



Investor Presentation

25 November 2016

Forward looking statements

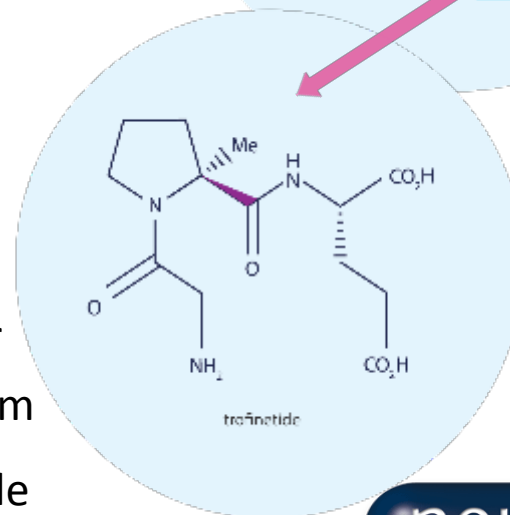
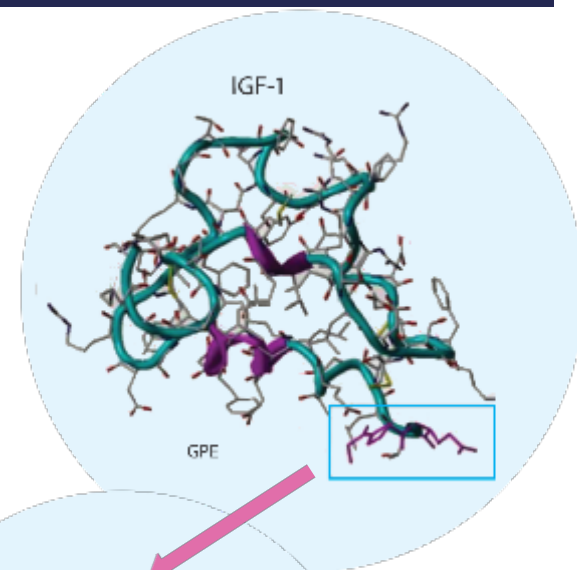
This presentation contains forward looking statements that involve risks and uncertainties. Although we believe that the expectations reflected in the forward looking statements are reasonable at this time, Neuren can give no assurance that these expectations will prove to be correct. Actual results 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.

Neuren snapshot

- Stock code ASX: NEU – market cap approximately A\$120 million
- Developing new treatments for neurological conditions
 - Significant unmet needs and commercial opportunities with no approved drugs
 - Regulatory advantages – candidates for *Fast Track, Orphan Drug, Breakthrough Therapy*
 - Strong support from advocacy groups and other stakeholders
- Lead drug candidate trofinetide
 - Utility in neurodevelopmental disorders, neurodegenerative diseases and brain Injury
 - Excellent safety and tolerability profile to date
 - Improvement observed in Rett syndrome and Fragile X syndrome Phase 2 trials
 - Broad range of clinical effects consistent with known normalising actions on brain function
 - Results from current Phase 2 trial in pediatric Rett syndrome expected in March 2017
- Strategy to realise value
 - Generate clinical data in Phase 2 trials
 - Define optimum pathway towards New Drug Applications
 - Optimise manufacturing processes for commercial product supply
 - Engage with commercial partners

