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Investor Presentation

6 October 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.

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Neuren snapshot

- Stock code ASX: NEU, market cap approximately A$160 million (US$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 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)
  - End of Phase 2 meeting with FDA Division of Neurology in October 2017

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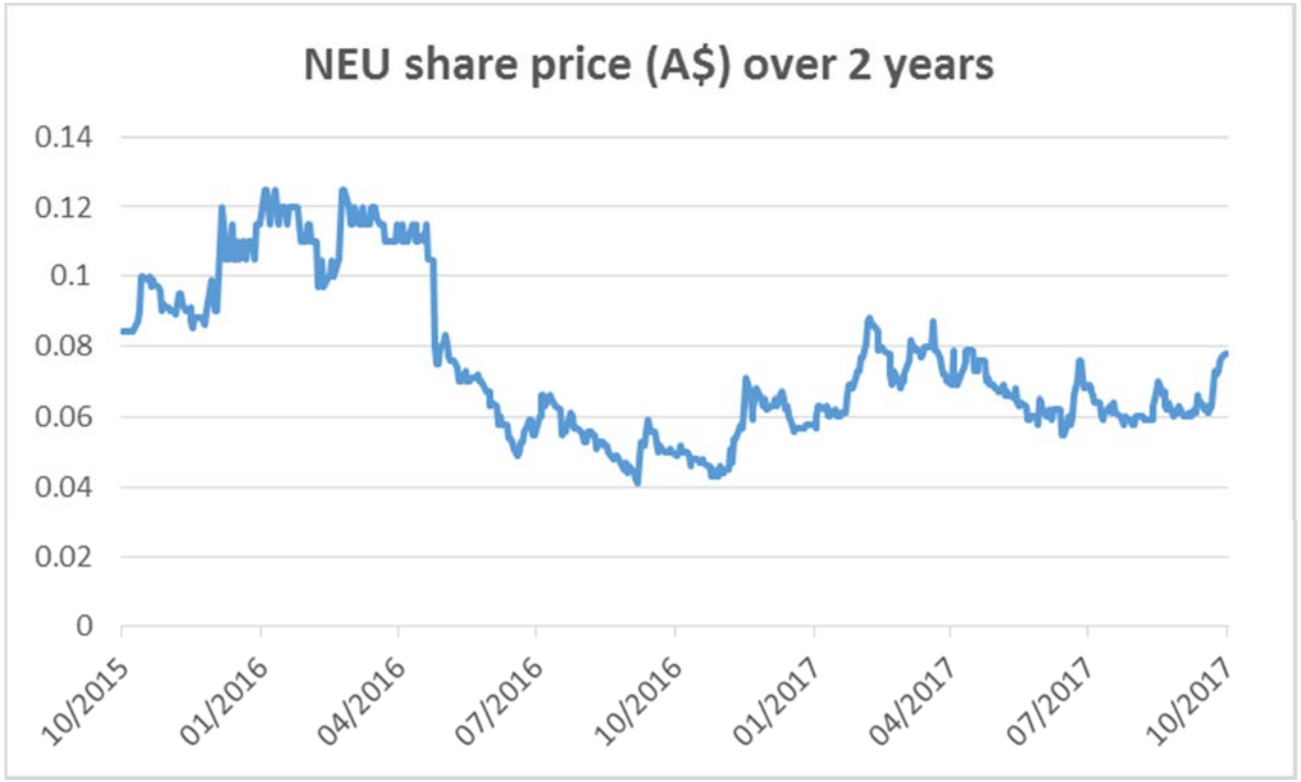
Neuren stock information (ASX: NEU)

