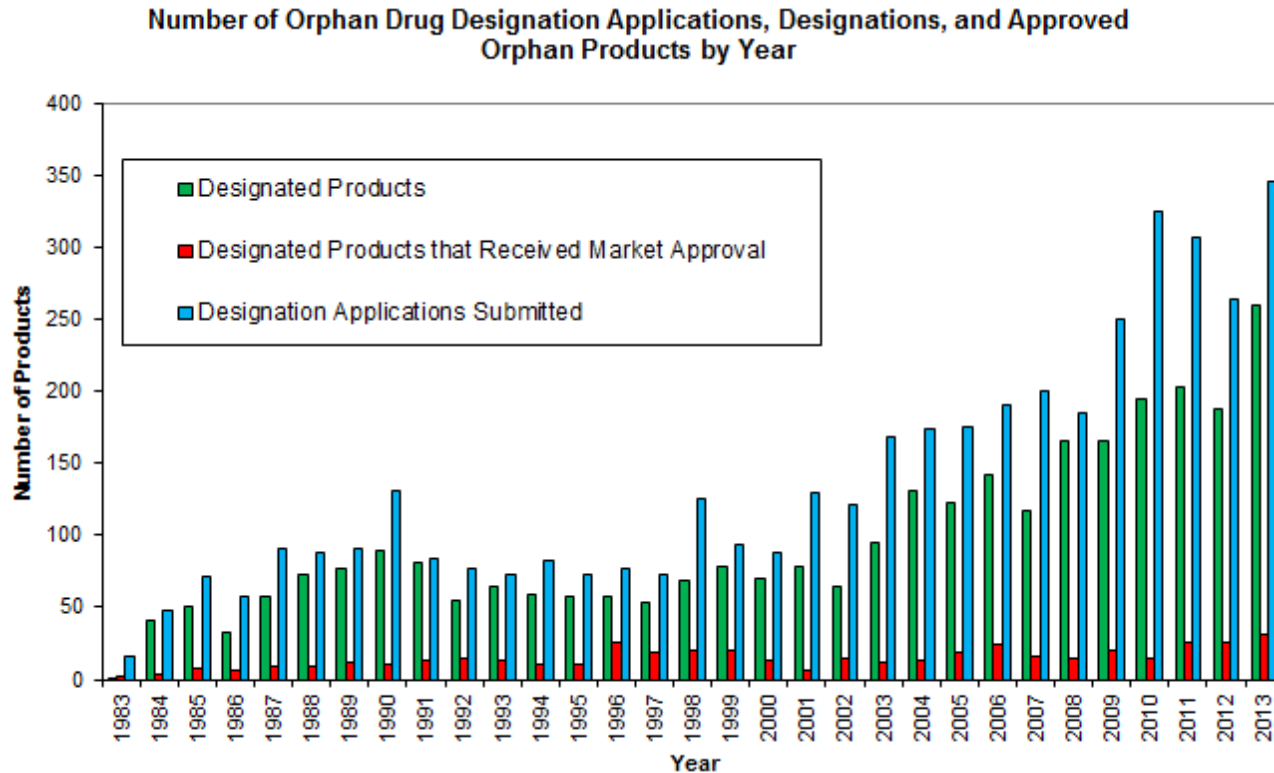


# Trofinetide current clinical strategy



# Importance of “orphan” drug designation

- FDA and EMA may grant “orphan” designation to a drug to treat a rare condition – provides marketing exclusivity following approval for 7 years in US and 10 years in EU
- Orphan granted to Neuren in US and EU for both Fragile X syndrome and Rett syndrome
- Pharma companies increasingly pursuing orphan drugs



# Trofinetide in Rett syndrome

- Mutation in a gene on the X chromosome - 1 / 10,000 females (20,000 USA)
- Most physically disabling of the autism spectrum disorders - symptoms include:
  - Intellectual disability, loss of speech and motor control
  - Compulsive hand movements
  - Disorders of breathing and cardiovascular function
  - Muscle rigidity
  - Seizures
- Profound disability and financial burden for >50,000 patients and families globally
- No approved treatments available and few in development
- NNZ-2566 in Rett syndrome
  - Successful Phase 2 trial with a pathway towards New Drug Application
  - Orphan Drug designations granted by FDA and EMA
  - Fast Track designation granted by the FDA