Scientific foundation

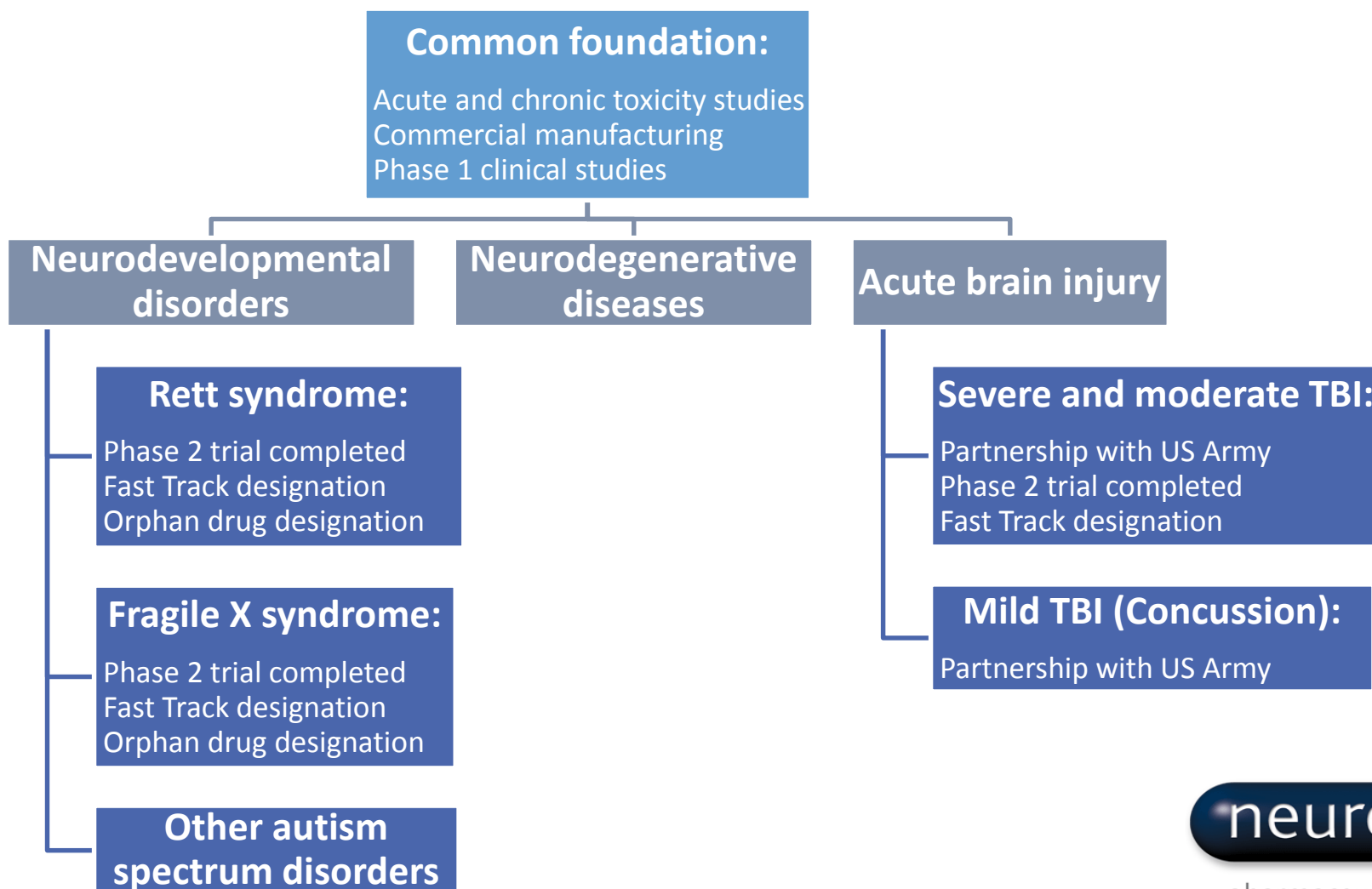
- ❑ **IGF-1** is a naturally occurring growth factor in the brain
- ❑ Glypromate (**GPE**) separates from IGF-1 in the brain
- ❑ IGF-1 and GPE maintain and restore equilibrium in the brain
- ❑ **Trofinetide** is a synthetic analogue of GPE with a longer half-life, better stability and suitability as 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** both potentially treat a wide range of neurological conditions