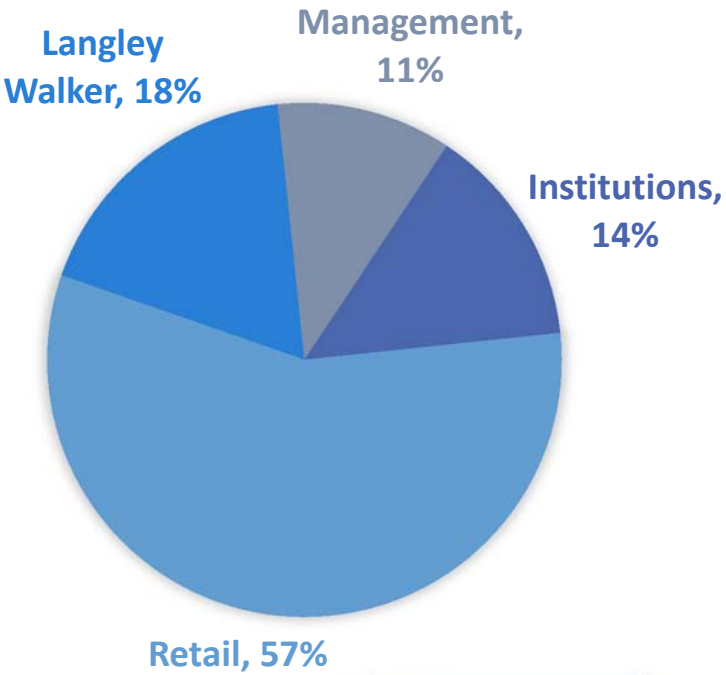
Issued shares: 2.0 billion

Closing price 5 Oct 2017: 7.7 cents

1 month VWAP : 6.9 cents

52 week range: 4.1 – 9.4 cents





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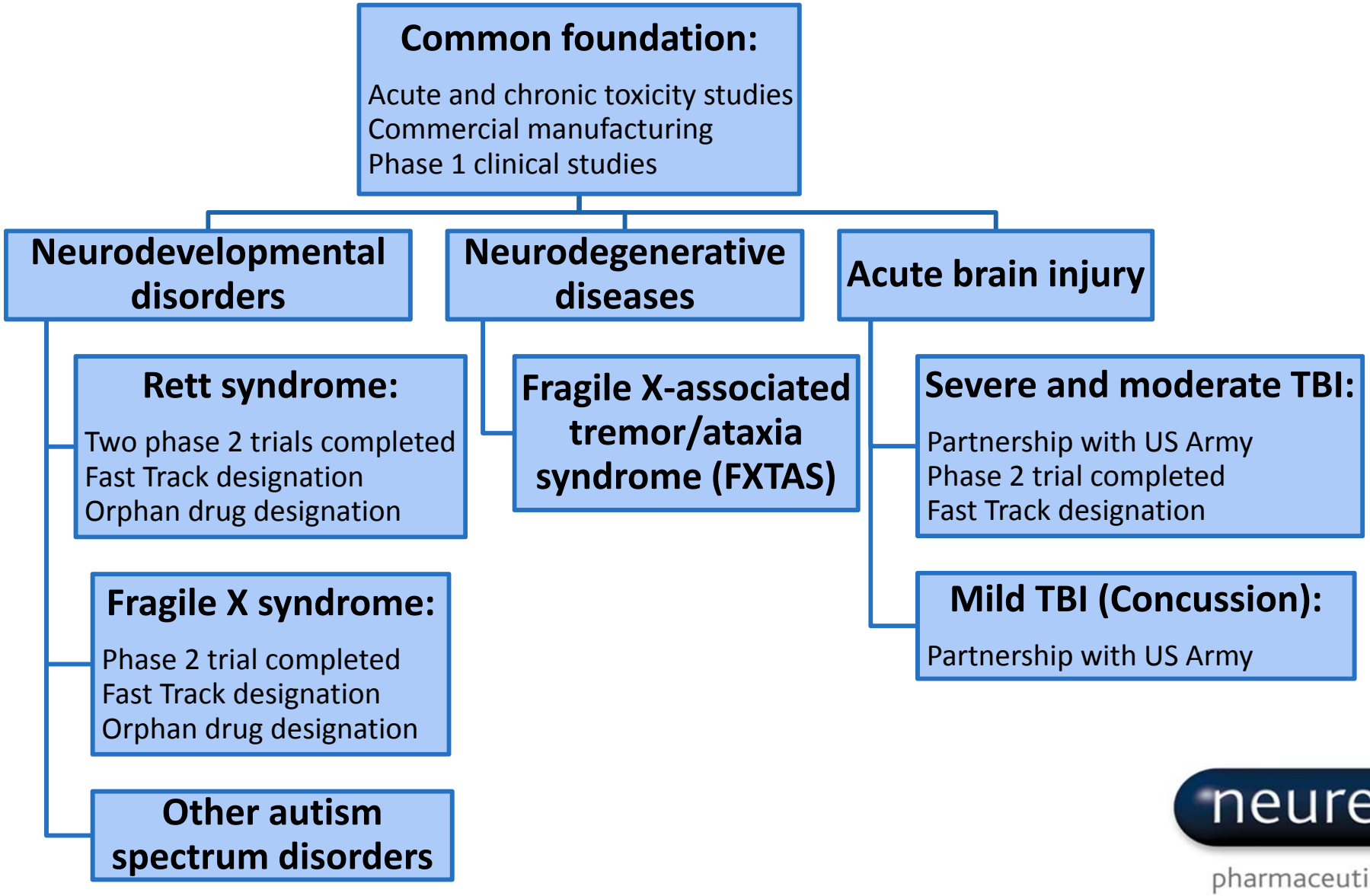
Trofinetide development strategy



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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

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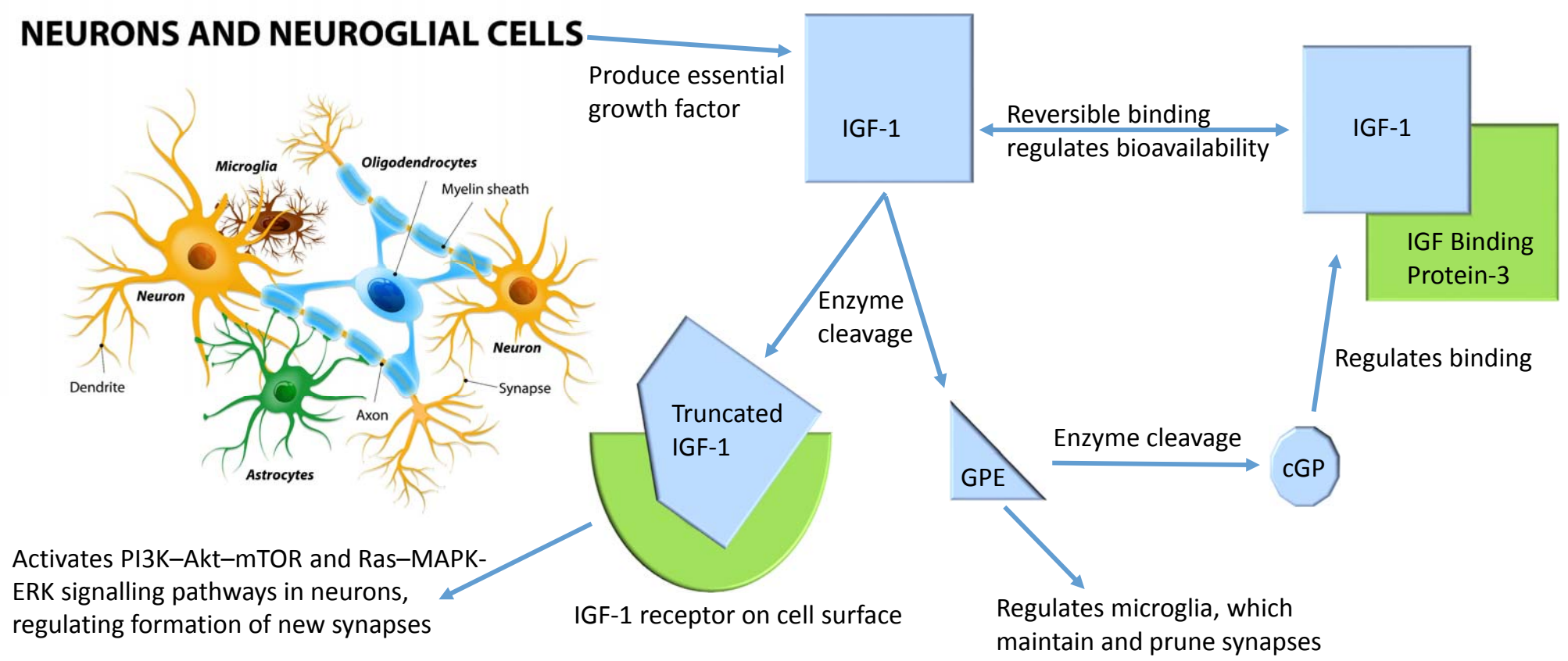
Normal biology of IGF-1 in the brain



Neuren's **trofinetide** and **NNZ-2591** are synthetic analogues of GPE and cGP:

- Replicate the activity of the natural molecules
- More stable and orally bioavailable
- Readily cross the blood-brain barrier

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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

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Impaired brain biology and trofinetide intervention

- In Rett syndrome, synapses are too few and underdeveloped, due to:
  - Insufficient formation of new synapses by neurons
  - Exaggerated maintenance of existing synapses by overactive microglia
- A mutation in the *MECP2* gene causes a deficit of the protein MeCP2
  - MeCP2 binds to the IGF Binding Protein-3 promoter, so insufficient MeCP2 allows excess IGF Binding Protein-3 to be produced
  - Too much IGF-1 binds to the excess IGF Binding Protein-3, so there is insufficient remaining available to bind to IGF-1 receptors and activate protein synthesis
  - Bound IGF-1 does not break down, so insufficient GPE is released
  - Excessive inflammatory cytokines are produced and microglia and astrocytes are overactive
- Introducing trofinetide:
  - Increases the amount of available IGF-1 that can bind to IGF-1 receptors
  - Inhibits the production of inflammatory cytokines
  - Inhibits the over-activation of microglia and astrocytes

