



Investor Presentation

2 June 2017

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 (US\$90 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 leading physicians
- Lead drug candidate trofinetide
 - Clinical improvement in Rett syndrome and Fragile X syndrome Phase 2 trials
 - Broad range of effects consistent with known normalising actions on brain function
 - Excellent safety and tolerability profile
- Lead Orphan Drug program – Rett syndrome
 - Seriously debilitating and life-threatening disorder, with no approved medicines
 - Statistically significant and clinically meaningful improvement in Phase 2 trial
 - Active collaboration and strong support from leading physicians and largest advocacy group (rettsyndrome.org)
 - Anticipating Phase 3 discussions with FDA Division of Neurology in Q3 2017

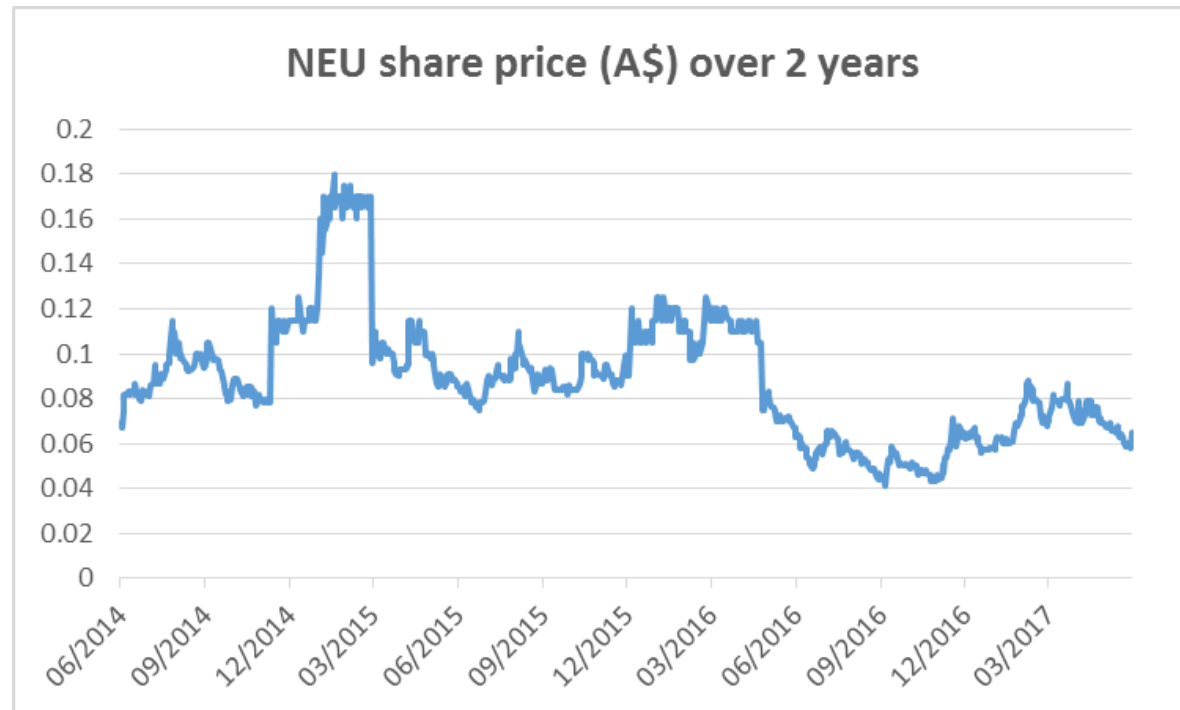
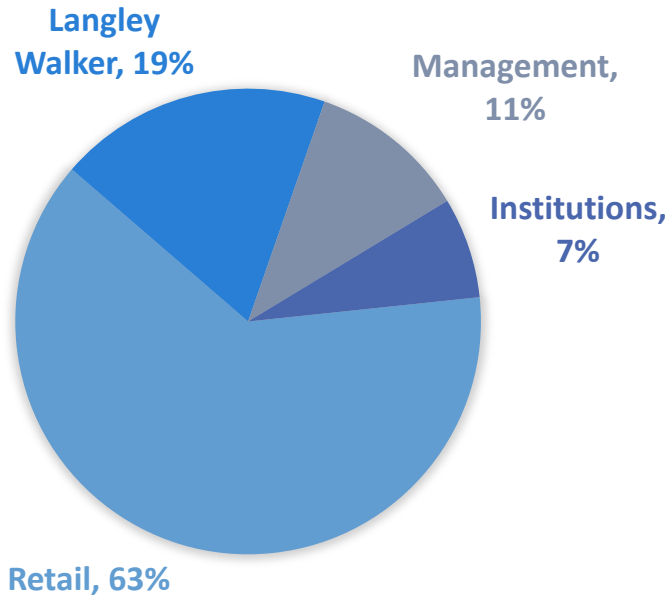
Neuren stock information (ASX: NEU)

