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Investor Presentation

6 September 2018

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

- New therapies for neurological conditions with high unmet need
  - Significant commercial opportunities with no approved drugs
  - Regulatory incentives – *Orphan Drug*, *Fast Track, Priority Review*
  - Strong support from advocacy groups and leading physicians
  - Trofinetide and NNZ-2591 - patented drugs with utility in neurodevelopmental disorders, neurodegenerative disorders and brain injury
- Strong position following partnership with ACADIA for trofinetide
  - ACADIA provides capabilities, strategic intent and funding required to bring trofinetide to market in the US for Rett syndrome and Fragile X syndrome
  - Significant participation for Neuren in future value of trofinetide in North America
  - Neuren retains 100% of value of trofinetide outside North America
  - ACADIA commencing Rett syndrome Phase 3 trial in 2019
  - Neuren able to advance NNZ-2591 - $24.8 million cash at 31 August

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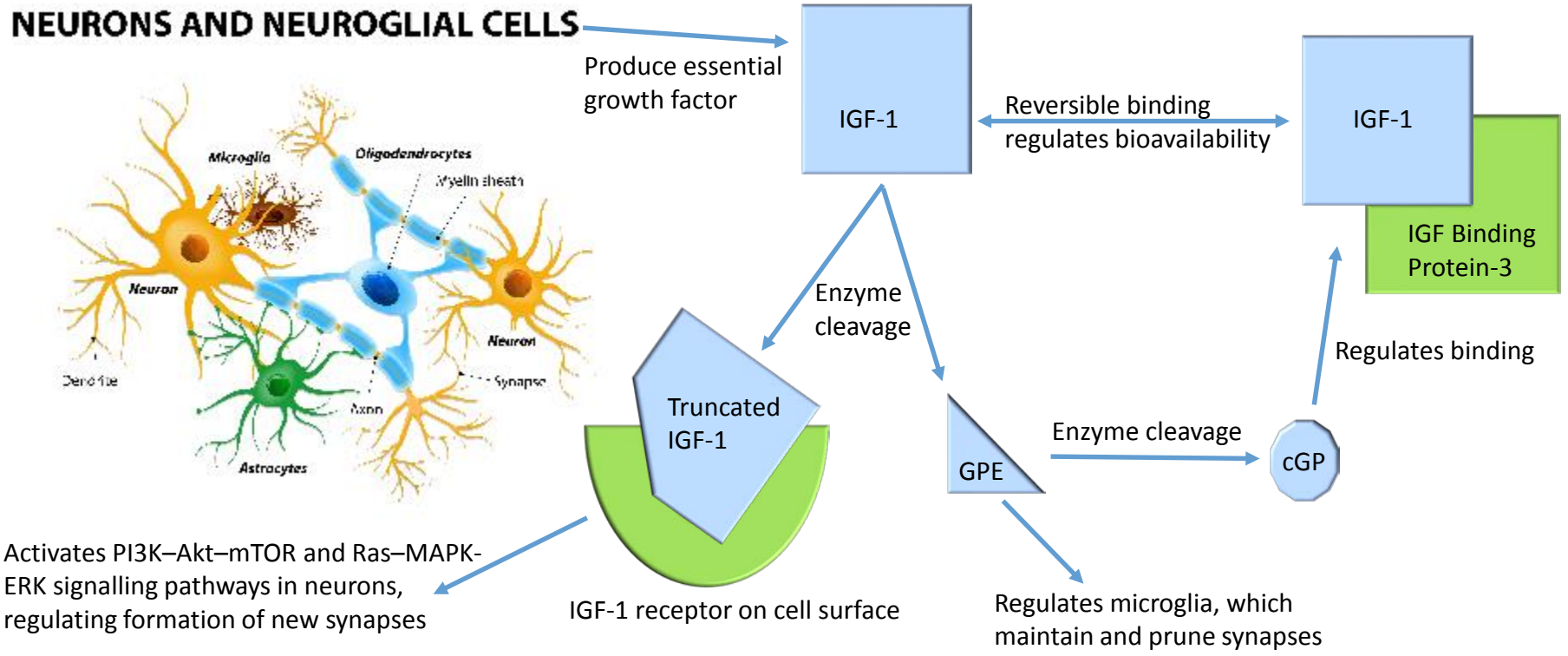
Normal biology of IGF-1 in the brain