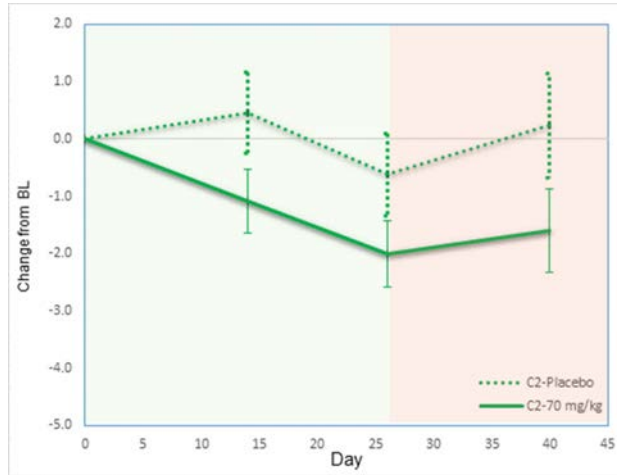


# Phase 2 trial highlights

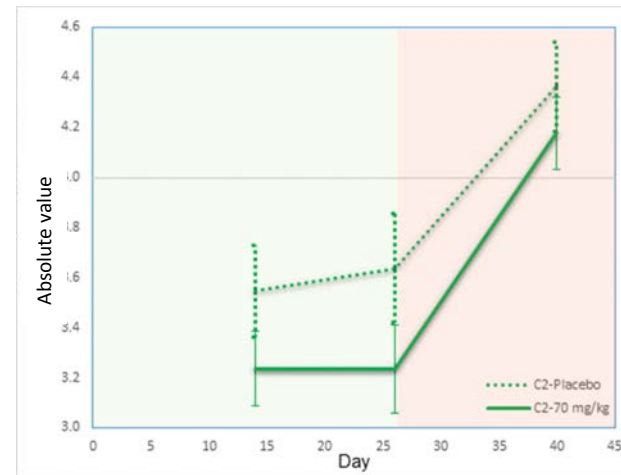
- Double-blind, placebo-controlled Phase 2 trial of 28 days of treatment with two dose levels (35 mg/kg and 70 mg/kg of body weight twice daily)
- 56 subjects aged 16 to 45 years randomized, with 53 subjects completing the trial
- Both dose levels were well tolerated and no safety concerns were identified
- Higher dose exceeded the pre-specified criteria for improvement in core efficacy measures compared with placebo
- Both doses showed trends of increasing effect with duration of treatment
- The clinical benefit in the trial encompassed core symptoms of Rett syndrome and was observed in both clinician and caregiver assessments

# Core efficacy measures that met target

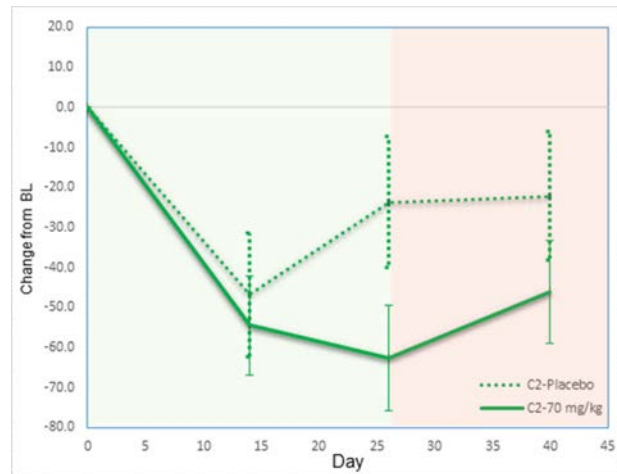
## Motor Behavior Assessment Change Index