Multiple disorders with common causes and effects

	Neuro-inflammation	Microglial Activation	Neuronal signaling	Apoptosis	Impaired Neurogenesis	Oxidative stress
Rett	■	■	■	■	■	■
Fragile X	■	■	■		■	■
Idiopathic autism	■	■	■		■	■
TBI	■	■	■	■	■	■
Depression	■	■	■	■	■	■
Post-traumatic Stress Disorder	■	■	■			■
Cognitive impairment	■	■	■	■	■	■
Parkinson's Disease	■	■	■	■	■	■
Multiple Sclerosis	■	■	■	■	■	■
Alzheimer's Disease	■	■	■	■	■	■
Stroke	■	■	■	■	■	■
Anxiety	■	■	■		■	■
Schizophrenia	■	■	■	■	■	■

Trofinetide development strategy



Trofinetide commercial exclusivity

- Issued composition of matter patents for trofinetide owned by Neuren
 - US and Europe – expire 2022, potential to extend to 2027
- Exclusivity periods from orphan drug designation for trofinetide in Rett syndrome and Fragile X syndrome
 - US – 7 years from marketing authorization, potentially plus 6 months if approved for pediatric use
 - European Union – 10 years from marketing authorization, potentially plus 2 years if approved for pediatric use
- Method of treatment applications for trofinetide in autism spectrum disorders (ASDs)
 - Issued US patent for Rett syndrome – expires 2032
 - Issued Australian patent for ASDs – expires 2032
 - Other applications pending in US, Europe and other territories

Trofinetide in Rett syndrome

- Non-inherited mutation on the X chromosome – estimated 1/10,000 females
- 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 patients and families
- No approved treatments available
- Trofinetide in Rett syndrome:
 - Clinical improvement observed in Phase 2 trial in adolescents and adults
 - Results from Phase 2 trial in girls aged 5 to 15 expected in March 2017
 - Commence Phase 3 trial in children, adolescents and adults in 2018



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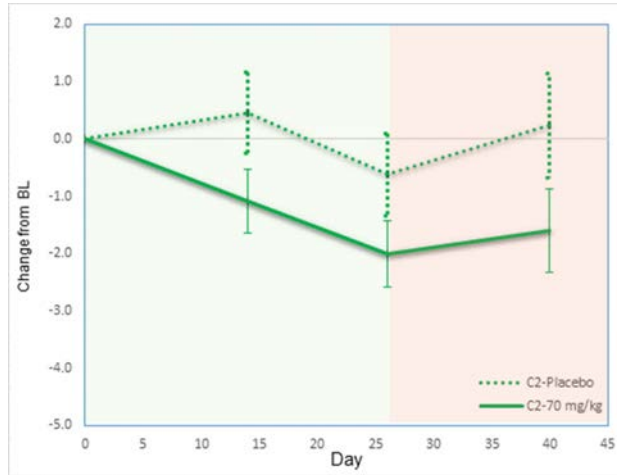
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Completed Phase 2 trial in adults and adolescents

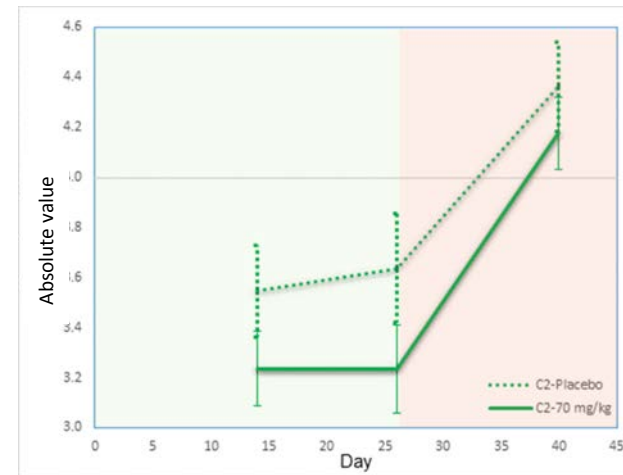
- Double-blind, placebo-controlled Phase 2 trial of 28 days of treatment with two dose levels (35 mg/kg and 70 mg/kg of body weight twice daily)
- 56 subjects aged 16 to 45 years randomized, with 53 subjects completing the trial
- Both dose levels were well tolerated and no safety concerns were identified
- 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 improvement in the trial encompassed core symptoms of Rett syndrome
 - Observed in both clinician and caregiver assessments
 - Included communication/speech, alertness and social interaction, anxiety, breathing abnormalities, hand movements/function, motor/muscular dysfunction, seizures and GI dysfunction