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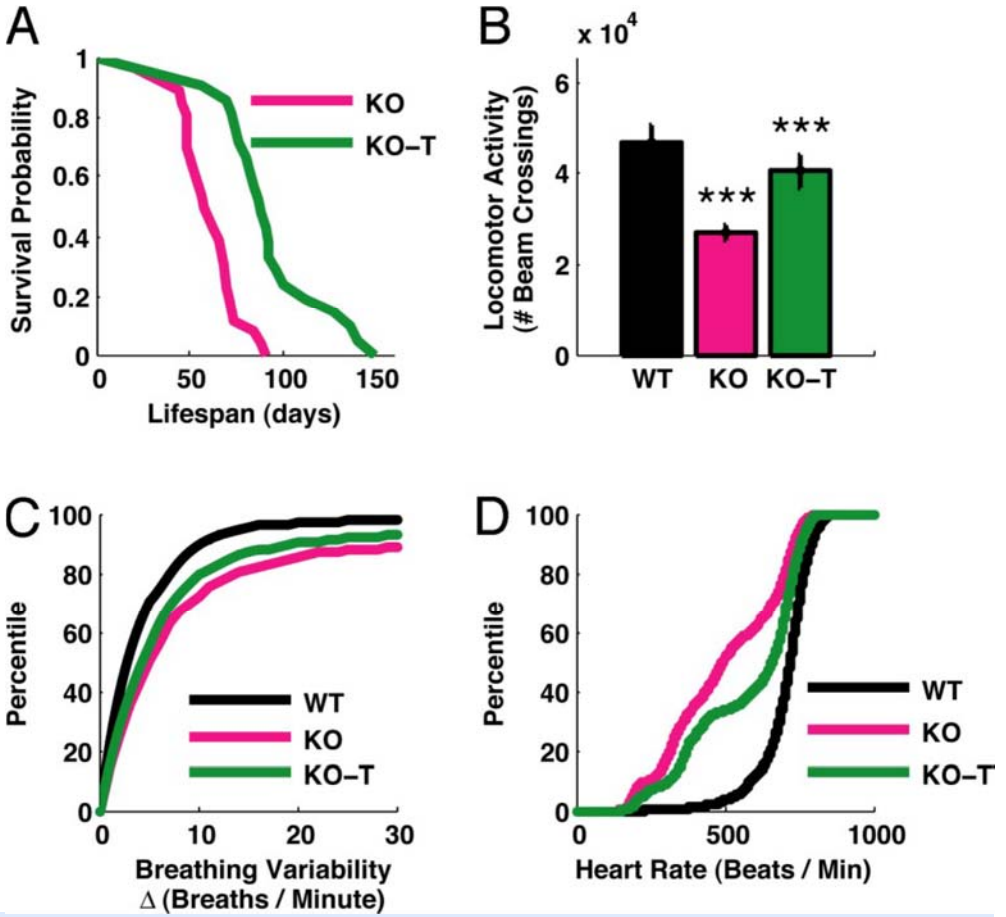
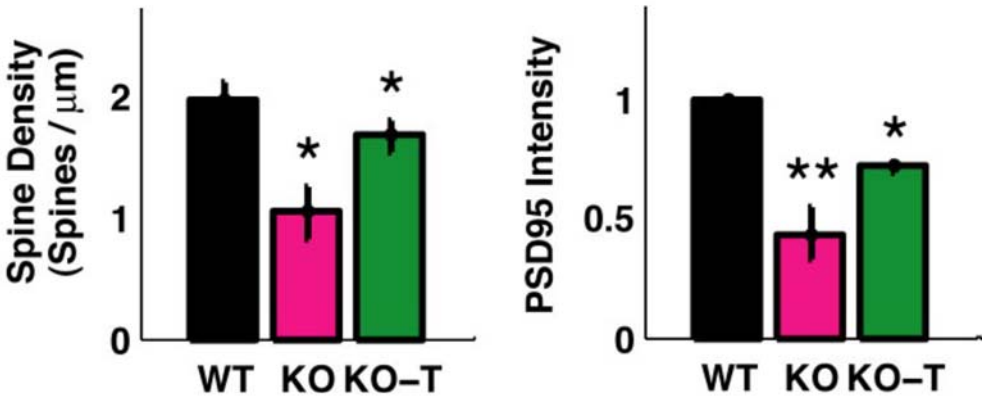
Impact in mouse model of Rett syndrome

In “Partial reversal of Rett syndrome like symptoms in MeCP2 mutant mice” (doi:10.1073/pnas.0812394106), Tropea et al reported that in the MeCP2 knockout mouse, introducing GPE:

- Extended life span, improved locomotor function, ameliorated breathing patterns and reduced irregularity in heart rate
- Increased the density of the dendritic spines that form synapses
- Increased levels of PSD-95, a key protein for synapse maturation
- Increased synaptic transmission signals





Notes: WT=wild type, KO=knockout, KO-T=knockout treated with GPE. Charts reproduced with permission.

Trofinetide development program

- 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)
- End of Phase 2 Type B meeting with FDA Division of Neurology scheduled in October 2017 to discuss Phase 3 development
- Investments ongoing 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

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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