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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Key features of ACADIA partnership

- ACADIA granted exclusive license for trofinetide in North America
- Neuren retains all rights outside North America
  - Free use of all data and regulatory information generated by ACADIA in the US for registration outside North America
- Neuren receives escalating tiered double-digit percentage royalties on net sales of trofinetide in North America
- Neuren receives milestone payments of up to US$465 million
  - US$10 million already received
  - Up to US$105 million on achievement of development milestones for Rett syndrome and Fragile X syndrome
  - Up to US$350 million on achievement of thresholds of annual net sales of trofinetide
- Neuren receives one third of the value of any Rare Pediatric Disease Priority Review Voucher awarded by the FDA
  - 5 vouchers sold for between US$110 million and US$150 million in 2017

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Key features of ACADIA partnership

- ACADIA team has proven record developing and commercializing therapies for CNS disorders in the US that have no approved therapies and high unmet need
- ACADIA will fund all development costs for trofinetide in North America (including ~US$55 million for Rett syndrome)
- Neuren will complete certain in-progress preparatory activities, funded by existing resources including ACADIA's exclusivity investment of US$4 million
- Neuren has equal membership of Joint Steering Committee to direct the development of trofinetide in all indications
- ACADIA has right of first negotiation for rights outside North America
- Neuren has an obligation not to develop a competing product in indications for which ACADIA develops and commercializes trofinetide

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Rett syndrome development program

- Statistically significant and clinically meaningful improvement demonstrated in pediatric Phase 2 clinical trial
- Phase 3 program with single trial agreed at End of Phase 2 Meeting with FDA Division of Neurology Products
- ACADIA to commence US Phase 3 trial in H2 2019, following completion of manufacturing of all drug substance required for the trial
  - Rett Syndrome Behaviour Questionnaire (RSBQ) and Clinical Global Impression of Improvement (CGI-I) as co-primary efficacy endpoints
  - ~180 subjects
  - Longer treatment than Phase 2 trial, with optimised weight-banded dosing
- Continuing strong support from leading Rett syndrome physicians and largest advocacy group (rettsyndrome.org)

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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
  - Patents in Europe, Japan and Australia for autism spectrum disorders, including Rett syndrome and Fragile X syndrome – expire 2032
  - Other applications pending in Canada, Brazil, Israel

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Advancing NNZ-2591

- Demonstrated efficacy in pre-clinical models of Parkinson's disease, stroke, traumatic brain injury, peripheral neuropathy, Fragile X syndrome, memory impairment and multiple sclerosis
- Funds now available to accelerate CMC and pre-clinical development required prior to clinical trials
- Issued composition of matter patents in US, Japan and all EPO countries except Turkey
  - Expire 2024, potential to extend to 2029
- Method of treatment patents and applications for NNZ-2591
  - Issued US patent for autism spectrum disorders and neurodevelopmental disorders and pending applications in Europe and Japan – expire 2034
  - 3 issued US patents for Parkinson's, peripheral neuropathy and cognitive impairment – expire 2024

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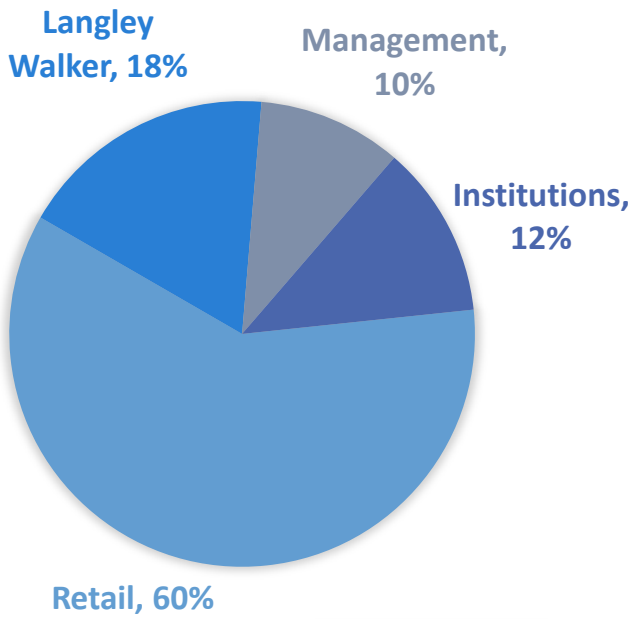
Neuren stock information (ASX: NEU)