## Clinical Global Impression of Improvement



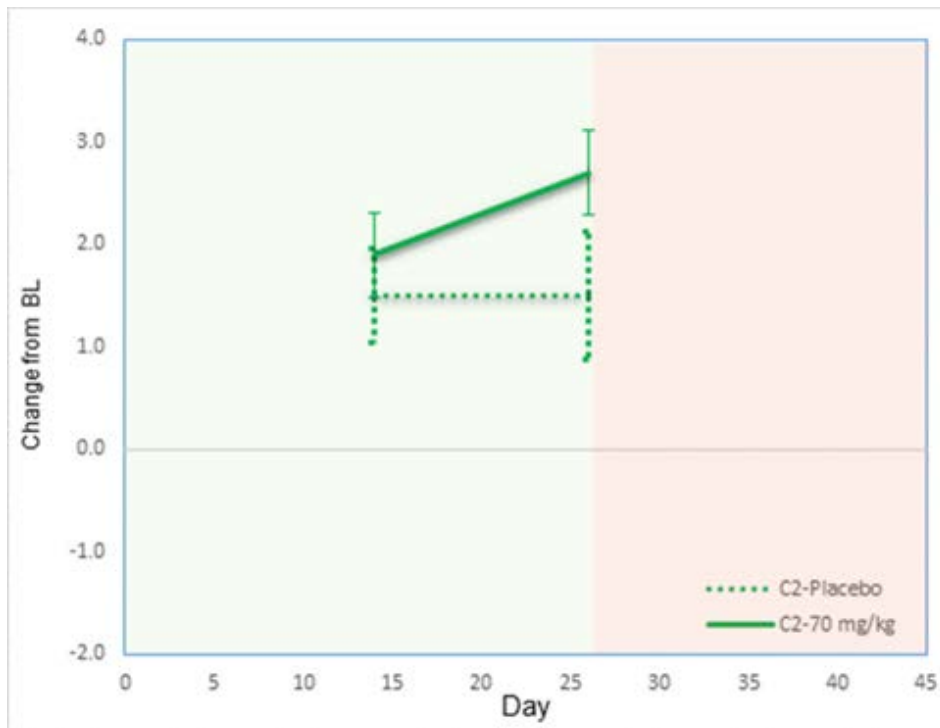
## Caregiver Top 3 Concerns



- Analysis of group mean values
- Solid line is 70mg/kg, dotted line is placebo
- The two different shaded areas indicate the treatment period and the period post-cessation of treatment
- A negative value on the y-axis indicates clinical benefit

# Subject-level efficacy analysis

Mean subject-level efficacy score



- ❑ Solid line is 70mg/kg, dotted line is placebo
- ❑ The two different shaded areas indicate the treatment period and the period post-cessation of treatment
- ❑ A positive value on the y-axis indicates clinical benefit
- ❑ Changes in all 6 core efficacy measures for each subject were combined in an efficacy score
- ❑ Mean efficacy scores were then compared with placebo

# Remaining development for Rett syndrome

- Meaningful guidance in all areas of development program from recent FDA meeting
- Neuren and FDA committed to reach agreement quickly on primary efficacy endpoint for pivotal trials, to be derived from the Motor Behavior Assessment (MBA)
  - MBA has been used to assess over 1,100 children, adolescents and adults with Rett syndrome enrolled in the Rett Natural History Study, a study sponsored by the NIH
  - MBA demonstrated a pattern of clinical benefit after 28 days' dosing in Neuren's Phase 2 clinical trial
- Neuren to propose to FDA a design for a single Phase 3 clinical trial to support a New Drug Application
- Neuren to conduct a brief tolerability trial in children and adolescents to test higher doses in a younger population
  - generate useful information on trofinetide in children and younger adolescents
  - confirm the optimum dose levels for the Phase 3 trial