Core efficacy measures that met target

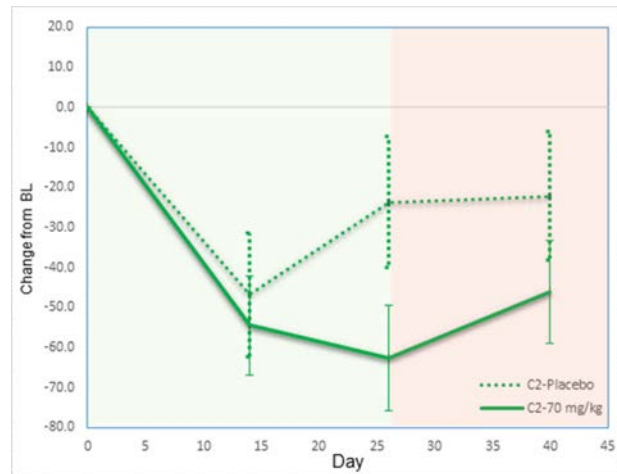
Motor Behavior Assessment Change Index



Clinical Global Impression of Improvement



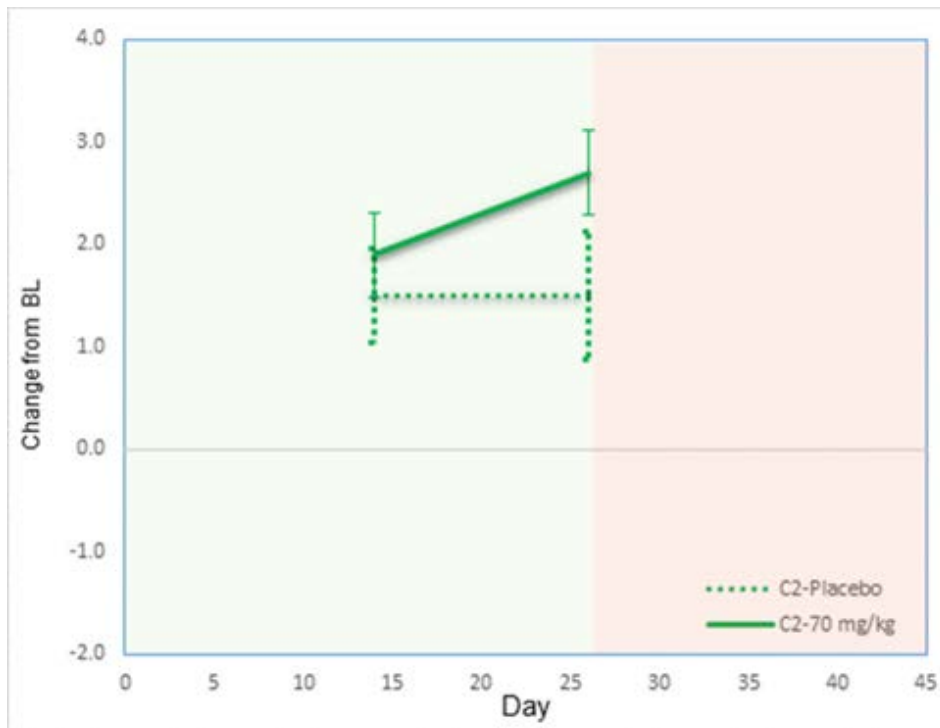
Caregiver Top 3 Concerns



- 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 improvement

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 improvement
- ❑ Changes in all 6 core efficacy measures for each subject were combined in an efficacy score
- ❑ Mean efficacy scores were then compared with placebo