Quoted shares: 100.2 million

52 week range: $1.04 - $3.56

2.5 million loan funded shares at exercise prices $1.62 - $1.84

(Fully diluted shares: 102.7 million)



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Neuren's near-term priorities

- Actively support ACADIA in development of trofinetide for North America
  - Complete second non-clinical chronic toxicology study
  - Assist with preparations for Rett syndrome Phase 3 trial:
    - Manufacture of drug supplies
    - Finalise protocol, sites and logistics
  - Optimise Fragile X syndrome development plan
- Advance Neuren's strategy to develop and commercialise trofinetide outside North America, including Europe and Japan
  - Engage with regulators to confirm requirements for registration in Rett syndrome
- Accelerate development of NNZ-2591
  - Advance CMC and toxicology studies to enable clinical trials
  - Confirm indication strategy to maximise value worldwide

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Trofinetide in Rett syndrome and Fragile X syndrome

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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Results of Phase 2 trial in girls aged 5 to 15

- Double-blind, placebo-controlled Phase 2 trial of treatment for 6 weeks in girls with Rett syndrome, aged 5 to 15 years
- Conducted at 12 US hospitals, led by world-leading clinicians in Rett syndrome and supported by rettsyndrome.org
- Statistically significant improvement for high dose (n=27) compared with placebo (n=24), 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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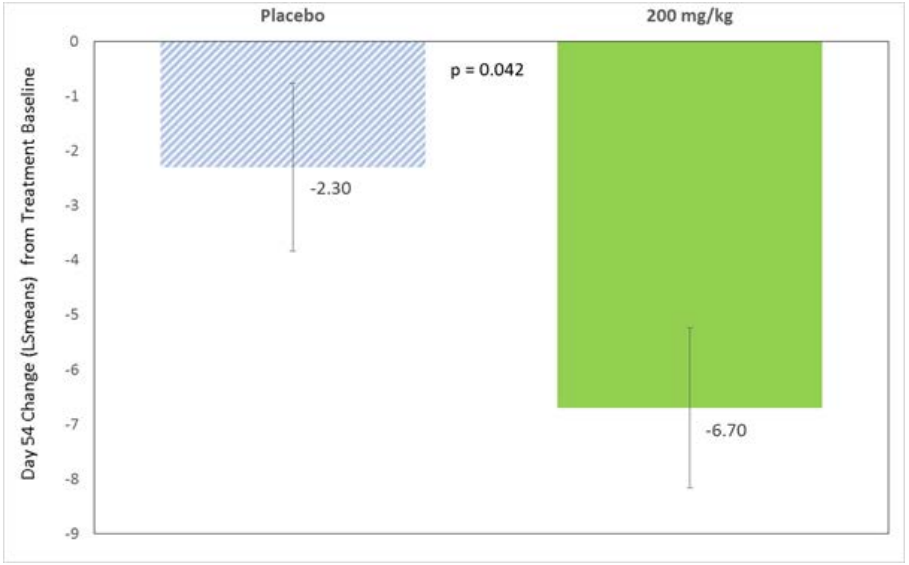
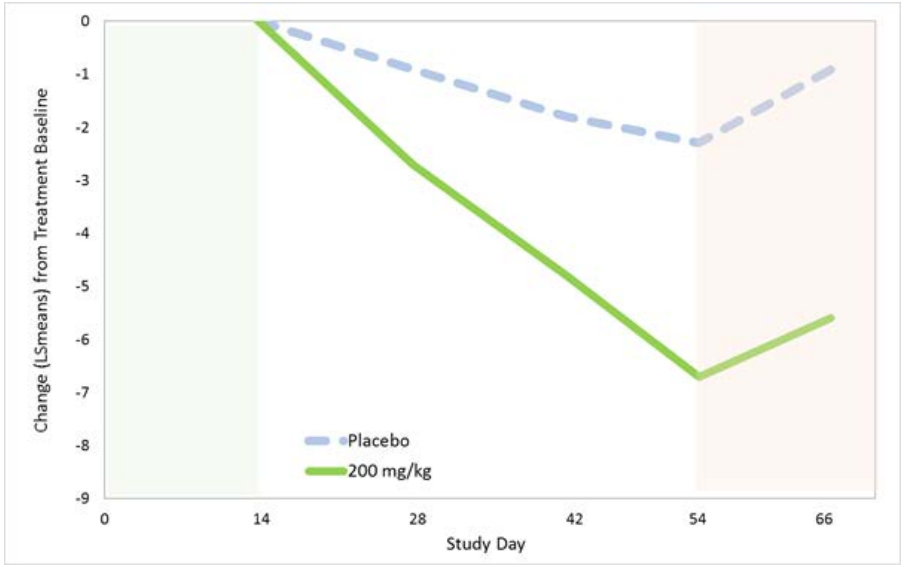
RSBQ – 200mg/kg versus placebo