Issued shares: 1.84 billion

1 month VWAP : 6.4 cents

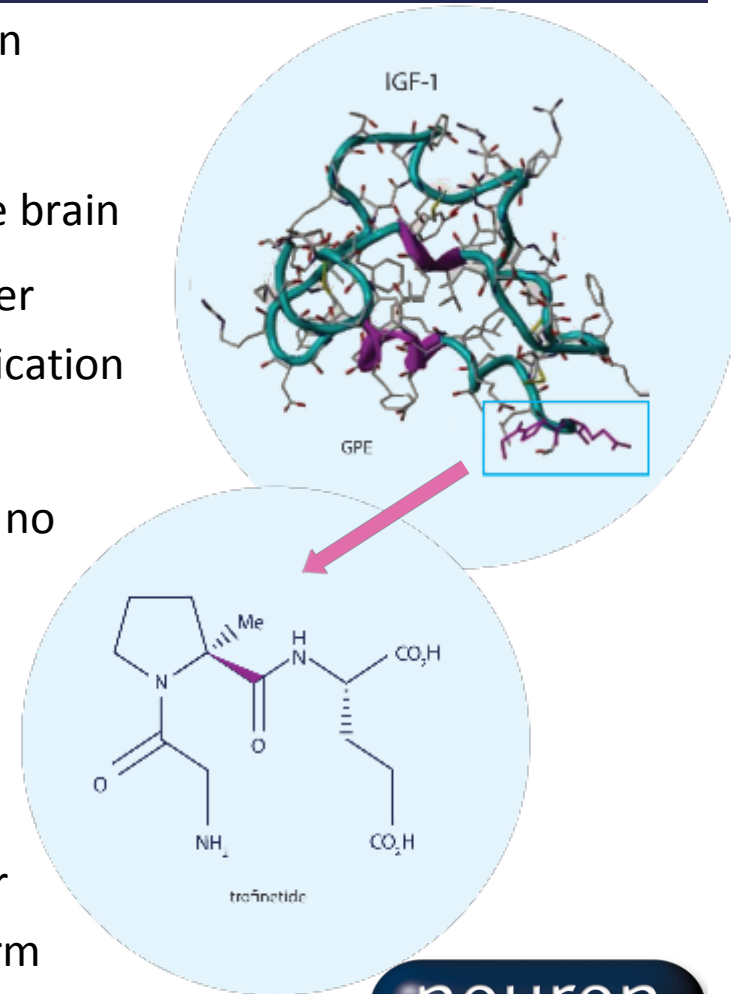
Closing price 31 May 2017: 6.5 cents

52 week range: 4.1 – 9.4 cents



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, but has virtually no effects in normal cells and animals:
 - Inhibits neuroinflammation
 - Normalises function of microglia
 - Normalises 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



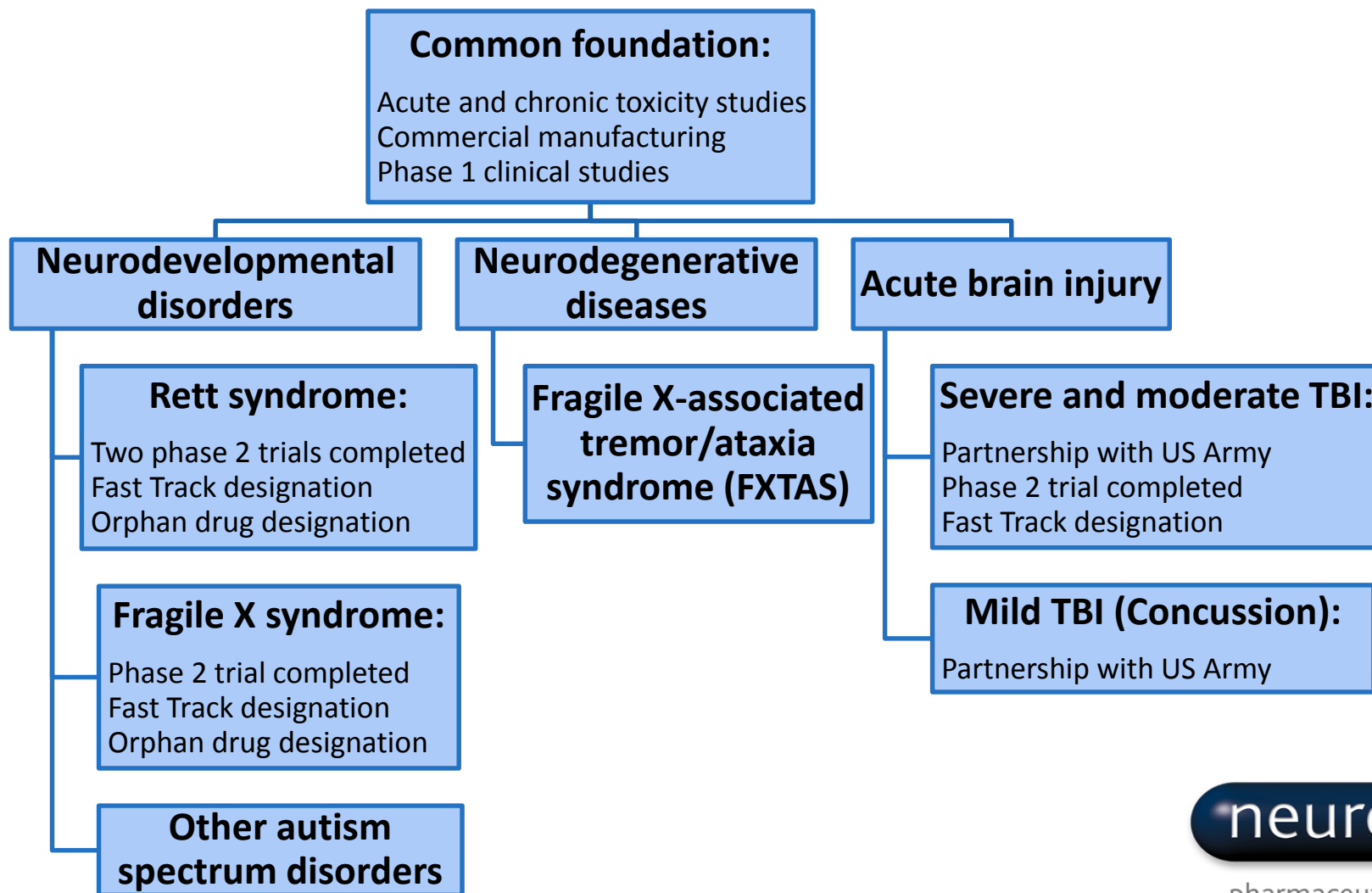
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Trofinetide commercial exclusivity