MBA Change Index

- No precedent for efficacy measures in Rett syndrome clinical trials for registration
- Motor Behavior Assessment (MBA) is a clinician completed instrument to measure the core signs and symptoms of Rett syndrome
 - 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
 - Composite score of 34 items
- MBA Change Index is a subset of items from the MBA, agreed with the FDA, selected based on:
 - Clinical meaningfulness
 - Functional impact
 - Sensitivity to change
 - Psychometric properties
- Neuren plans to use MBA Change Index as primary efficacy measure in Phase 3 trial

Current Phase 2 trial in girls aged 5 to 15

- Double-blind, placebo-controlled Phase 2 trial in subjects aged 5 to 15 years
 - Evaluate safety and efficacy of higher doses in younger population with longer treatment
 - To confirm optimum dose levels for subsequent Phase 3 trial in children, adolescents and adults
 - Conducted at 12 US hospitals, led by world-leading clinicians in Rett syndrome
 - Supported by funding of US\$1m from rettsyndrome.org
- Top-line results expected in March 2017 - fast enrolment enabled expansion of trial beyond original target of 64 subjects:
 - 62 subjects randomised to 4 groups (50 mg/kg, 100 mg/kg, 200 mg/kg or placebo)
 - 20 further subjects randomised to 200 mg/kg or placebo
 - Efficacy measures include MBA Change Index, CGI-I and Caregiver Top 3 Concerns
 - Primary endpoint safety compared with placebo in this younger population

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Trofinetide in Fragile X syndrome

- Inherited X chromosome mutation – full mutation causes Fragile X syndrome
 - 1 / 4,000 males and 1 / 6,000 females estimated to have full mutation
 - More severe in males, ~50% of females have some features of the syndrome
- 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 behavior
- No approved treatments available
- Trofinetide in Fragile X syndrome:
 - Clinical improvement observed in Phase 2 trial in adolescents and adults
 - Validation of FXS Rating Scale for use in pivotal clinical trials is in progress
 - Commence next trial in children aged 3 to 12 in 2018, followed by Phase 3 trial in children, adolescents and adults