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

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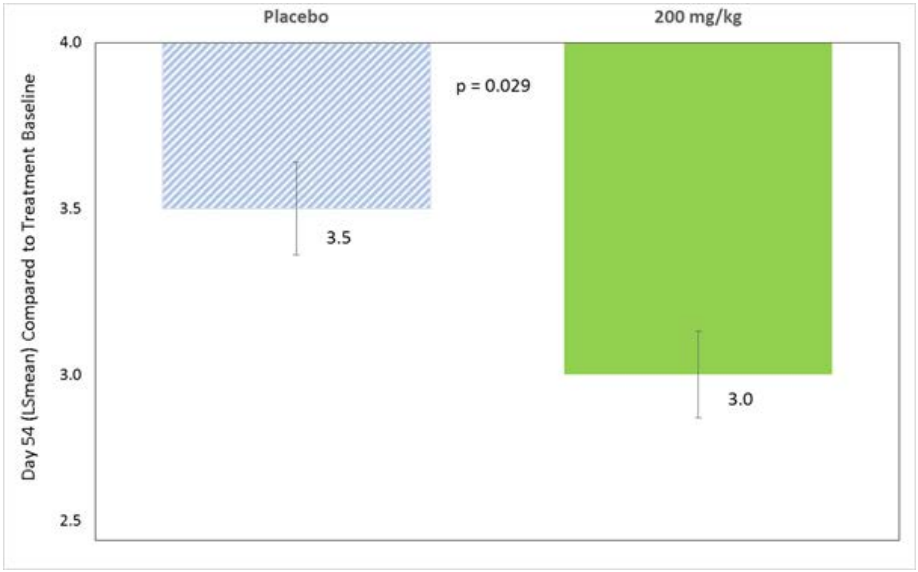
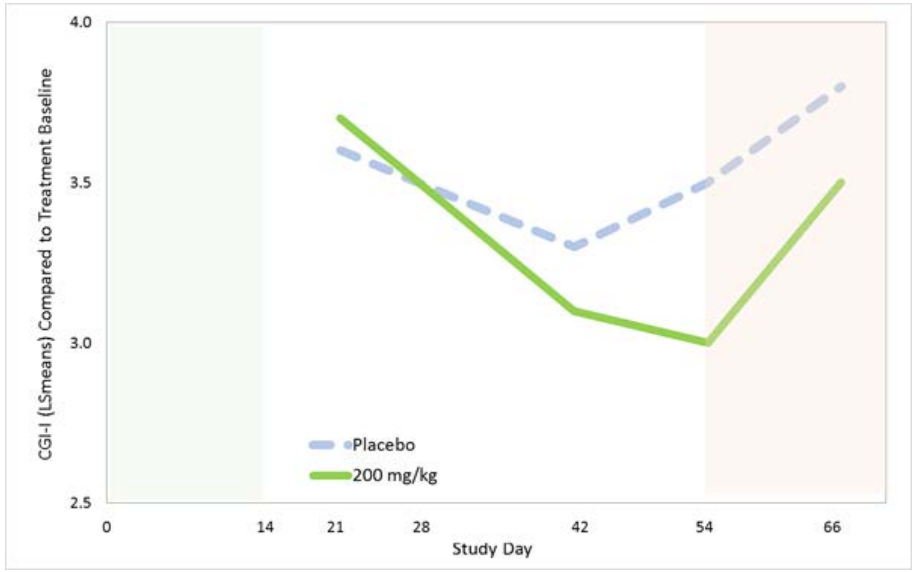
CGI-I – 200mg/kg versus placebo