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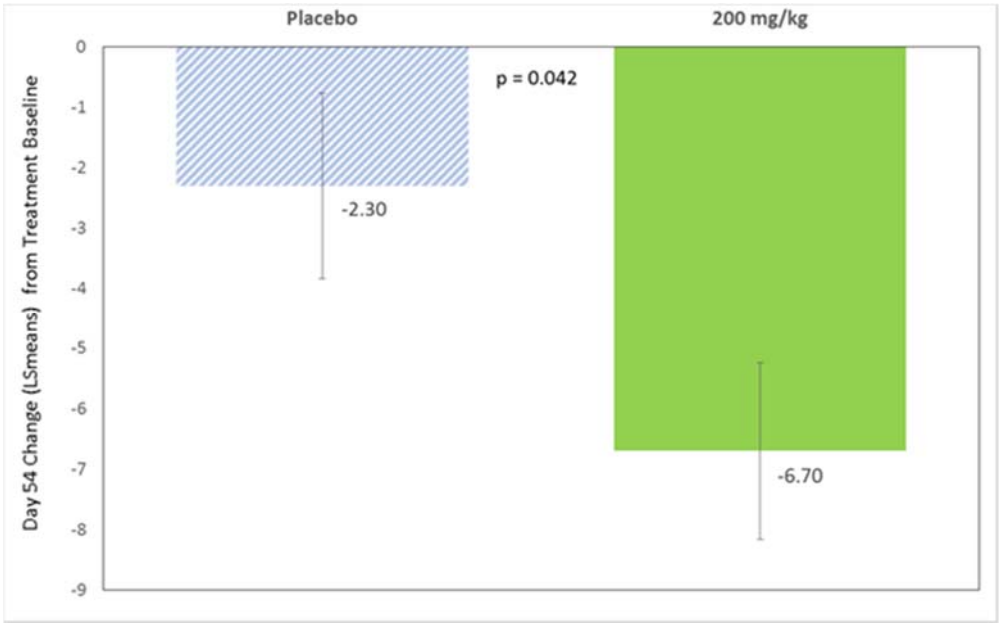
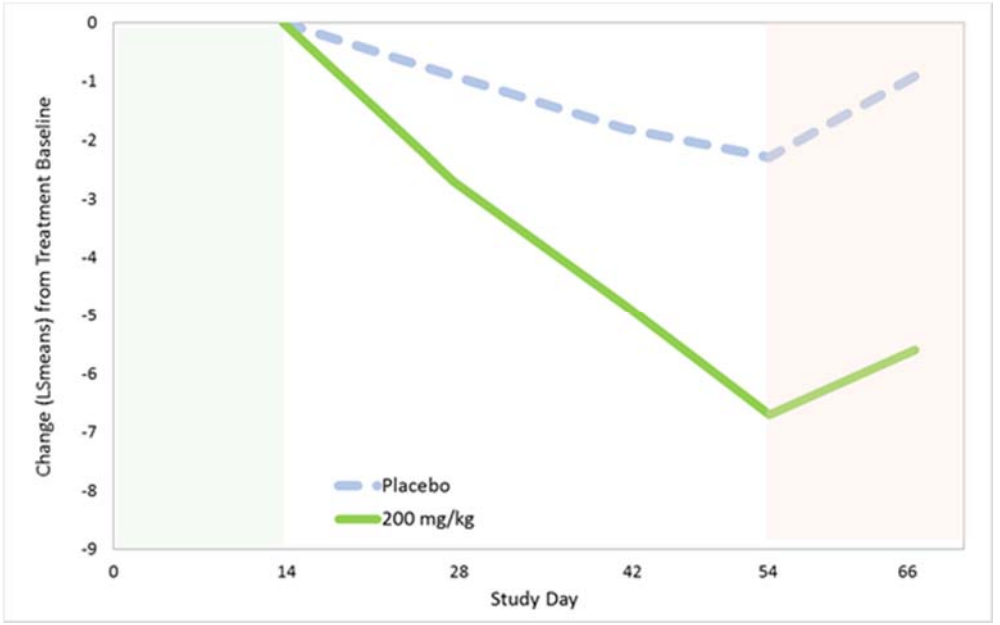
RSBQ – 200mg/kg versus placebo

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

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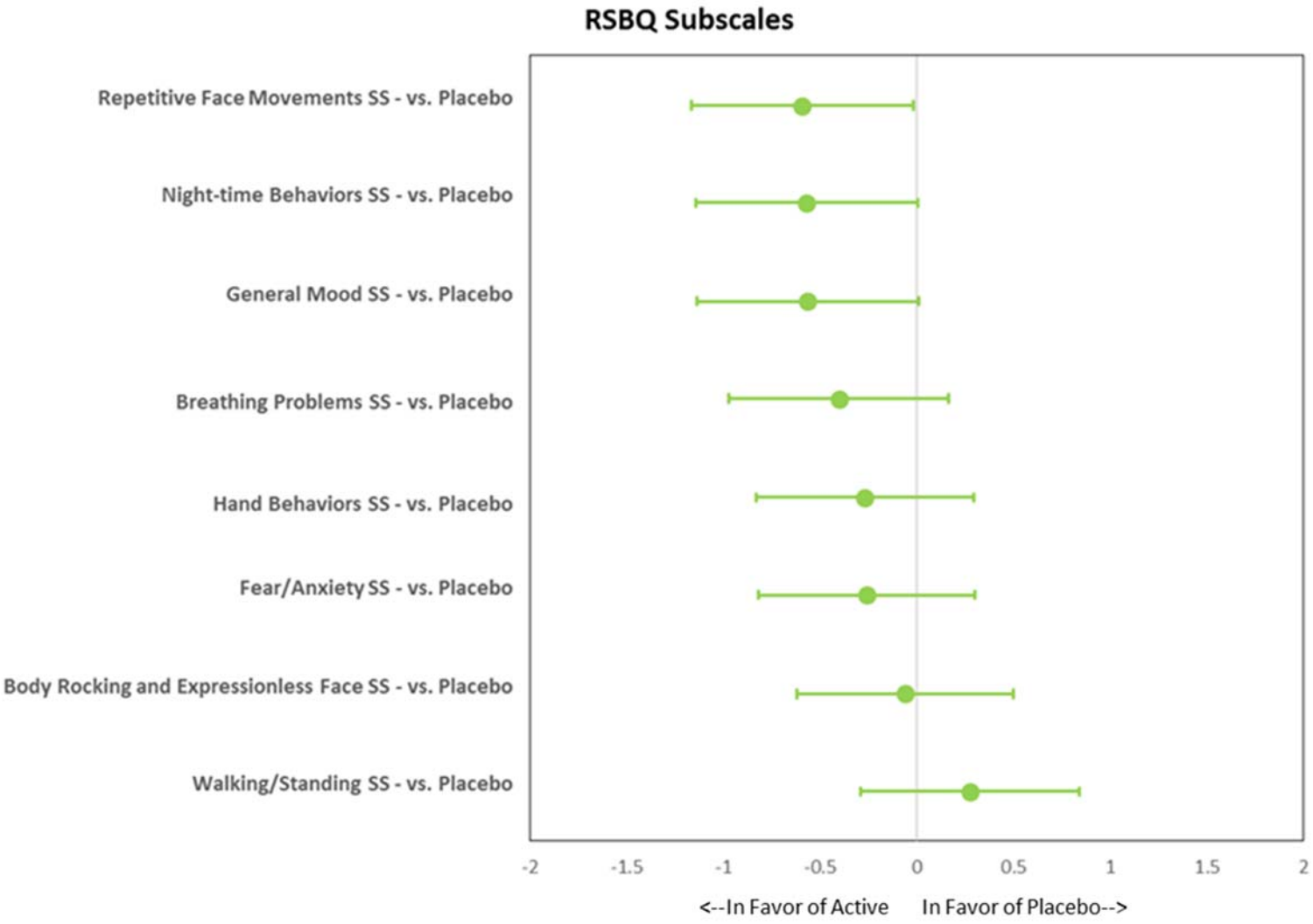
RSBQ subscales – Cohen's D effect sizes