- ▣ Issued composition of matter patents owned by Neuren
 - US and Europe – expire 2022, potential to extend to 2027
- ▣ Exclusivity periods from orphan drug designation
 - 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 patents and applications
 - US patents for Rett syndrome and Fragile X syndrome – expire 2032
 - European patent and Australian patent for autism spectrum disorders, including Rett syndrome and Fragile X syndrome – expire 2032
 - Other applications pending in Japan, Canada, Brazil, Israel

Trofinetide development strategy





Rett syndrome program

About Rett syndrome

- Seriously debilitating and life-threatening neurological disorder, with no approved medicines
- Caused by non-inherited mutation on the X chromosome – estimated 1 in 10,000 to 15,000 live female births in all racial and ethnic groups
- After apparently normal development for the first six months of life, girls experience a period of rapid regression between 6 to 18 months of age
- Profoundly disabling range of symptoms:
 - Loss of speech and motor control
 - Neurobehavioral, cognitive and intellectual disability
 - Seizures
 - Autonomic dysfunction – breathing, cardiovascular and gastrointestinal abnormalities
- Most require life-long medical care and 24 hour supportive care - profound financial and emotional impact on families



Development program status

- Statistically significant and clinically meaningful improvement demonstrated in pediatric Phase 2 clinical trial; positive trends observed in earlier Phase 2 trial in adults
- Active collaboration and strong support from leading Rett syndrome physicians and largest advocacy group (rettsyndrome.org)
- Anticipating meeting with FDA Division of Neurology in Q3 2017 to discuss Phase 3 development
- Investments required before commencement of Phase 3 trial:
 - Conclude optimization of API manufacturing process for commercial supply
 - Conclude stability testing and analytical validation of to-be-marketed liquid drug formulation
 - Conduct non-clinical toxicity study in second species with 6 months' dosing, required for NDA and Phase 3 trial with longer dosing
 - Schedule manufacturing to supply the Phase 3 trial

Recently completed Phase 2 trial in girls aged 5 to 15

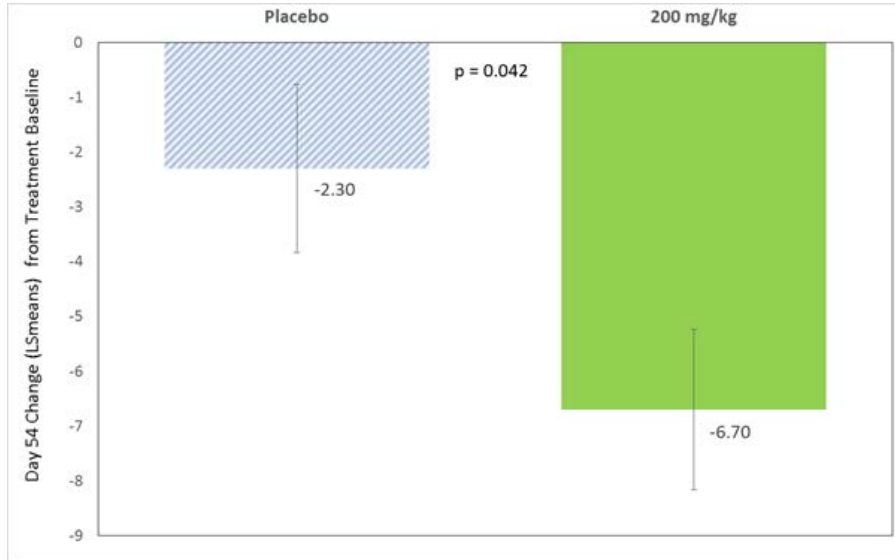
- Double-blind, placebo-controlled Phase 2 trial in girls aged 5 to 15 years
 - Conducted at 12 US hospitals, led by world-leading clinicians in Rett syndrome, supported by rettsyndrome.org
 - 62 subjects randomised to 4 groups (50 mg/kg, 100 mg/kg, 200 mg/kg or placebo); still blinded, 20 further subjects randomised to 200 mg/kg or placebo
- 200mg/kg dose group achieved statistically significant clinical improvement compared with placebo in 3 syndrome-specific measures completed by clinicians and caregivers:
 - Rett Syndrome Behaviour Questionnaire (RSBQ), Clinical Global Impression of Improvement (CGI-I), Rett Syndrome Domain Specific Concerns (RTT DSC)
- Improvement considered clinically meaningful by leading physicians
 - ~15% mean improvement from treatment baseline in a short duration trial
 - Improvement continued increasing through to end of treatment, indicating longer dosing may achieve further improvement
 - Evidence of biological activity across multiple symptom areas
- Trofinetide was well tolerated with no safety concerns identified

Rett Syndrome Behaviour Questionnaire (RSBQ)

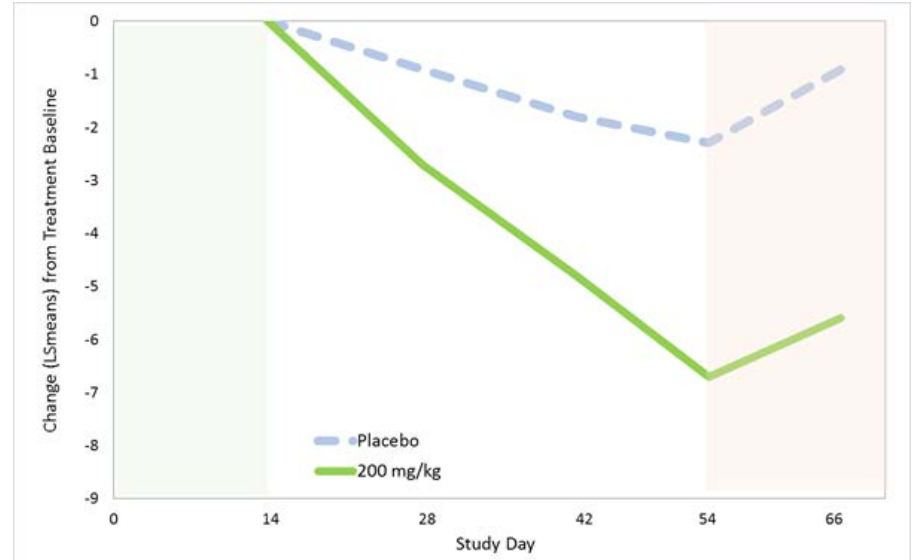
- The RSBQ is a well-validated instrument that has been used in other Rett syndrome clinical trials, has been correlated with quality of life outcomes and has been characterized and validated in peer-reviewed publications
- The RSBQ is designed to measure the frequency of 45 neurobehavioral items, reflecting the severity of the syndrome. The items are rated from 0 to 2 by the caregiver:
 - 0: the item is not true for an individual
 - 1: the item is somewhat or sometimes true in the individual
 - 2: the item is often or very true in the individual
- The items are organized into eight subscales: General Mood, Breathing Problems, Hand Behaviors, Repetitive Face Movements, Body Rocking and Expressionless Face, Night-time Behaviors, Fear/Anxiety, and Walking/Standing
- The RSBQ was not used in Neuren's earlier trial in ages 16 to 45

