Neuren (NEU) - ASX Announcement **29 June 2020**

Chairman's Address at 2020 Annual Meeting of Shareholders

Since the last Annual Shareholders' Meeting Neuren has made important progress in our ambition to achieve approval of novel drug therapies for a range of serious neurodevelopmental conditions for which there are currently no approved medicines. The team at Neuren has not lost sight of the importance of their work, which aims to make life better for the people who are impacted by these debilitating illnesses.

In order to fund our plans to generate valuable Phase 2 clinical trial data for NNZ-2591 we have this morning announced the successful completion of a capital raise of 20 million Australian dollars. These funds were raised via a Placement at $1.40 per share to institutional and sophisticated investors in Australia, New Zealand, Hong Kong and the United Kingdom. Bids for participation in the Placement materially exceeded the available shares on offer and we have significantly enhanced the composition of our share register, with new international and domestic institutions participating in the Placement. The expansion of institutional shareholders on our register is seen as a logical progression for Neuren and we have been very active in our institutional investor communications, so we are pleased to see many new international and domestic investors participate in the Placement. We welcome these new shareholders to Neuren and we are grateful for the strong support that they and existing holders have shown for the strategic direction we are pursuing.

In addition to the placement Neuren will also offer participation in a Share Purchase Plan to existing shareholders in Australia and New Zealand. The Share Purchase Plan has also been set at $1.40, the same price as the Placement, which offers our existing loyal shareholders the opportunity to invest further in Neuren should they so desire. Funds received from the Placement and the Share Purchase Plan will ensure Neuren is able to pursue its exciting development activities with confidence.

We have been very mindful of the current volatility in global equity markets, which is clearly something we cannot control, and after careful consideration of all options available to us we made the decision that a Placement and Share Purchase Plan at this time is the right choice for Neuren. It was clear that we needed to raise additional funds in the near term to execute our plan for NNZ-2591 and we are glad to have now removed this material uncertainty from the equation.

Over the last 12 months Neuren has made strong progress on a number of important matters and Jon will give you more information in his presentation shortly but I'd like to mention a few highlights.

Trofinitide commenced its Phase 3 trial in the United States and notwithstanding an interruption to new enrolments due to the impact of Covid19 we are delighted that our partner ACADIA has recently confirmed that new enrolments are again commencing at various sites. It was also confirmed that trofinitide has been awarded Rare Pediatric Designation, which further enhances the commercial value of the product and Neuren has attractive commercial rights to benefit from this designation if marketing

approval is achieved. Outside North America, we chose to defer partnering in order to capture substantially greater value by selecting the best commercial outcome after the US Phase 3 trial results.

There has been much progress for NNZ-2591 with the achievement of three Orphan drug designations from the FDA, compelling results in 3 animal models, successful manufacturing development, execution of non-clinical toxicology studies and the key milestone of commencing the Phase 1 trial.

The focus for the near term is very clear. We have three key value drivers. We want to realise Neuren's share of trofinetide value in the US through ACADIA's Phase 3 results and New Drug Application; we will pursue the optimum commercial strategy for trofinetide ex-North America, using the US data for registration; and with critical funds now secure we have enhanced confidence to execute our plans for NNZ-2591 on its journey to Phase 2 data for three valuable indications.

As most of you will know, last month Richard Treagus resigned from his role as Executive Chair of Neuren after more than 7 years to enable him to concentrate on his other business interests. I would again like to acknowledge Richard's contribution to Neuren and thank him for his efforts over many years. I am happy to report that the transition of Jon Pilcher to the role of CEO has gone very smoothly and reflects the depth of knowledge that Jon has of Neuren's business, our strategy, our partners and our investors. The success of the capital raise being undertaken so shortly after Jon's appointment underlines this point.

On behalf of the Board I'd like to acknowledge the team at Neuren and to thank them for their enthusiasm and unwavering commitment to realising Neuren's full potential. To my fellow Directors, thank you for your support and counsel, it is very enjoyable working with you and I look forward to the year ahead with confidence.

About Neuren

Neuren is developing new therapies for neurodevelopmental disorders with high unmet need, utilizing synthetic analogs of neurotrophic peptides that occur naturally in the brain. Trofinetide is currently in a Phase 3 clinical trial for Rett syndrome and has completed a Phase 2 clinical trial in Fragile X syndrome. The programs have each received Fast Track designation by the US Food and Drug Administration and Orphan Drug designation in both the United States and the European Union. Neuren has granted an exclusive license to ACADIA Pharmaceuticals Inc. for the development and commercialization of trofinetide in North America, whilst retaining all rights outside North America. Neuren is advancing the development of NNZ-2591 for Phelan-McDermid, Angelman and Pitt Hopkins syndromes, each of which has received Orphan Drug designation in the United States.