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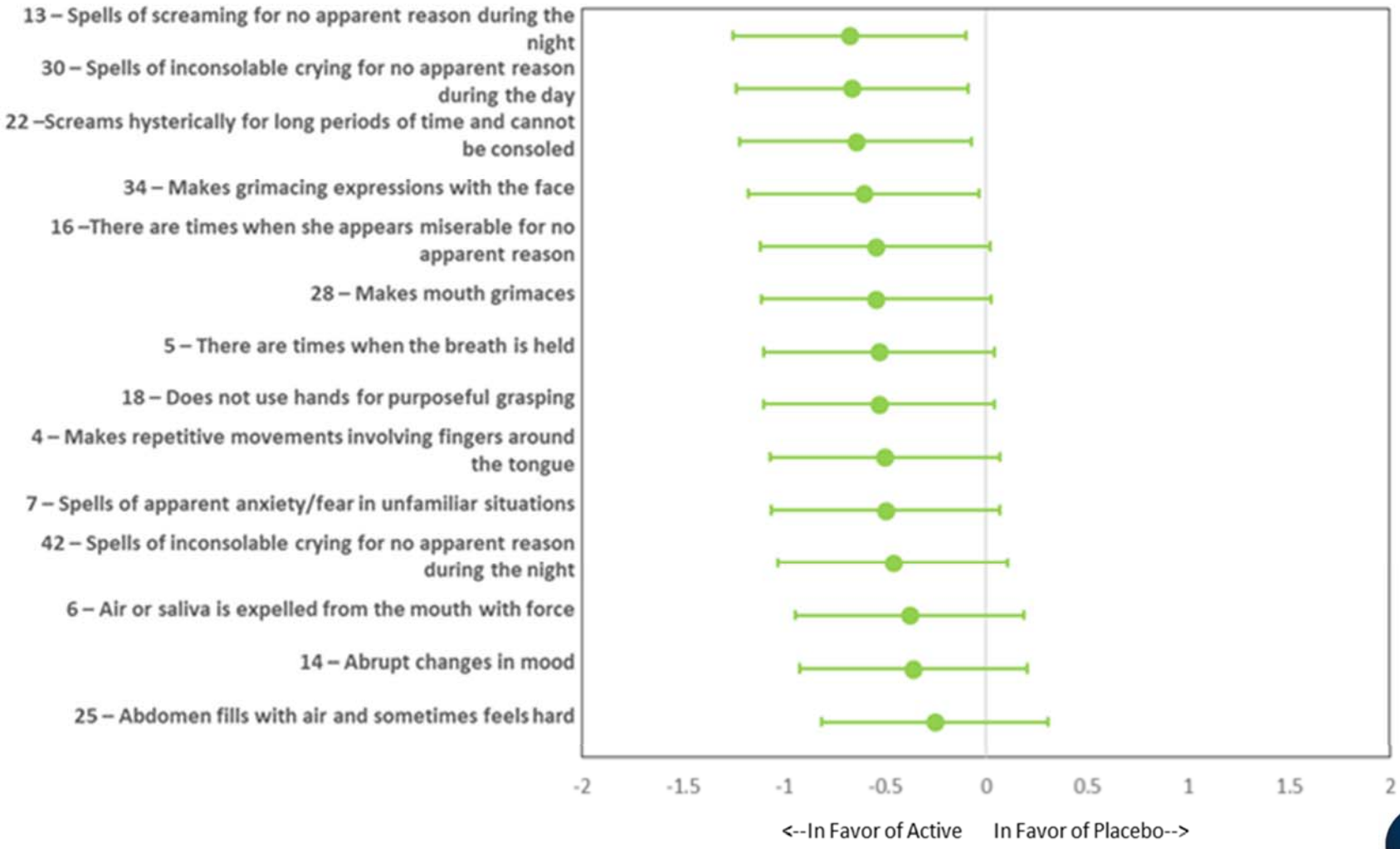
RSBQ items – Cohen's D effect sizes

RSBQ items with largest effect size in favour of active



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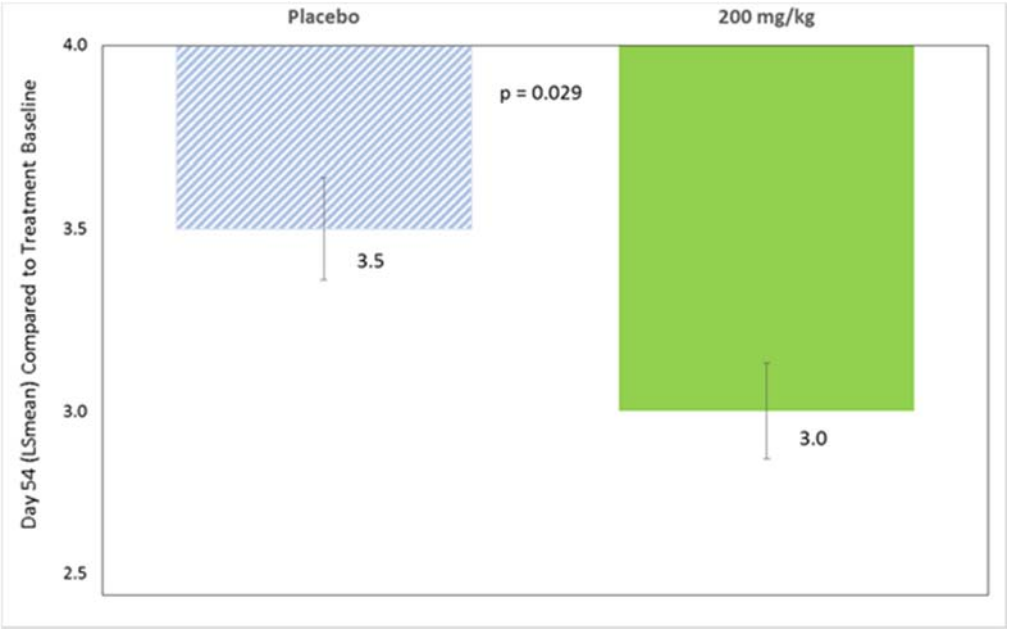
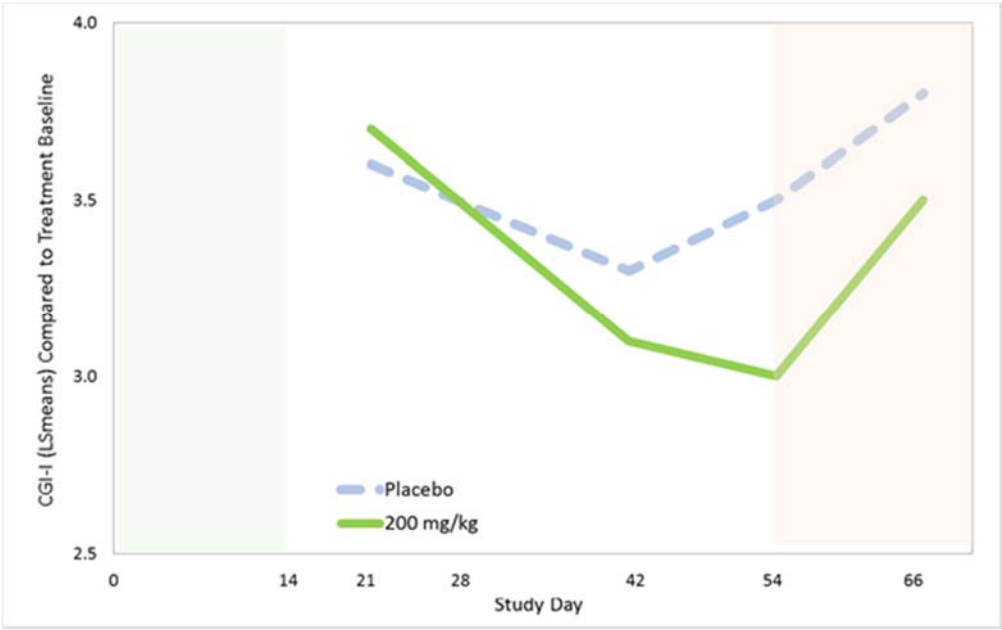
CGI-I – 200mg/kg versus placebo