RSBQ – 200mg/kg versus placebo

Mean improvement after 6 weeks of treatment



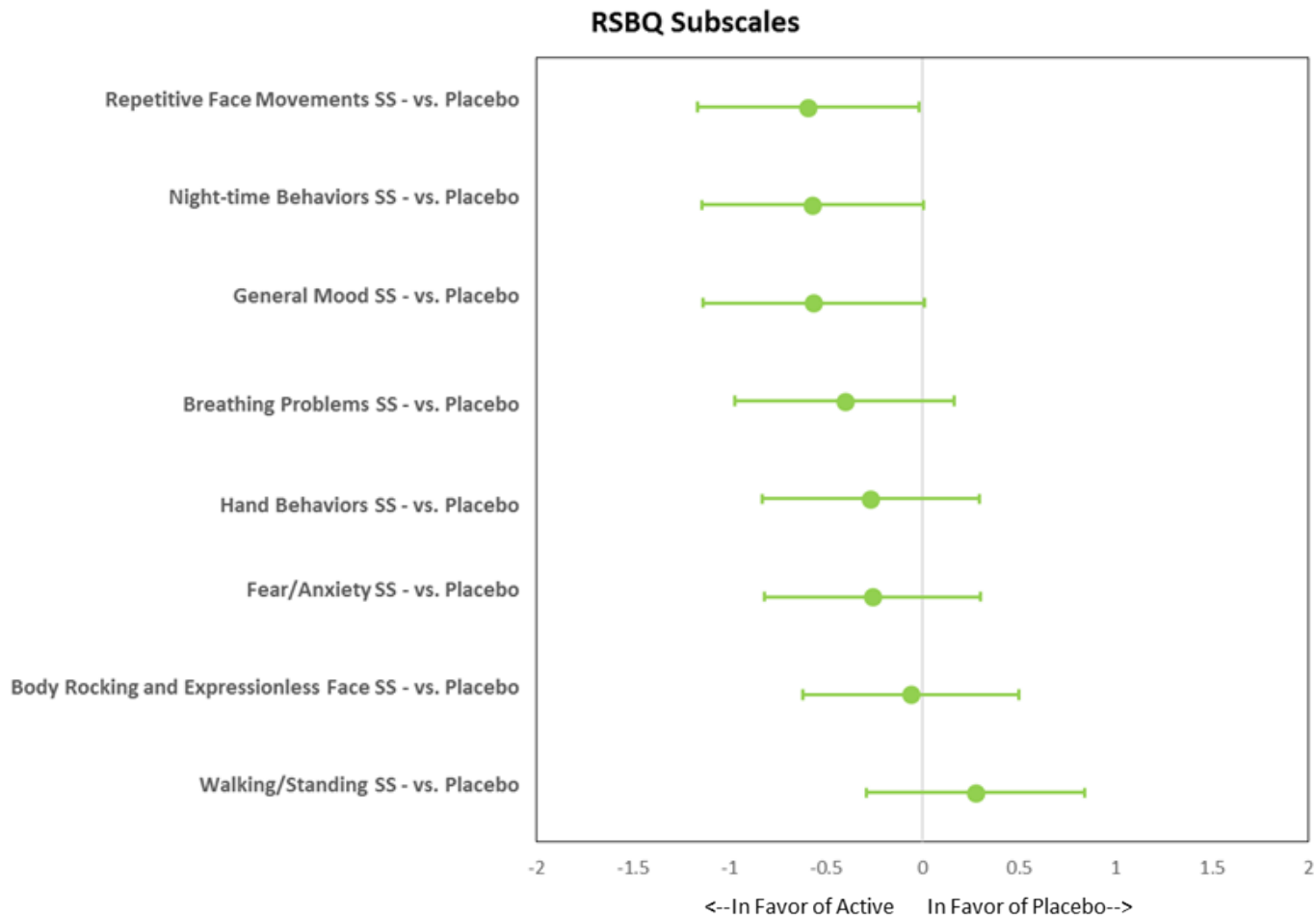
Time course of Improvement



- ❑ A decrease on the y-axis indicates clinical improvement
- ❑ Mean improvements for 200mg/kg and placebo were, respectively, 16% and 6% of the treatment baseline
- ❑ Caregiver rates the frequency of 45 neurobehavioral items, reflecting the severity of the syndrome
- ❑ Neuren intends to use RSBQ as a primary efficacy measure in pivotal trial