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

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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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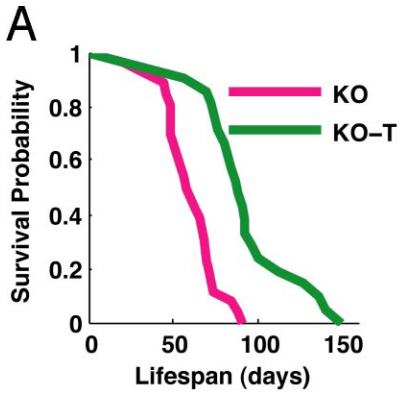
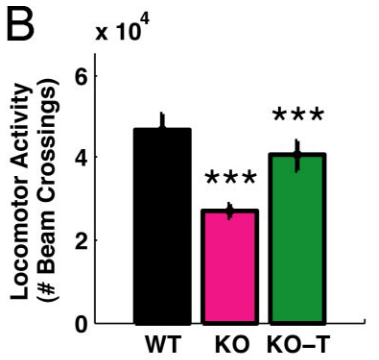
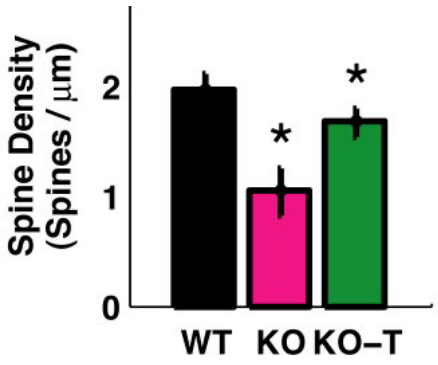
Impact in mouse model of Rett syndrome

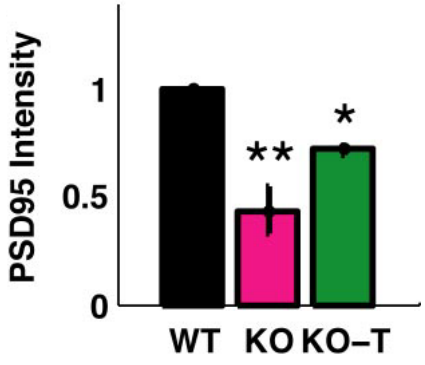
In "Partial reversal of Rett syndrome like symptoms in MeCP2 mutant mice" (doi:10.1073/pnas.0812394106), Tropea et al reported that in the MeCP2 knockout mouse, introducing GPE:

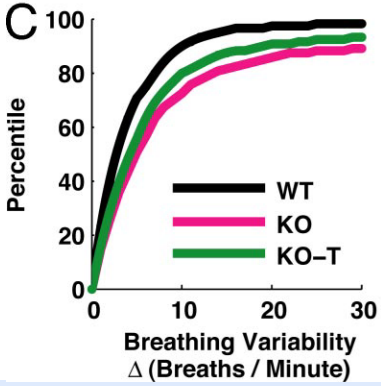
- Extended life span, improved locomotor function, ameliorated breathing patterns and reduced irregularity in heart rate
- Increased the density of the dendritic spines that form synapses
- Increased levels of PSD-95, a key protein for synapse maturation
- Increased synaptic transmission signals

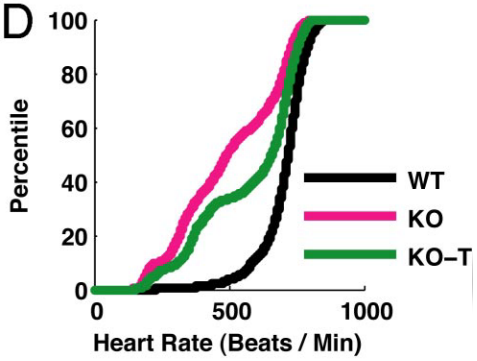












Notes: WT=wild type, KO=knockout, KO-T=knockout treated with GPE. Charts reproduced with permission.