# Trofinetide in Fragile X syndrome

- Mutation on the X chromosome affecting both males and females - 1 / 4,000 males and 1 / 6,000 females (58,000 USA)
- The most common inherited cause of intellectual disabilities and the most common known cause of autism - symptoms include:
  - Intellectual disabilities
  - Anxiety and unstable mood
  - Seizures (approximately 1 in 4)
  - Attention deficit, hyperactivity and autistic behaviour
- Phase 2 trial in males aged 12-45 with Fragile X syndrome
  - Safety and efficacy of treatment with two dose levels of oral NNZ-2566 for 28 days
  - 72 subjects enrolled; top-line results expected in December 2015
- Orphan Drug designations granted by the FDA and the EMA
- Fast Track designation granted by the FDA



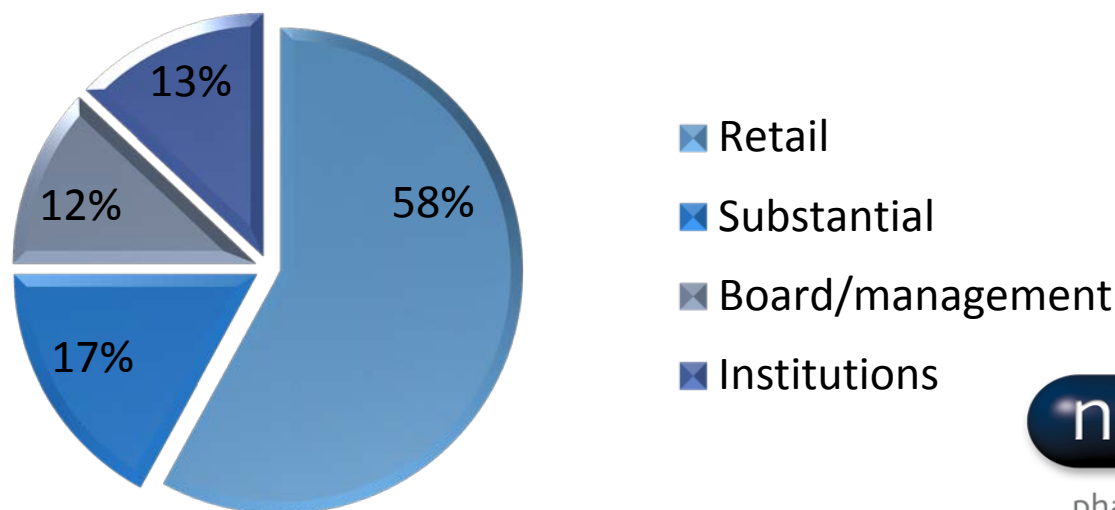
# Trofinetide in Traumatic Brain Injury (TBI)

- ▣ > 1.5 million head injuries annually in the US alone; >75% are mild (Concussion)
- ▣ Leading cause of death and disability, especially in young and elderly
- ▣ Serious health and economic effects of Concussion in sporting codes
- ▣ Partnership funding of ~US\$25 million by US Army
- ▣ Phase 2 trial (“INTREPID”) in moderate to severe TBI
  - Safety and efficacy of treatment with intravenous NNZ-2566 for 72 hours
  - 260 subjects to be enrolled in US trauma centres – 245 enrolled to date
  - “Fast Track” designation granted by the FDA
- ▣ Phase 2 trial in mild TBI (Concussion)
  - Safety and efficacy of treatment with two dose levels of oral NNZ-2566 for 7 days
  - 132 subjects with mild TBI to be enrolled at US military training facility and civilian hospitals
  - Trial timeline under review

# Shareholdings and financial position

- Fully funded through to completion of Phase 2 trials in 4 different indications
- A\$18m cash reserves at 30 June 2015

Shares outstanding:	1.7 billion
Options outstanding:	73 million (1.3 cents to 3.8 cents per share)
Closing price 30 July 2015	9.8 cents
52 week range:	7.4 cents – 18.5 cents



# Neuren 2015 expected milestones

FDA meeting on remaining development for Rett Syndrome

Achieved

Orphan Drug designation in Europe for Rett syndrome and Fragile X syndrome

Achieved

Top-line results for Fragile X Phase 2

December 2015

Top-line results for *INTREPID* Phase 2

H2 2015