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 secondary efficacy measure in pivotal trial

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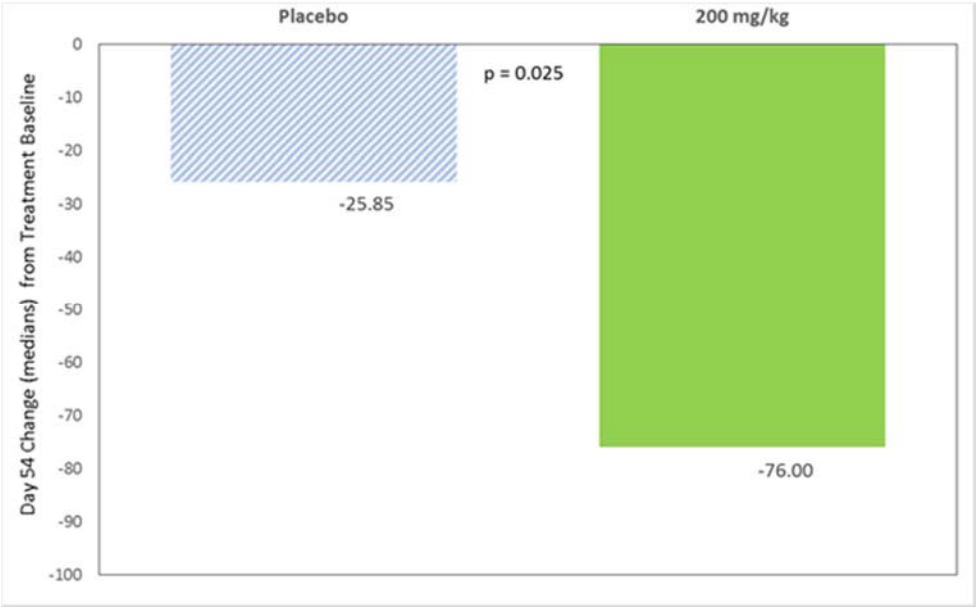
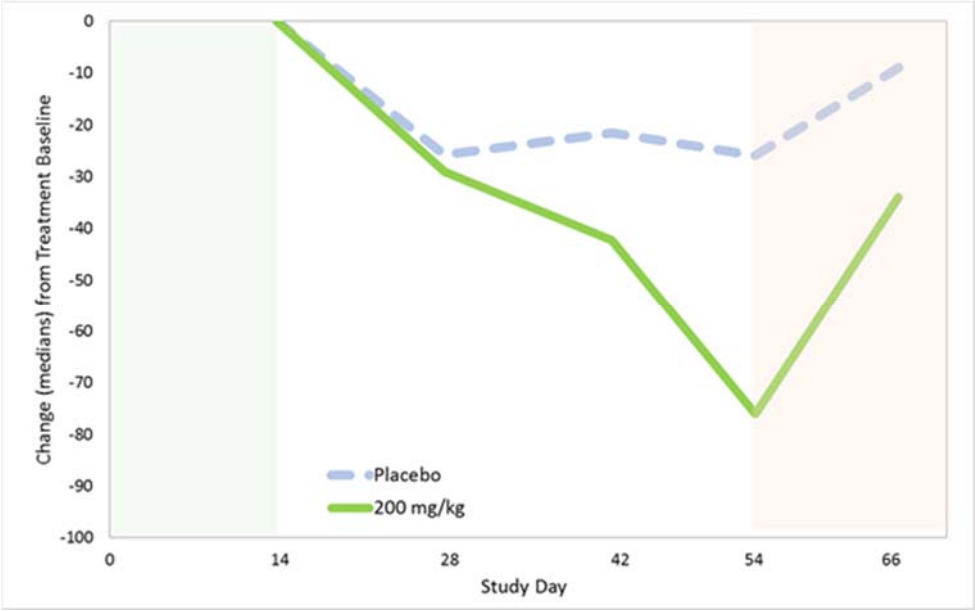
RTT DSC – 200mg/kg versus placebo

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

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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."

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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

Study publication: Glaze et al, Pediatric Neurology DOI: http://dx.doi.org/10.1016/j.pediatrneurol.2017.07.002

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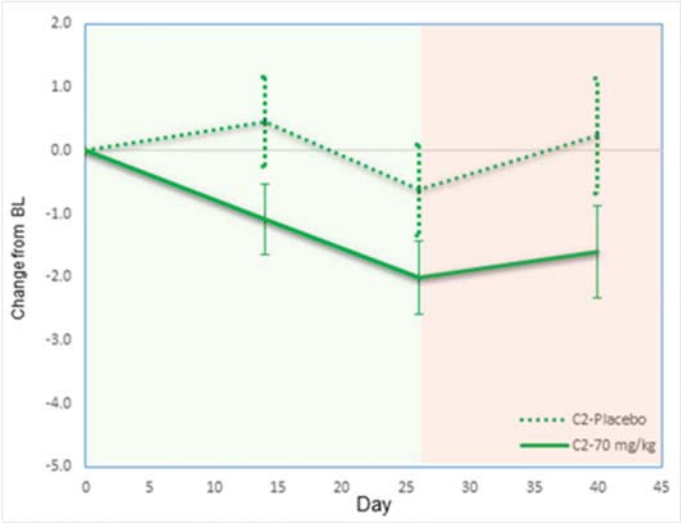
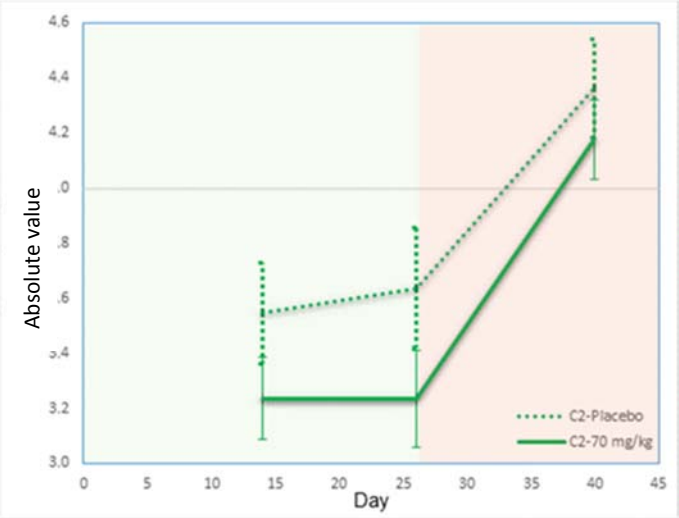
Core efficacy measures