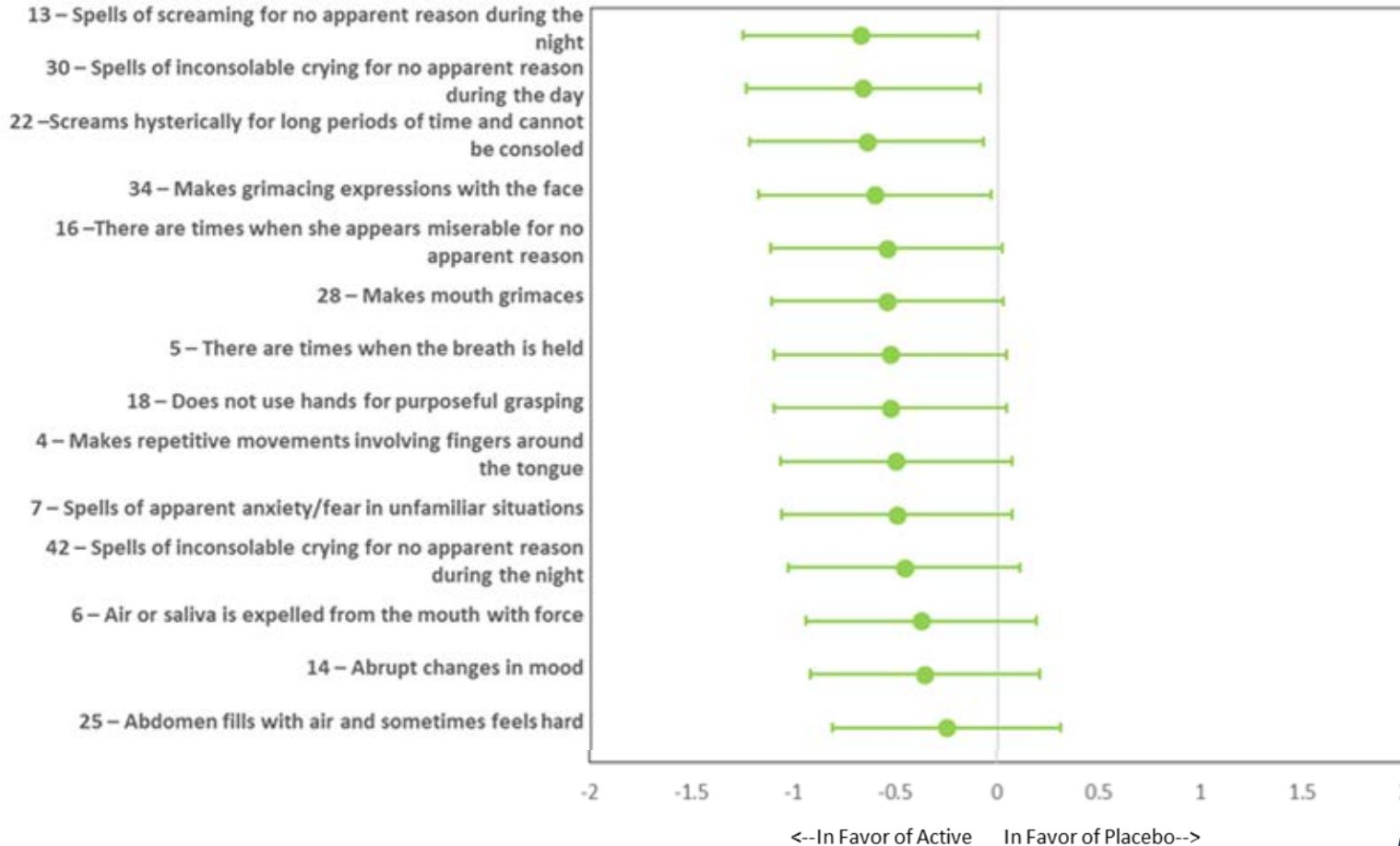


RSBQ subscales – Cohen's D effect sizes



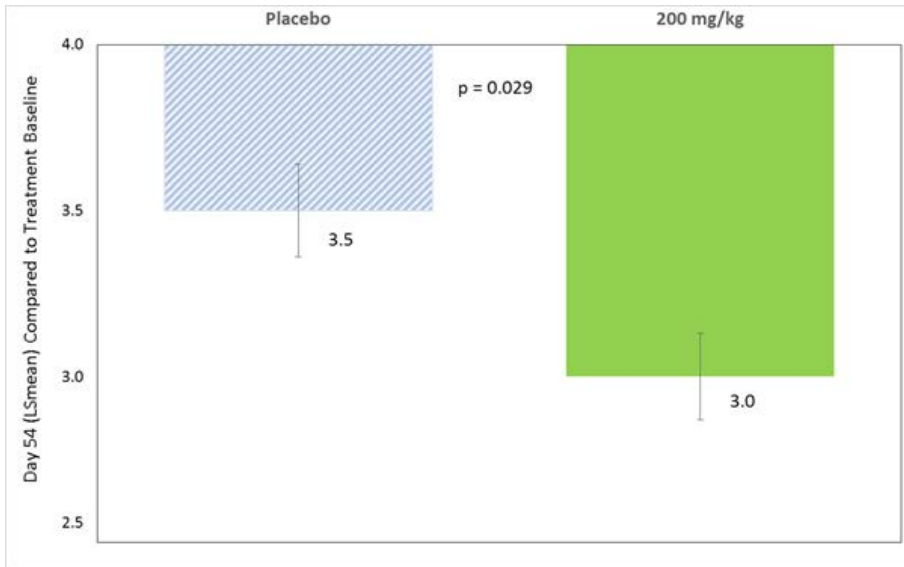
RSBQ items – Cohen's D effect sizes

RSBQ items with largest effect size in favour of active

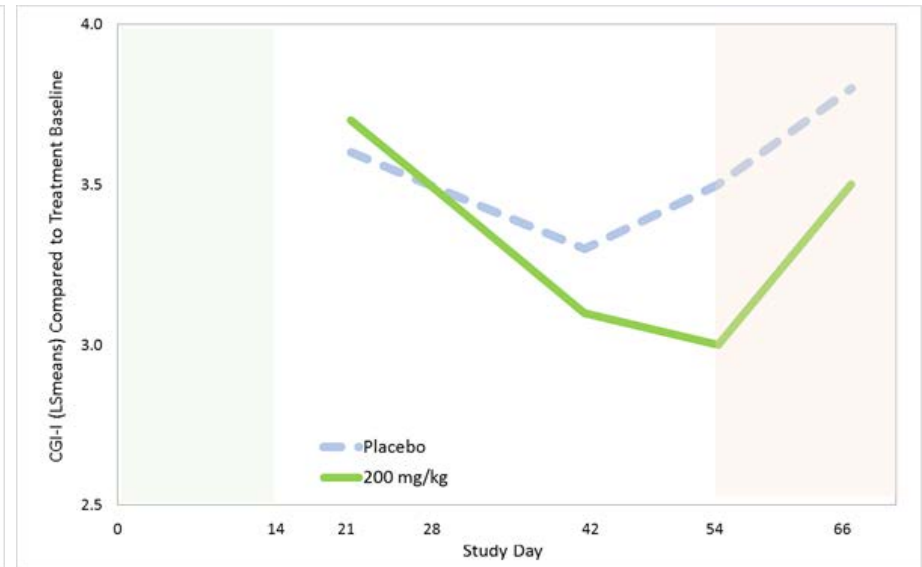


CGI-I – 200mg/kg versus placebo

Mean improvement after 6 weeks of treatment



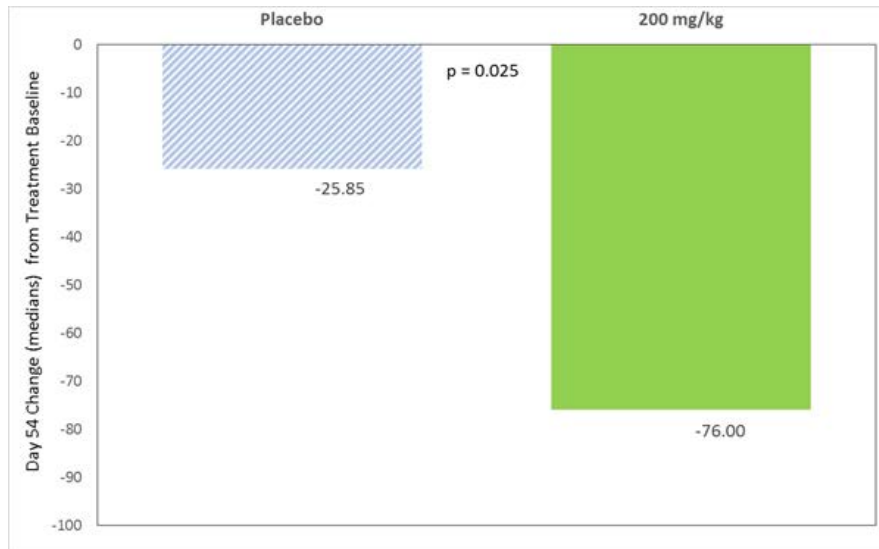
Time course of Improvement



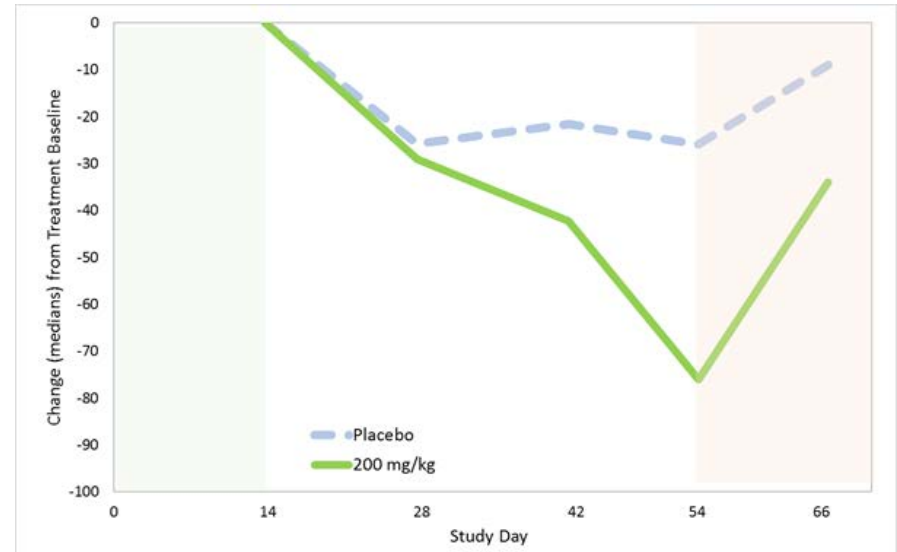
- ❑ A decrease on the y-axis indicates greater clinical improvement
- ❑ Clinician rates how much the subject's overall illness has improved or worsened, relative to baseline, with ratings anchored to Rett syndrome symptom descriptions
- ❑ 22% of subjects in the 200mg/kg dose group received a CGI-I score of 2 ("much improved") compared with 4% of subjects in the placebo group
- ❑ CGI-I expected to be a key secondary efficacy measure in pivotal trial

RTT DSC – 200mg/kg versus placebo

Median improvement after 6 weeks of treatment



Time course of Improvement



- ❑ A decrease on the y-axis indicates clinical improvement
- ❑ Median improvements for 200mg/kg and placebo were, respectively, 15% and 5% of the treatment baseline
- ❑ Clinician assesses on a visual analog scale the severity of concerns identified for each subject on an individual basis

Views of leading physicians and rettsyndrome.org

Walter Kaufmann, MD:

“The outcome of this trial is very encouraging. Safety, the primary goal, was achieved. As important and with broad implications, there was a clear clinical improvement covering several common symptoms in Rett syndrome, which are known to impair the quality of life of girls affected by the disorder. The variety of improved symptoms suggests that trofinetide is a drug that targets mechanisms underlying the disorder rather than a symptomatic medication. Similar to the previous adult trial, the results are particularly significant because of the relatively short duration of the trial. The impact of the study goes beyond the suggested efficacy of trofinetide, since it shows the potential of neurobiologically-based drugs for the treatment of Rett syndrome and other neurodevelopmental disorders.”