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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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
- Clinical improvement observed in Phase 2 trial in adolescents and adults

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Completed Phase 2 trial in adolescents and adults

- Double-blind, placebo-controlled Phase 2 trial of 28 days of treatment with two dose levels
- 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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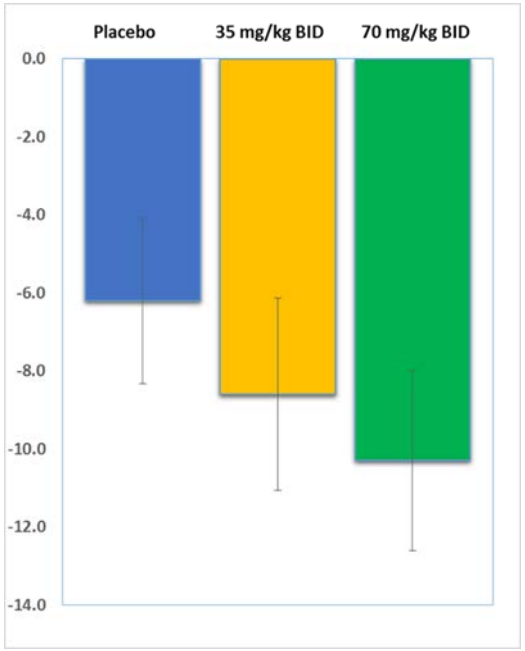
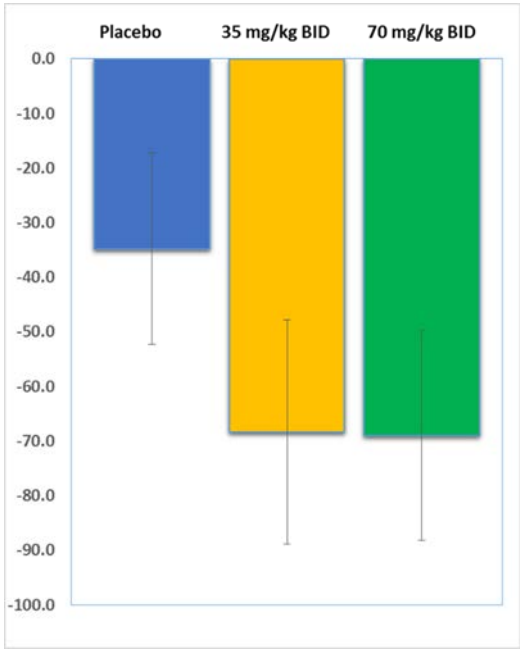
Core efficacy measures that met target