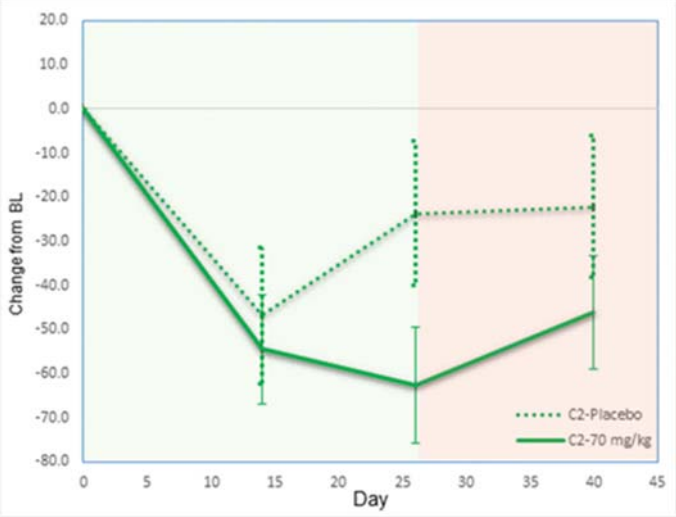
Motor Behavior Assessment Change Index



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

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Fragile X syndrome program

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 development program status:
  - 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

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Impaired brain biology and trofinetide intervention

- Mutations in the *fmr1* gene cause a deficit in production of the Fragile X Mental Retardation Protein (FMRP), which leads to too many and immature dendritic spines and abnormal synaptic transmission:
  - Impaired functioning of microglia and astrocytes
  - Overactive PI3K–Akt–mTOR and Ras–MAPK-ERK signalling pathways in neurons
  - Increased oxidative stress
  - Low production of IGF-1 and therefore GPE
- Intervention with trofinetide addresses each of these factors:
  - Inhibits the over-activation of microglia and astrocytes
  - Reduces the PI3K–Akt–mTOR and Ras–MAPK-ERK signalling
  - Increases the activity of Nrf2, a transcription factor that regulates the expression of antioxidant elements in response to oxidative stress
  - Increases bioavailable IGF-1 in the brain

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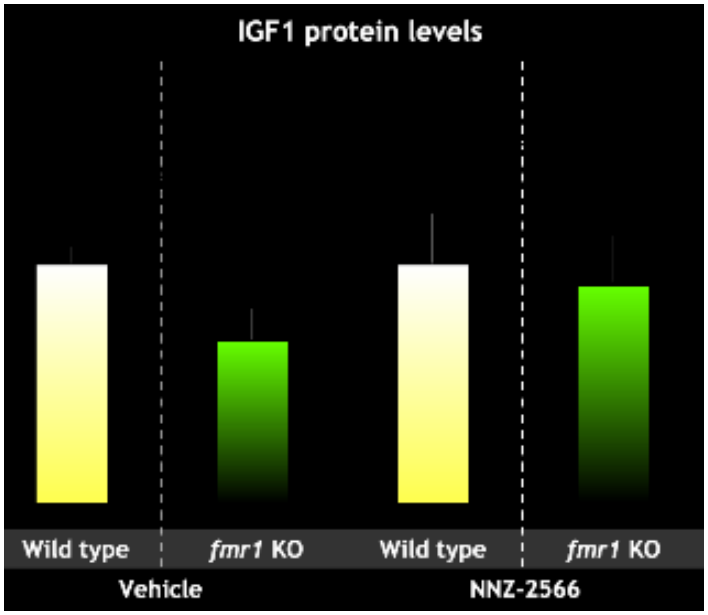
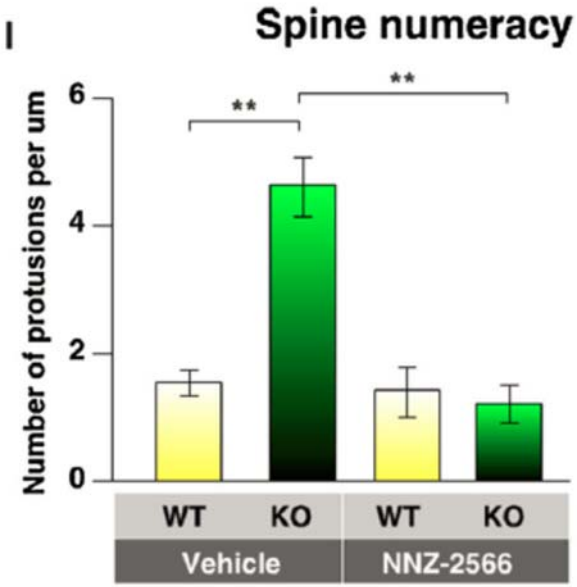
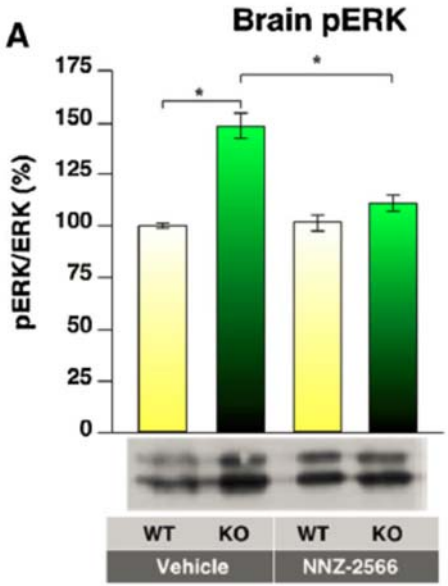
Impact in mouse model of Fragile X syndrome

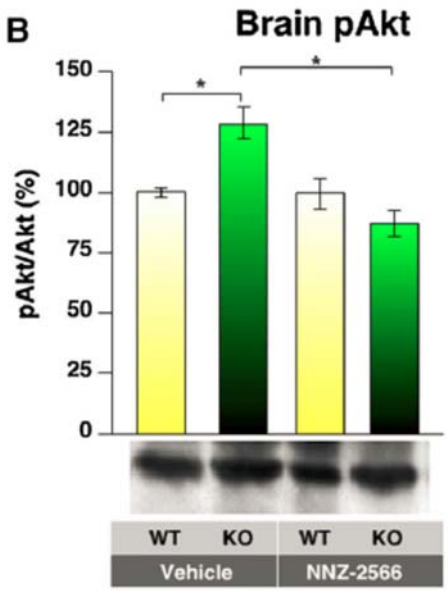
In the *fmr1* knockout mouse model, trofinetide normalised mutant mice, but had no effect on wild type mice:

- Corrected learning and memory deficits, hyperactivity and social behaviour
- Reduced dendritic spine density
- Normalised overactive ERK and Akt signalling in the brain
- Normalised the level of IGF-1 in the brain









Notes: WT=wild type, KO=knockout. Trofinetide is also known as NNZ-2566.