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ASX Listing Rules information

This announcement was authorized to be given to the ASX by the board of directors of Neuren Pharmaceuticals Limited, Suite 201, 697 Burke Road, Camberwell, VIC 3124

Forward-looking Statements

This announcement contains forward-looking statements that are subject to risks and uncertainties. Such statements involve known and unknown risks and important factors that may cause the actual results, performance or achievements of Neuren to be materially different from the statements in this announcement.

neuren pharmaceuticals

ANNUAL SHAREHOLDERS MEETING

29 June 2020

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.

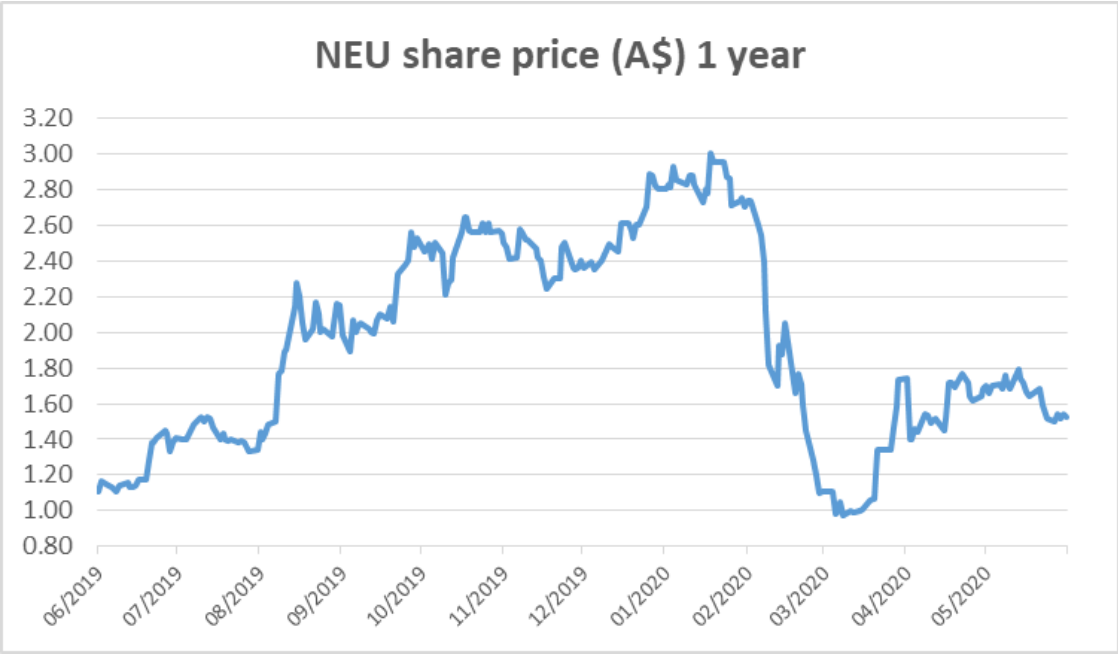
NEUREN'S CURRENT STRONG POSITION

- Neuren is developing **2 drugs** to treat **5 debilitating childhood disorders**, which have no approved therapies
- Drugs based on naturally occurring molecules target the underlying **impairment in signalling between brain cells**; no royalties payable
- **Orphan Drug** provides regulatory incentives and commercial protection
- **Trofinetide** partnered with **ACADIA** (NASDAQ:ACAD) for North America
  - Up to US$455m milestone payments plus double digit % royalties
  - Free and full access to US data for ex-North America registration
- **Trofinetide** in **Phase 3 trial for Rett syndrome**, funded by ACADIA:
  - Results expected in 2021, potential marketing approval in 2022
  - FDA Fast Track, Priority Review, Rare Pediatric Disease designation
- Neuren preparing for Phase 2 trials of **NNZ-2591 for 3 disorders**