Alan Percy, MD:

“The clear results from this trial of trofinetide in children support and strengthen the promising results that were obtained in the Neuren trial in older individuals with Rett syndrome. I now look forward to the pivotal trial.”

Steve Kaminsky, PhD, Chief Science Officer of Rettsyndrome.org:

“These pediatric study results are very exciting. The data suggest that trofinetide is having a positive change on a number of challenges of Rett syndrome. We at Rettsyndrome.org are very proud to have supported this game-changing study, believing that the best is yet to come.”

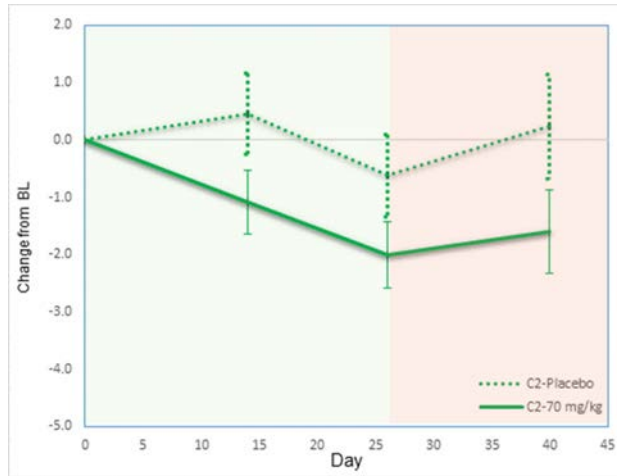


First Phase 2 trial in ages 16 to 45

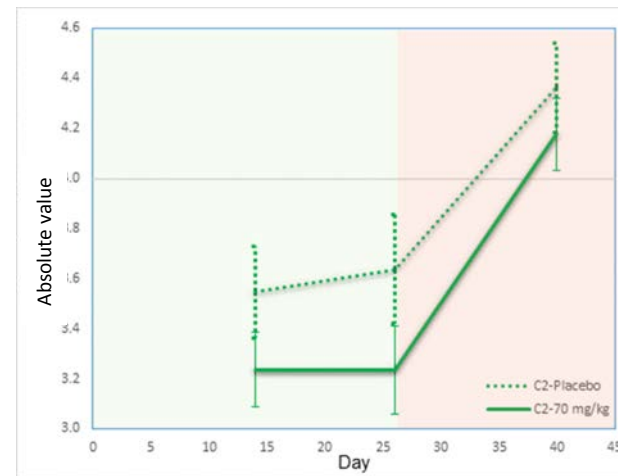
- Double-blind, placebo-controlled Phase 2 trial of 4 weeks of treatment with two dose levels (35 mg/kg and 70 mg/kg of body weight twice daily)
- 56 subjects aged 16 to 45 years randomized, with 53 subjects completing the trial
- Both dose levels were well tolerated and no safety concerns were identified
- 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

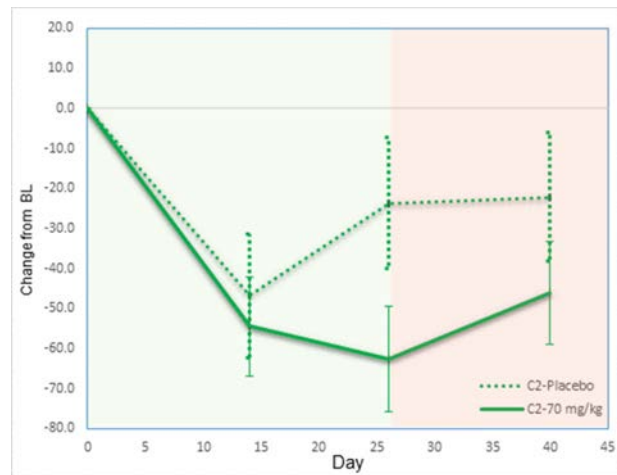
Motor Behavior Assessment Change Index



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



Other programs

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
 - Evaluation of rating scales for use in pivotal clinical trials is in progress
 - Non-clinical toxicity study and CMC investments for Rett program will enable next Fragile X clinical trial in children aged 3 to 12