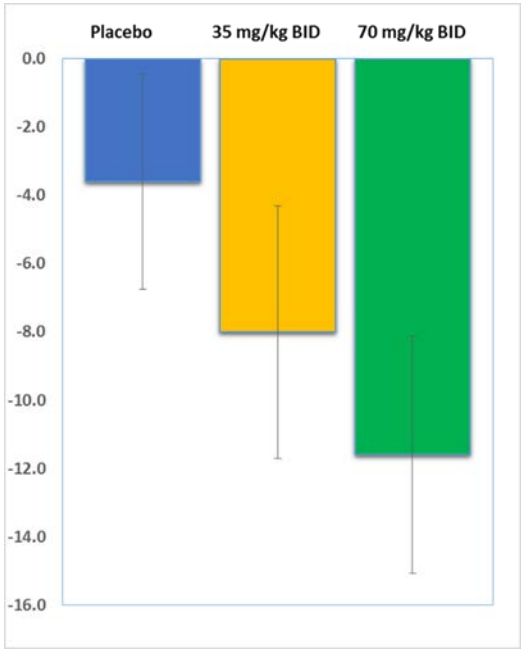
Fragile X Syndrome Rating Scale



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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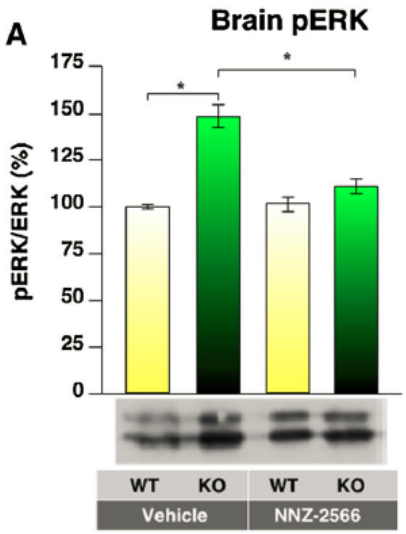
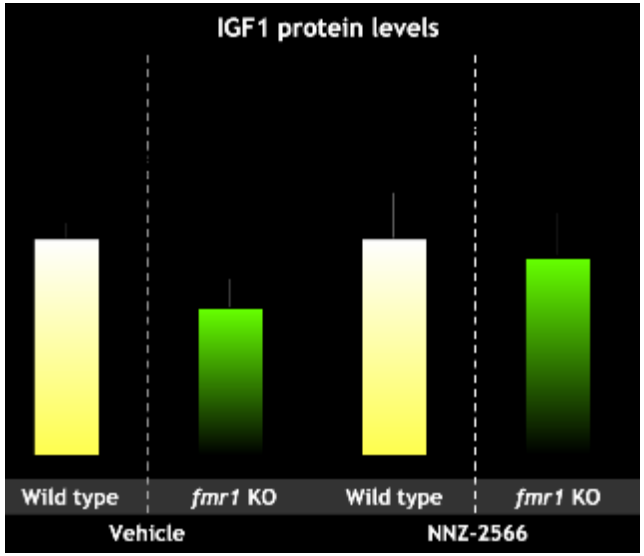
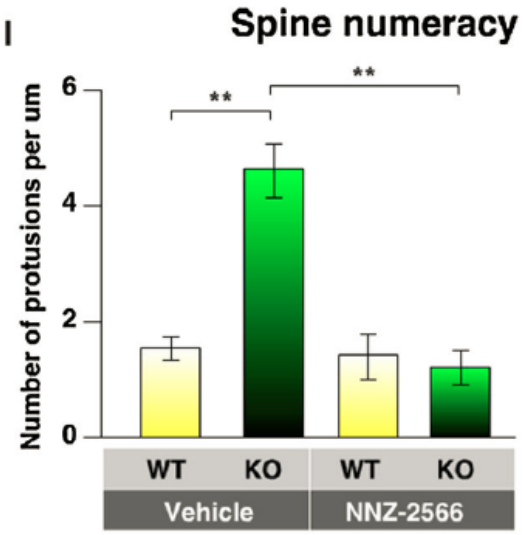
Impact in mouse model of Fragile X syndrome

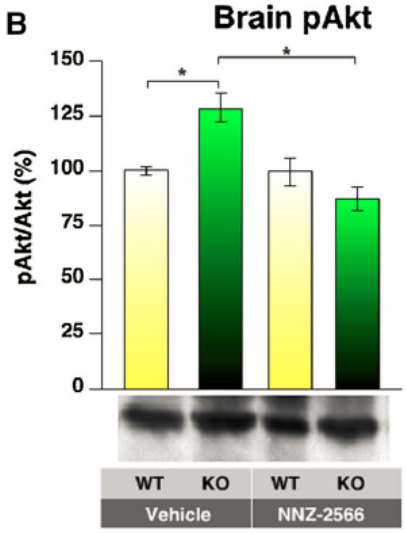
In the *fmr1* knockout mouse model, trofinetide normalised mutant mice, but had no effect on wild type mice:

- 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.

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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