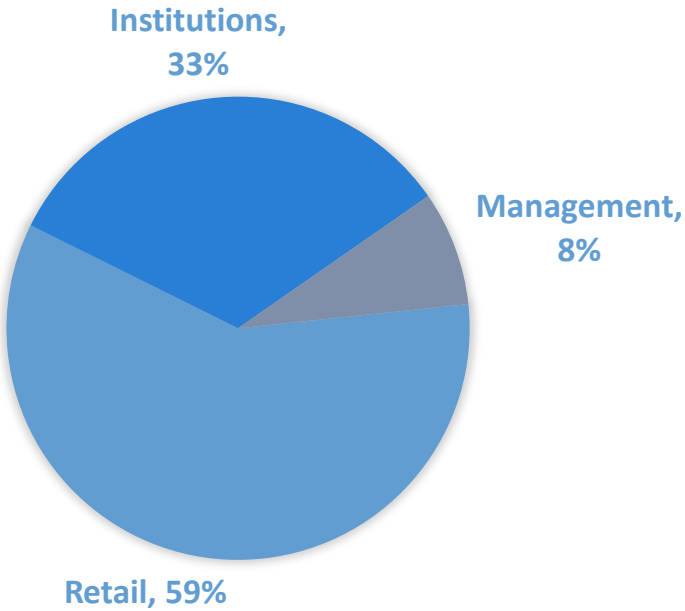
STOCK INFORMATION POST-RAISING (ASX: NEU)

Pro-forma cash post-raising: circa A$30 million

52 week price range: A$0.97 - A$3.04



Estimated share register composition (115 million quoted shares)



THE FUTURE - THREE KEY VALUE DRIVERS

KEY VALUE DRIVER 1

Realise Neuren's share of trofinetide value in the US through ACADIA's Phase 3 results and New Drug Application

Achieved last year:

- ✓ Successful manufacturing scale-up
- ✓ Phase 3 trial commenced on time
- ✓ Rare Pediatric Disease designation

Key future milestones:

- LAVENDER Phase 3 results 2021
- Potential US marketing approval 2022

KEY VALUE DRIVER 2

Achieved last year:

- ✓ Deferred partnering to capture more value post-Phase 3
- ✓ New patent granted in Israel

Key future milestones:

- EU national agency meetings H2 2020
- EMA interactions 2021
- Execute commercial strategy 2021/22

KEY VALUE DRIVER 3

Achieved last year:

- ✓ 3 Orphan drug designations from FDA
- ✓ Compelling results in 3 animal models
- ✓ Successful manufacturing development
- ✓ Non-clinical toxicology studies
- ✓ Commenced Phase 1 trial
- ✓ New patents granted in US, Europe and Japan

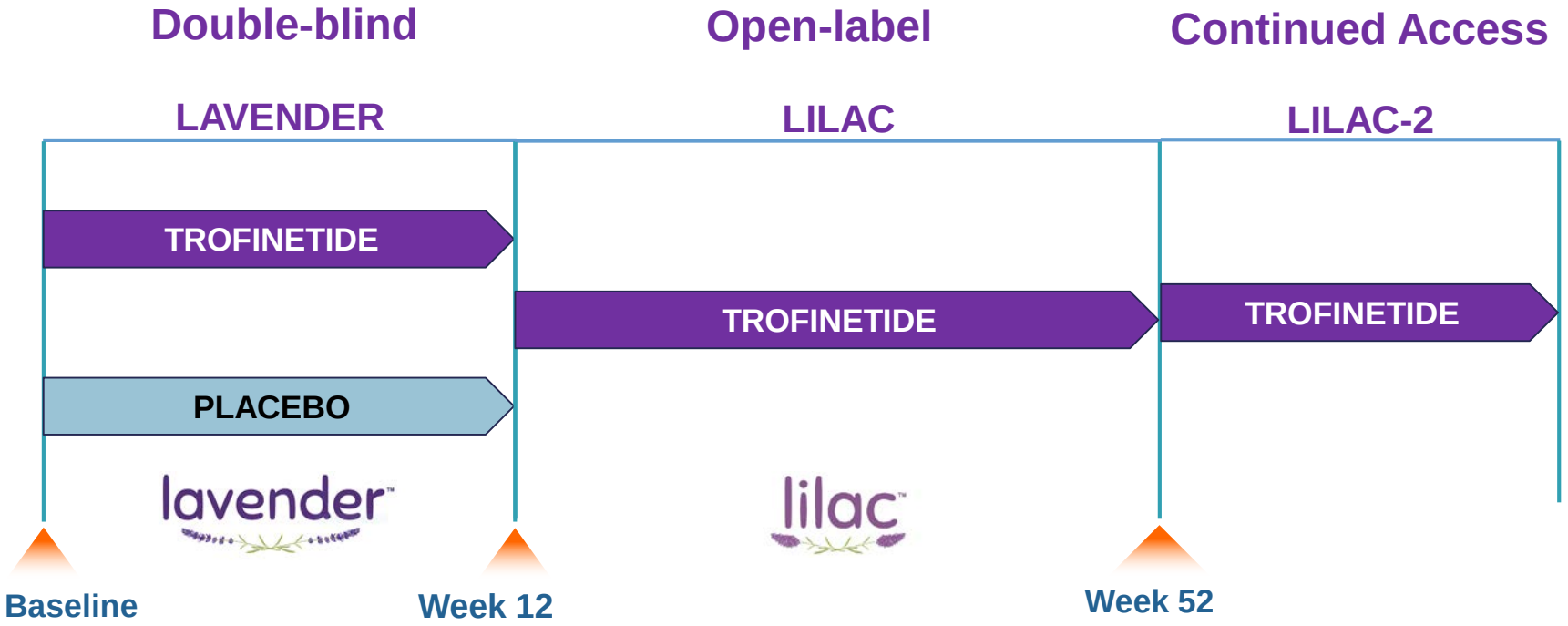
Confirm efficacy of NNZ-2591 in Phase 2 trials for 3 valuable indications