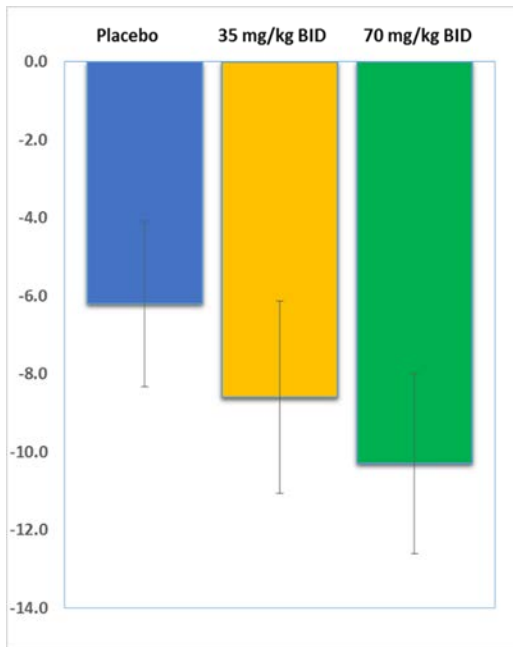


Completed Phase 2 trial in adolescents and adults

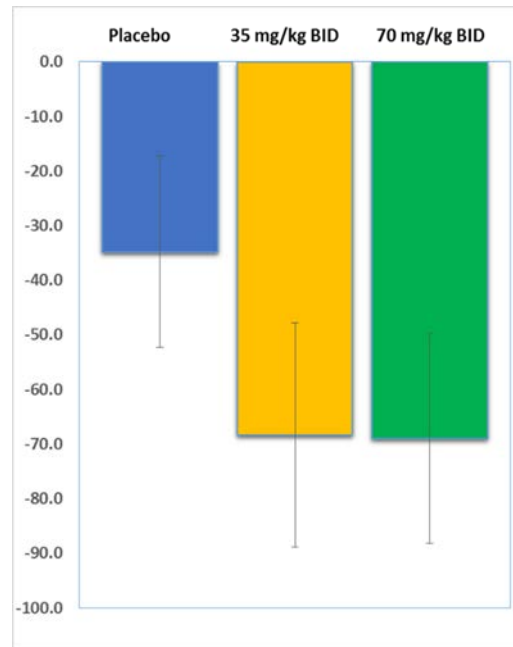
- Double-blind, placebo-controlled Phase 2 trial of 28 days of treatment with two dose levels (35 mg/kg and 70 mg/kg of body weight twice daily)
- 70 subjects aged 12 to 45 years received treatment, with 68 subjects completing the trial
- Both dose levels were well tolerated and no safety concerns were identified
- Higher dose exceeded pre-specified targets and demonstrated consistent trends 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

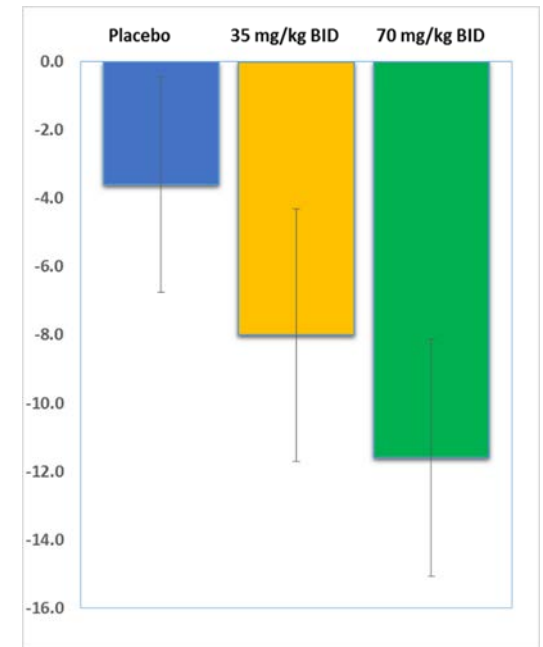
Fragile X Syndrome Rating Scale



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

Trofinetide in FXTAS

- Initiating development of trofinetide for Fragile X-associated tremor/ataxia syndrome (FXTAS) in H2 2017:
 - neurodegenerative disorder with no approved therapy.
 - expected to meet the criteria for Orphan Drug designation.
- Individuals with FXTAS are carriers of a premutation of the Fragile X Mental Retardation 1 (FMR1) gene. Full mutation causes Fragile X syndrome.
- Approximately 1 in 800 males and 1 in 250 females in the US are premutation carriers. Of these, 40% of males over 50 and 8% of females over 40 will go on to develop FXTAS.
- Symptoms include ataxia, cognitive dysfunction (ranging from memory loss to dementia), psychiatric disorders (such as depression, anxiety, agitation, and disinhibition), behavioural disorders (due to impaired executive function), falls and intention tremor.

Trofinetide in Traumatic Brain Injury (TBI)

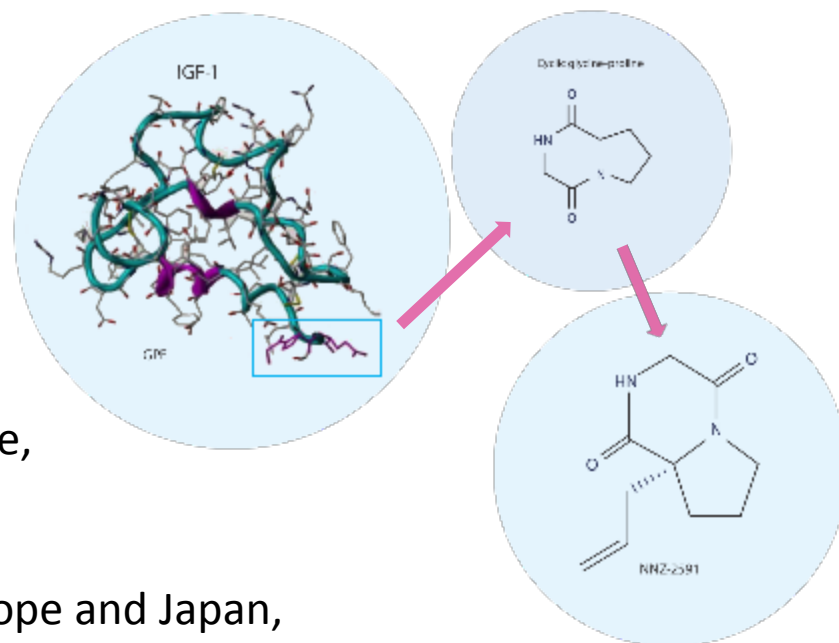
- >1.5 million head injuries annually in the US alone
- Leading cause of death and disability, especially in young and elderly
- No approved treatments available
- Partnership funding of ~US\$25 million has been contributed by US Army
- Phase 2 trial (“INTREPID”) in 260 subjects with moderate to severe TBI
 - Favourable safety profile confirmed
 - Statistically significant ($p=0.008$) and clinically relevant benefit of active over placebo in patients with severe TBI who completed RBANS
 - 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)
 - A positive pk/pd relationship was seen in patients with severe TBI

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
- Consideration of potential Orphan Drug qualification for severe TBI

Second drug candidate: NNZ-2591

- Synthetic analog of cyclic dipeptide derived from GPE, 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
- Potential either to target different indications, or to improve on trofinetide



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