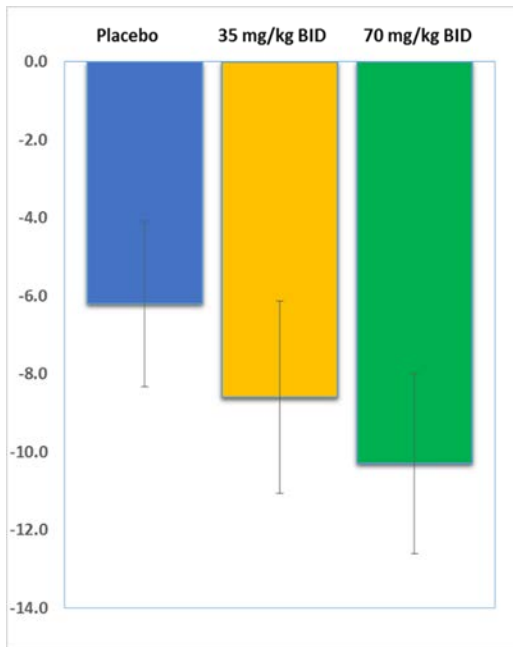


Completed Phase 2 trial in adolescents and adults

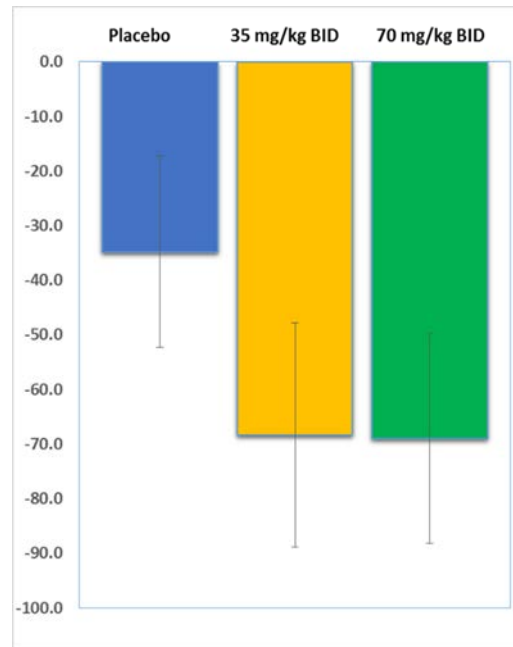
- Double-blind, placebo-controlled Phase 2 trial of 28 days of treatment with two dose levels (35 mg/kg and 70 mg/kg of body weight twice daily)
- 70 subjects aged 12 to 45 years received treatment, with 68 subjects completing the trial
- Both dose levels were well tolerated and no safety concerns were identified
- Higher dose exceeded pre-specified targets and demonstrated a consistent pattern of clinical improvement, observed in both clinician and caregiver assessments
- Improvements across a range of core symptoms of Fragile X syndrome
 - Captured by new Fragile X-specific measures as well as by the Aberrant Behavior Checklist
 - Included higher sensory tolerance, reduced anxiety, better self-regulation, more social engagement
- Improvements observed with the low dose were less consistent and did not meet pre-specified targets, but there was evidence of a dose response

Core efficacy measures that met target

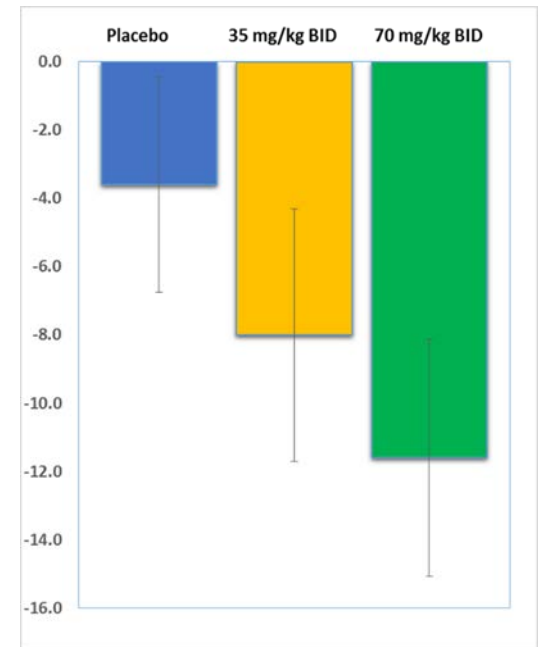
Fragile X Syndrome Rating Scale



Fragile X Domain Specific Concerns



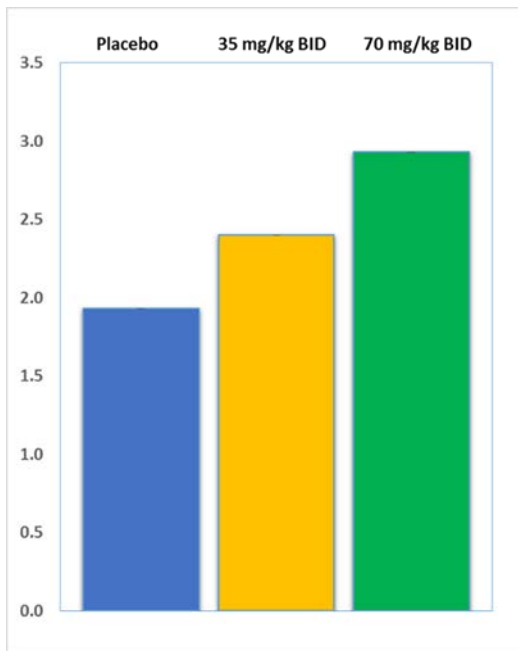
Aberrant Behavior Checklist (ABC) Total Score