Key future milestones:

- Submit IND application H1 2021
- Commence Phase 2 trials 2021
- Phase 2 trial results 2022

TROFINETIDE FOR RETT SYNDROME

RETT SYNDROME PHASE 3 PROGRAM



- Lavender results expected in 2021, potential US marketing approval in 2022
- 180 females with Rett syndrome aged 5 to 20 years
- Rett Syndrome Behaviour Questionnaire (RSBQ) and Clinical Global Impression of Improvement (CGI-I) at 12 weeks are co-primary efficacy endpoints
- Strong support from leading Rett syndrome physicians and Rettsyndrome.org
- First patients have completed Lavender and commenced Lilac; new patient enrolment into Lavender recently recommenced after temporary pause for Covid-19

MAXIMISING PROBABILITY OF SUCCESS

- The Phase 3 co-primary endpoints were both positive in the Phase 2 trial
- In the Phase 2 trial clinical improvement continued increasing through to end of treatment - the Phase 3 trial at 12 weeks is twice the duration of the Phase 2 trial
- The Phase 3 sample size at approx. 90 per group is more than 3 times the Phase 2 sample size – much greater statistical power to detect a difference between active and placebo
- The dosing regimen in the active group for the Phase 3 trial is optimised, informed by the PK-PD analyses of the Phase 2 subjects
- The age range for the Phase 3 trial is 5 to 20 years, compared with 5 to 15 years in the Phase 2 trial
- Both trials are US sites only, with most Phase 2 sites participating in Phase 3

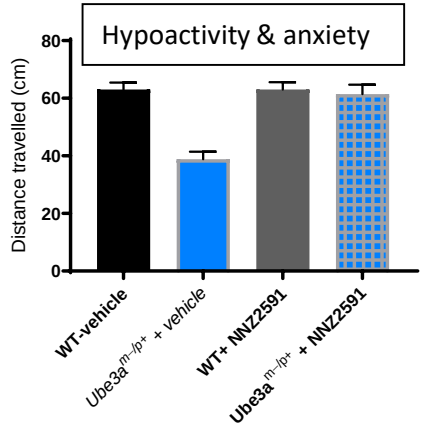
NNZ-2591 FOR PHELAN-MCDERMID, ANGELMAN AND PITT HOPKINS SYNDROMES

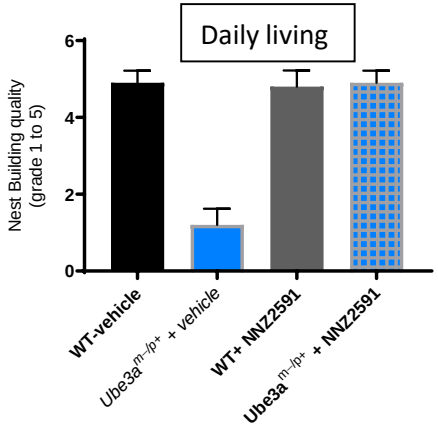
ADVANCING NNZ-2591 FOR 3 INDICATIONS

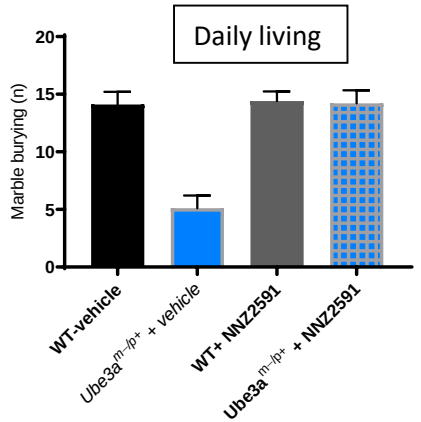
- FDA granted Orphan Drug designation for Phelan-McDermid, Angelman and Pitt Hopkins
- Compelling data package assembled in preparation for clinical trials:
  - Clear and consistent efficacy in mouse models of each syndrome (*SHANK3, UBE3A, TCF4*)
  - Biochemical effects in the brain confirmed in Phelan-McDermid model
  - High oral bioavailability and blood/brain barrier penetration
  - Optimum dose clearly demonstrated in Phelan-McDermid model
- Neuren is leveraging extensive and highly relevant experience from Rett and Fragile X programs across CMC, non-clinical, clinical and regulatory
- The program of non-clinical toxicology and CMC studies required to open an IND and enable clinical trials in pediatric patients is currently in progress
- Phase 1 trial in adult healthy volunteers in Australia currently in progress
- Planning Phase 2 trials in patients in 2021 for all three indications:
  - 12 weeks treatment of pediatric patients
  - Confirm safety and tolerability
  - Establish size of clinical response to drug, measured by CGI-I and other potential endpoints
  - Confirm optimum dose for the subsequent pivotal trials