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

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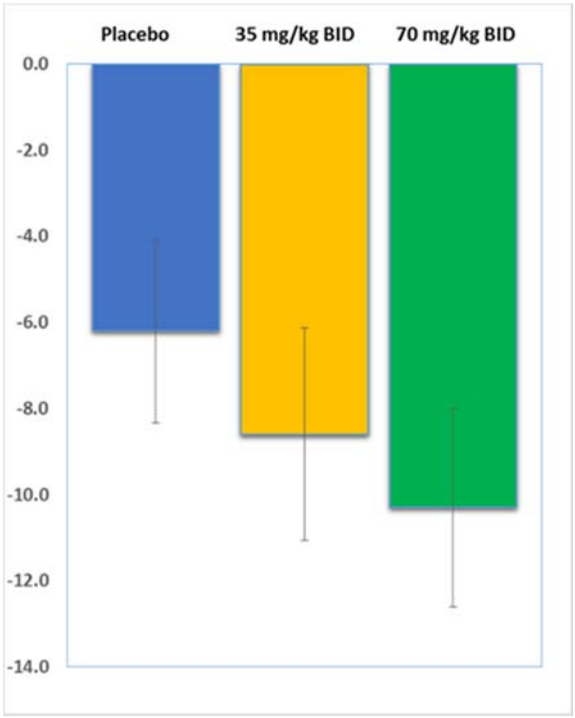
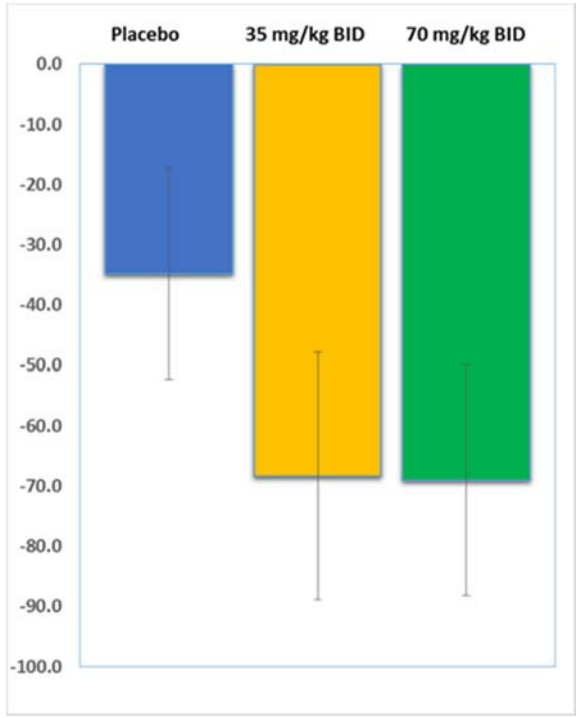
Core efficacy measures that met target

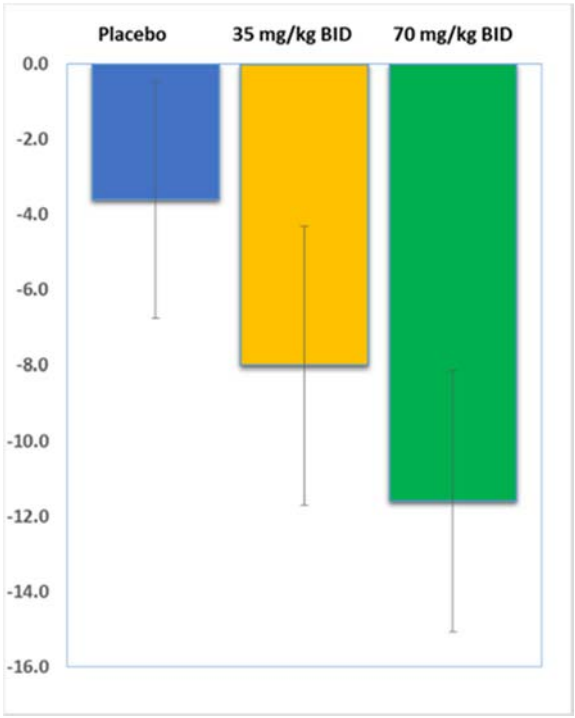
Fragile X Syndrome Rating Scale



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

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Other programs

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.

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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

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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

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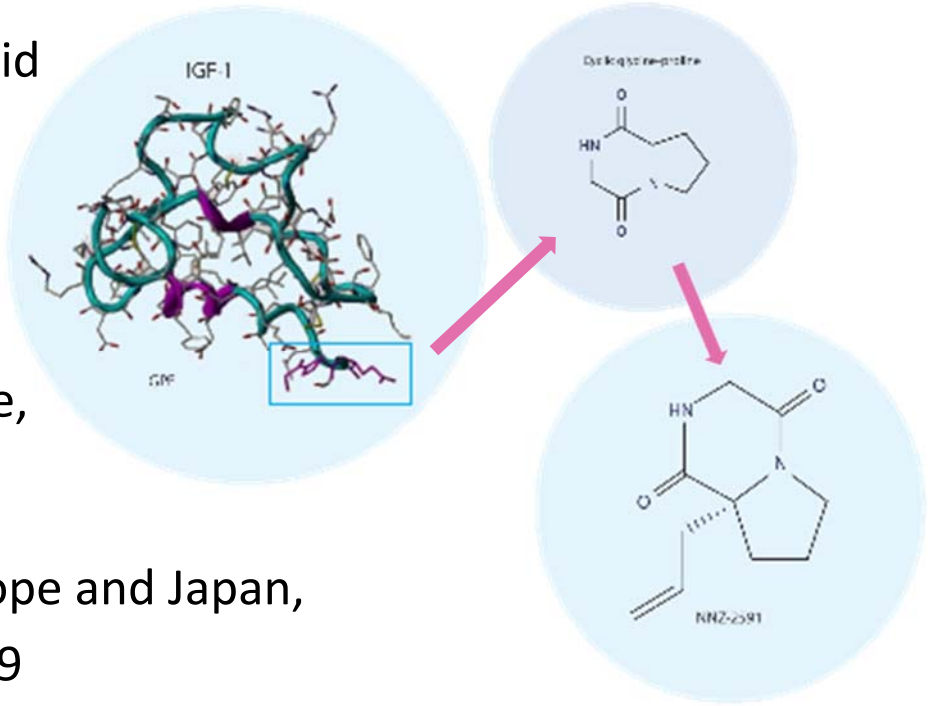
Preclinical drug candidate: NNZ-2591

- Improved stability and higher oral bioavailability, compared with trofinetide - 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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Appendix

Scientific publication references

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10. Tropea et al, Partial reversal of Rett Syndrome-like symptoms in MeCP2 mutant mice, doi:10.1073/pnas.0812394106
11. Deacon et al, NNZ-2566, a Novel Analog of (1–3) IGF-1, as a Potential Therapeutic Agent for Fragile X Syndrome, doi:10.1007/s12017-015-8341-2

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