- ❑ Analysis of mean clinical responses at end of treatment for each treatment group
- ❑ A negative value on the y-axis indicates clinical improvement

Subject-level efficacy analysis

Mean of individual subject scorecards



- A positive value on the y-axis indicates clinical improvement
- Changes in all 5 core efficacy measures at end of treatment were combined in an efficacy score for each subject
- Mean efficacy scores were then calculated for each treatment group

Trofinetide in Traumatic Brain Injury (TBI)

- >1.5 million head injuries annually in the US alone
- Leading cause of death and disability, especially in young and elderly
- No approved treatments available
- Partnership funding of ~US\$25 million has been contributed by US Army
- Results of Phase 2 trial (“INTREPID”) in moderate to severe TBI
 - Favourable safety profile confirmed
 - Highly statistically significant and clinically relevant benefit of active over placebo in patients with severe TBI who completed RBANS ($p=0.008$)
 - series of tests completed by the patient for assessing cognitive impairment
 - validated for use in TBI and extensively used to diagnose and track dementia
 - No difference between active and placebo in patients with severe TBI and moderate TBI, assessed by the primary efficacy measures that were used in past TBI trials:
 - GOS-E (measure of global function)
 - MPAI-4 (measure of daily living activities)

Next steps in TBI

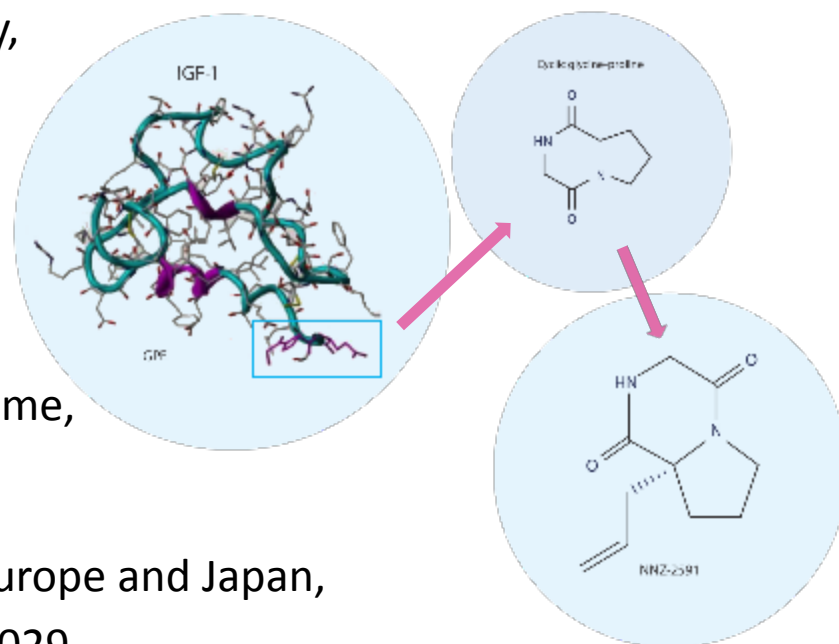
- Neuren and US Army discussing feasibility of a second trial in severe TBI, or moderate to severe TBI, optimised by including:
 - RBANS as primary efficacy endpoint
 - More targeted definition of trial population
 - Randomisation stratified by injury severity
 - Substantially higher doses and longer treatment, enabled by safety profile
- Development in mild TBI (Concussion) being conducted by Neuren and US Army is on hold while future strategy is considered