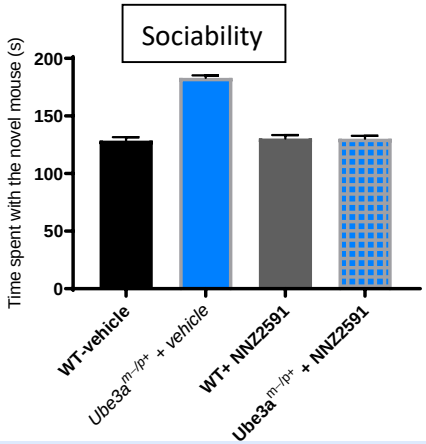
NNZ-2591 EFFICACY IN AS MOUSE MODEL (*UBE3A*)

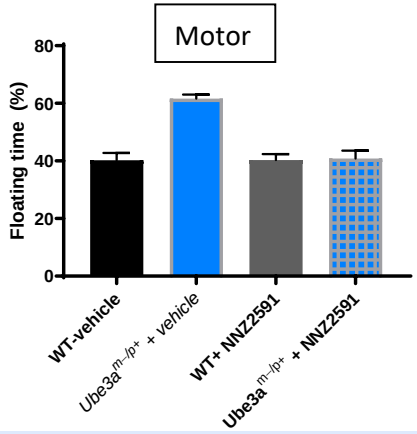
AS is caused by a deletion or mutation in the ubiquitin protein ligase E3A (*UBE3A*) gene on chromosome 15. In the *ube3a* knockout mouse model, which resembles features of AS in humans, wild type and knockout mice were each treated with placebo or NNZ-2591 for 6 weeks. Treatment with NNZ-2591 normalized all the deficits in the knockout mice, including eliminating seizures, and had no effect on the wild type mice.

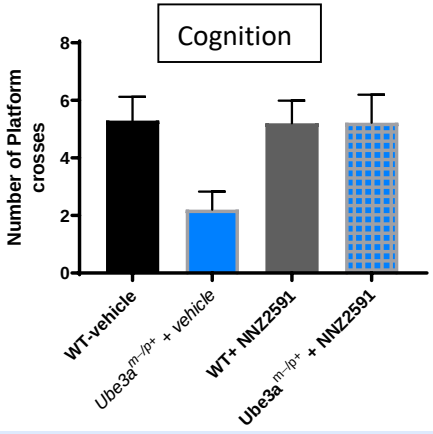






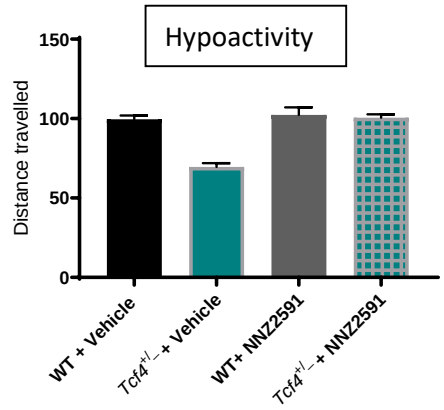


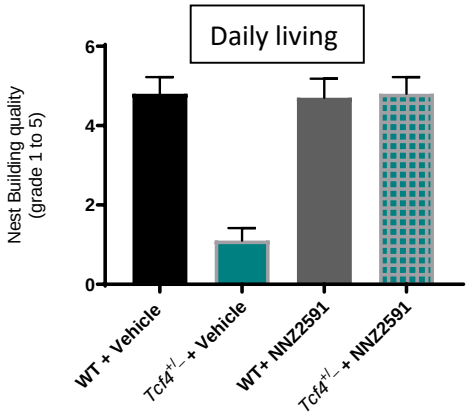


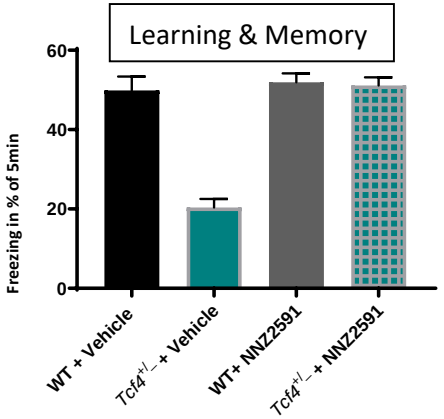


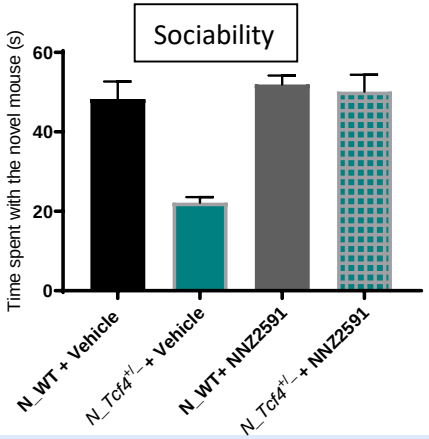
NNZ-2591 EFFICACY IN PTHS MOUSE MODEL (*TCF4*)

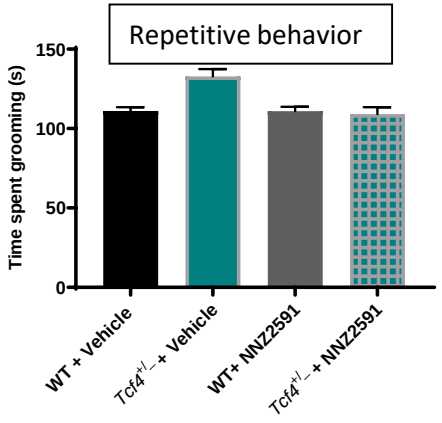
PTHS is caused by the loss of one copy or a mutation of the *TCF4* gene on chromosome 18. In the *tcf4* mutation mouse model, which exhibits features of PTHS in humans, wild type mice and knockout mice were treated with placebo or NNZ-2591 for 6 weeks. Treatment with NNZ-2591 normalized all the deficits in the knockout mice and had no effect on the wild type mice.

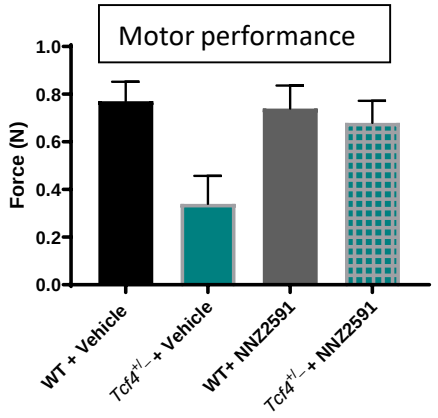








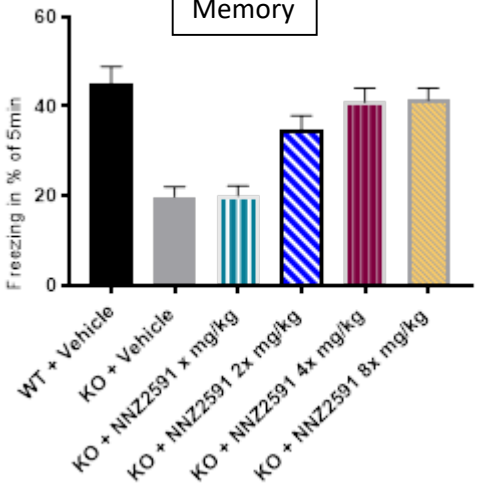




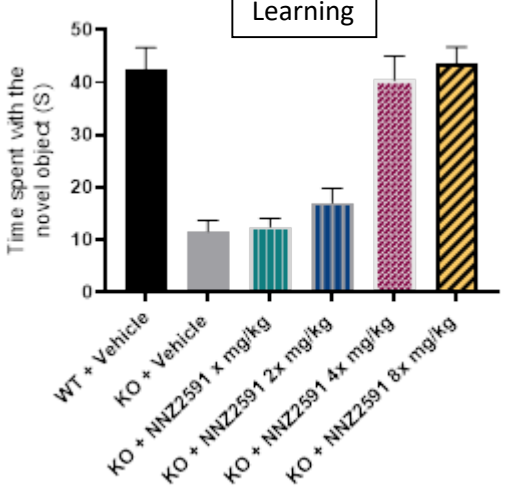
EFFICACY AND OPTIMUM DOSE IN PMS MODEL (*SHANK3*)

PMS is caused by a deletion or other change in the 22q13 region of chromosome 22, which includes the *SHANK3* gene, or a mutation of the gene. In the *shank3* knockout mouse model, wild type mice and knockout mice were treated with placebo or 4 escalating dose levels of NNZ-2591 for 6 weeks. Results clearly indicate 2nd highest dose as optimum dose, informing dose selection for clinical trials in patients.