Other development activities for trofinetide

- Manufacturing process required for pivotal trials, New Drug Application (NDA) and commercial supply
 - Optimization and scale-up of API synthesis and isolation continuing
 - To-be-marketed drug product stability testing in progress
 - Phase 3 trial manufacture using commercial process will commence in H2 2017
- Chronic toxicity studies required for NDA's and Phase 3 trials
 - First species will conclude in H1 2017, second species will be completed in H1 2018
- Investments in manufacturing and toxicity studies will benefit NDA's for all trofinetide indications

Second drug candidate: NNZ-2591

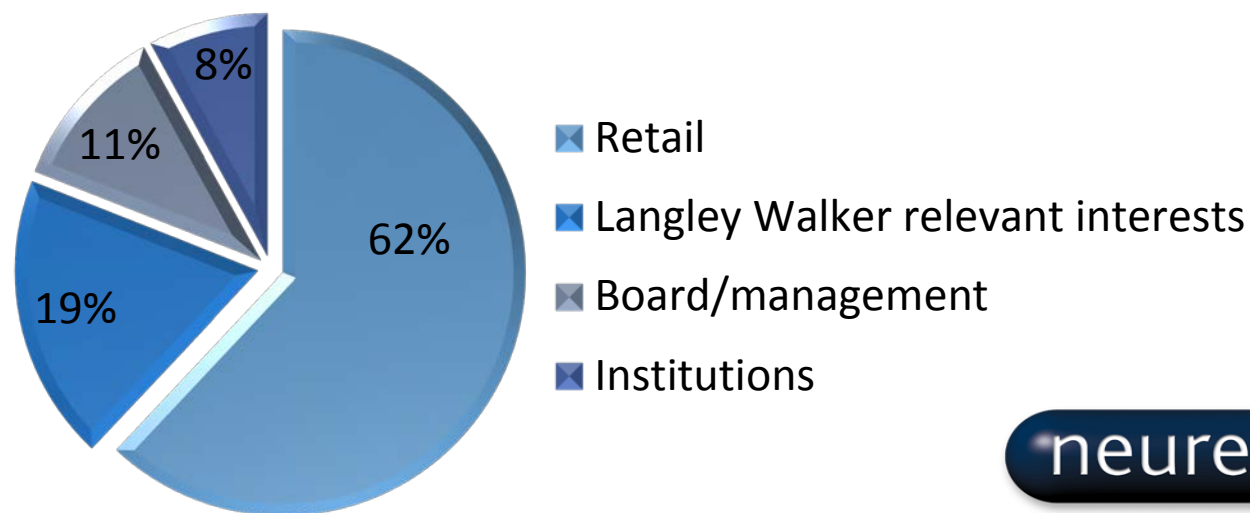
- Cyclic dipeptide with higher oral bioavailability, improved stability and potential for oral solid dosage form
- Demonstrated efficacy in pre-clinical models of Parkinson's disease, stroke, traumatic brain injury, peripheral neuropathy, Fragile X syndrome, memory impairment and multiple sclerosis
- Issued composition of matter patents in US, Europe and Japan, expiring in 2024, with potential to extend to 2029
- Issued US patents for methods of treating Parkinson's disease, peripheral neuropathy and cognitive impairment; international applications pending for methods of treating autism spectrum disorders



Share information

Issued shares:	1.84 billion ¹
Closing price 24 November 2016:	6.5 cents
52 week range:	4.1 cents – 13.0 cents

¹ Includes 90 million loan funded shares, which will provide additional funds of \$6 million when loans are repaid.



Key milestones

Milestone	Estimated timing
Top-line results from Rett syndrome pediatric Phase 2 trial	March 2017
Complete chronic toxicity studies for NDA's and Phase 3 trials: <ul style="list-style-type: none">• First species• Second species	H1 2017 H1 2018
Commence manufacture for Rett syndrome Phase 3 trial	H2 2017
Commence Rett syndrome Phase 3 trial	2018
Commence Fragile X syndrome pediatric trial	2018