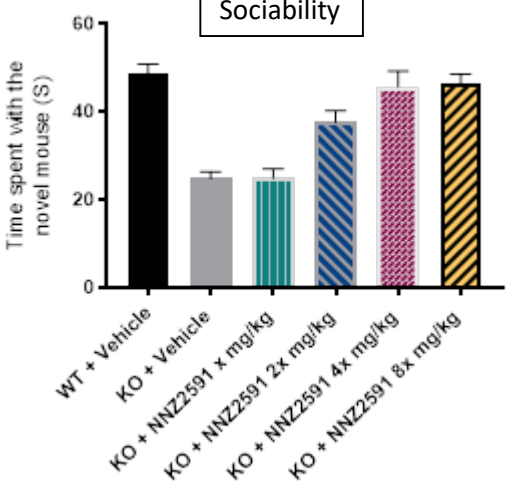
Memory



Learning



Sociability

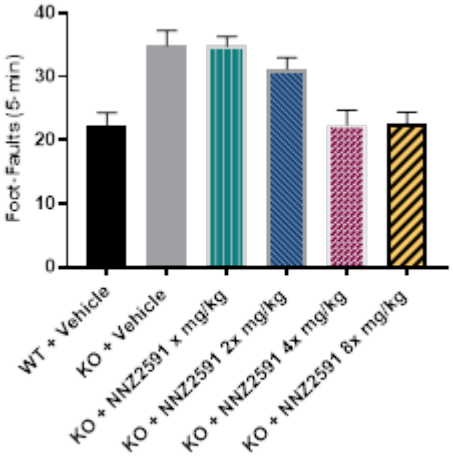


Incidence of seizures

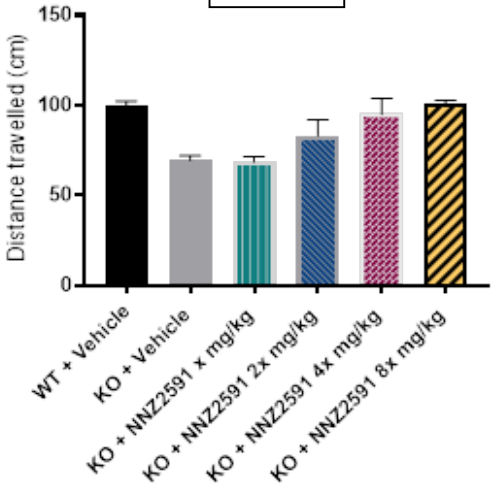
WT + vehicle	KO + vehicle	KO + x mg/kg	KO + 2x mg/kg	KO + 4x mg/kg	KO + 8x mg/kg
0%	60%	50%	30%	10%	10%

EFFICACY AND OPTIMUM DOSE IN PMS MODEL (*SHANK3*)

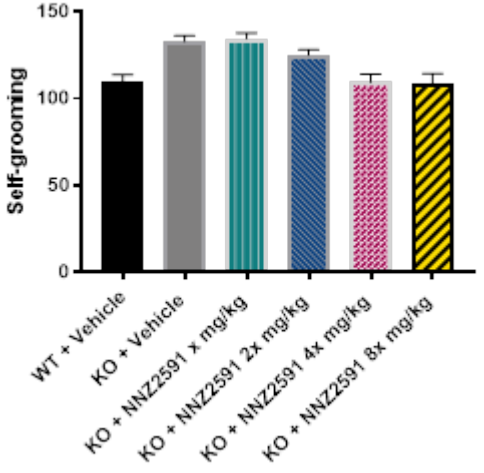
Motor function



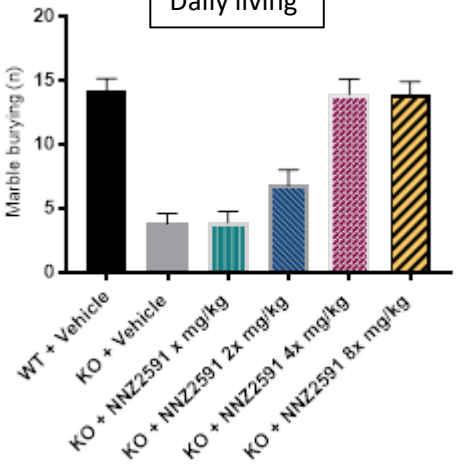
Anxiety



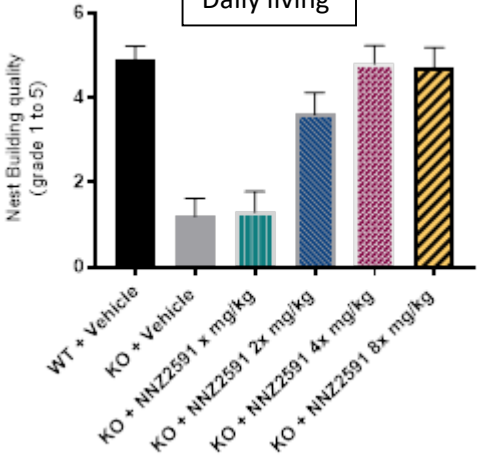
Repetitive behavior



Daily living

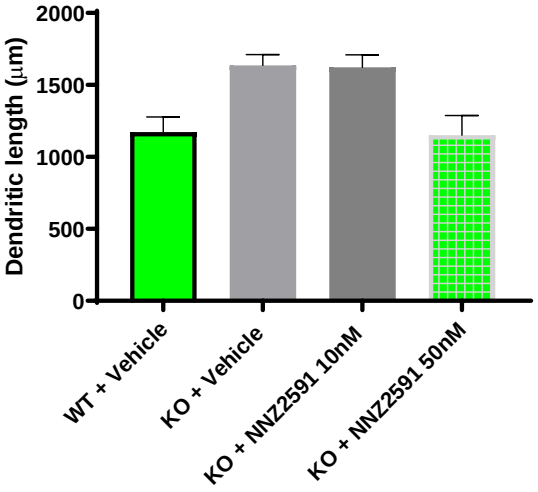


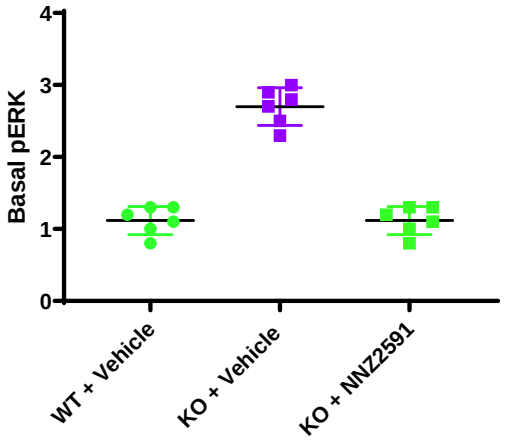
Daily living

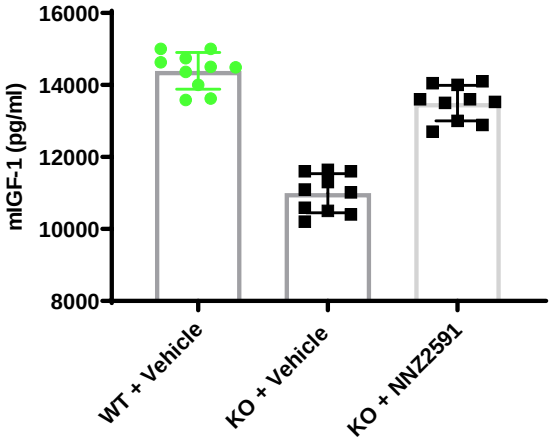


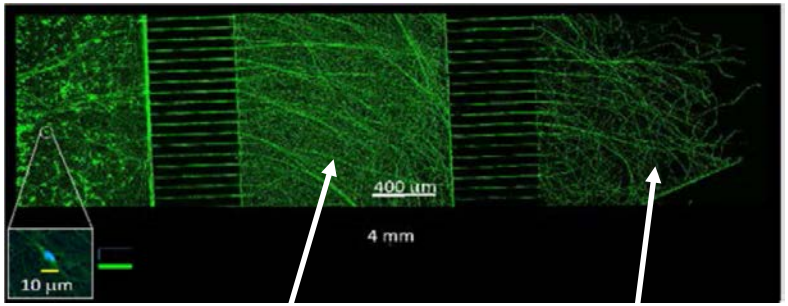
BIOCHEMICAL EFFECTS CONFIRMED IN *SHANK3* MODEL

In additional biochemical testing, NNZ-2591 was shown to normalise the abnormal length of dendrite spines between brain cells, the excess activated ERK protein (pERK) and the depressed level of IGF-1 in *shank3* knockout mice.









Abnormal dendrites in shank3 knockout mice

Normalisation after treatment with NNZ-2591

CONTACT

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