Neuren (NEU) - ASX Announcement **30 May 2022**

Chairman's Address at 2022 Annual Meeting of Shareholders

Since our Annual Shareholders' Meeting last year, we have made substantial progress on the key areas that we have consistently said are of high importance to the success of Neuren. In a moment I'll highlight some of these achievements and our Chief Executive Officer Jon Pilcher will further elaborate on the company's progress and prospects in his presentation.

I would however like to start with a sincere message of thanks to Jon and the entire team at Neuren who have navigated through these most unusual times with unbroken energy and importantly have maintained their good humour throughout. I would also like to thank our many partners in particular the patient communities and key opinion leaders we work with who give us their valued input and who are a constant reminder of the ultimate ambition that we strive to achieve. The illnesses that Neuren's products are aiming to treat have no approved medicines today and every member of our team is deeply motivated to make a positive impact on the lives of the patients and families most affected by these debilitating conditions.

The most significant individual milestone achieved in the last twelve months came in December last year when our partner for trofinetide in North America, Acadia Pharmaceuticals, announced robustly positive top-line results from the pivotal, Phase 3 Lavender™ study evaluating the efficacy and safety of trofinetide in girls and young women with Rett syndrome. Acadia plans to submit the New Drug Application for trofinetide to the United States Food and Drug Administration around the middle of this year, with potential for approval in the first quarter of 2023. Consequently, we expect to receive revenue over 2022 and 2023 for Rett syndrome in the US alone of A$115 million plus double-digit percentage royalties on net sales.

Beyond this Neuren's additional ongoing revenue from sales has two components. Firstly, double digit percentage royalties on sales of trofinetide in all indications. The potential peak annual net sales for trofinetide in Rett syndrome has been estimated by Acadia as at least US$500 million. Neuren also stands to receive payments of up to US$350 million on achievement of a series of 4 thresholds of total annual sales for all indications.

No royalties or similar costs are payable by Neuren to third parties, which means that Neuren's revenue from Acadia will flow through to pre-tax profit. It is so exciting to see the progression of trofinetide in the United States and on approval of the NDA Neuren would be one of only a handful of companies in Australia that has a new pharmaceutical product approved by the FDA.

The market responded very positively to the Phase 3 trial results news, our share price lifted materially and despite the extremely volatile environment for biotech valuations across the world we have not suffered the same severe declines that many others have over the last several months. That said, our current share price does not reflect the risk adjusted value that the Board, Management and external analysts see in the assets we are developing at Neuren. It has been encouraging to have new external financial research coverage initiated on Neuren over the last year. The share price targets from all these research reports are well above our share price with a range of current valuations from $5.10 to $8.10, which indicates the growing confidence that others also have in Neuren's potential.

With trofinetide in North America well and truly on the right path we have been working hard on evaluating our options for trofinetide in the rest of world markets, having received a high level of interest from multiple parties. This process is progressing as planned, narrowing the options down to those that will maximise the risk adjusted value for Neuren.

It has also been a period of important progress for our second product NNZ-2591. In March we received approval from the FDA for Investigational New Drug applications to commence Phase 2 clinical trials of NNZ-2591 for each of Phelan-McDermid syndrome, Angelman syndrome and Pitt Hopkins syndrome. The trials are scheduled to commence imminently, with results anticipated in the first half of 2023. In addition to these three trials, we are planning a Phase 2 trial in a fourth disorder, Prader-Willi syndrome, to commence later this year with results in the second half of 2023.
Neuren has Orphan Drug designation from the FDA for NNZ-2591 in all four syndromes, which are serious illnesses with no approved medicines. The estimated number of potential patients being targeted across these four disorders is more than five times larger than Rett syndrome and we retain global rights to NNZ-2591.

To allow further expansion of our NNZ-2591 development plans we undertook a successful capital raising in September last year by way of both a placement to sophisticated investors and a share purchase plan to retail investors.

Total gross proceeds of $23.3 million from the placement and Share Purchase Plan enabled us to accelerate the development and increase the value of NNZ-2591 across four indications, by funding a Phase 2 clinical trial in Prader-Willi syndrome and importantly the foundational work for Phase 3 development across Prader-Willi, Phelan-McDermid, Angelman and Pitt Hopkins syndromes.

We were most grateful for the support of participating shareholders, which resulted in both the placement and the Share Purchase Plan being oversubscribed. In particular, applications received from eligible shareholders under the Share Purchase Plan totaled approximately $3.3 million, compared with the targeted amount of $2 million, and we elected to accept the oversubscriptions, rather than implement a scale-back procedure at the time. The funds

are being deployed in line with our plans and we are confident that it was the right move to secure these funds to avoid any unnecessary delay or risk in pursuing the full development potential of NNZ-2591.

We continue to expand our investor relations activities and in my opinion this has been a very productive pursuit as we spread the Neuren story as widely as possible. We are fortunate that many of our shareholders, some of whom have been on our register for many years, are great advocates for our company and we are most appreciative of their support in this regard.

In closing I would like to thank my fellow Directors for their efforts over the last year. It really is a pleasure working with each of them and I am most appreciative of the positive contributions they make to the Board. We have very exciting opportunities ahead of us and we are well placed to pursue them.

I now invite Jon to make his presentation.

About Neuren

Neuren is developing two new drug therapies to treat multiple serious neurological disorders that emerge in early childhood, none of which have any approved medicines.

The lead compound, trofinetide, achieved positive results in a Phase 3 clinical trial for Rett syndrome and has also completed a Phase 2 clinical trial in Fragile X syndrome. Both programs have Fast Track designation from the US Food and Drug Administration (FDA). Neuren has granted an exclusive licence to Acadia Pharmaceuticals Inc. for the development and commercialisation of trofinetide in North America, while retaining all rights outside North America.

Neuren is preparing to initiate Phase 2 trials of its second drug candidate, NNZ-2591, for each of Phelan-McDermid syndrome, Angelman syndrome, Pitt Hopkins syndrome and Prader-Willi syndrome.

Recognising the urgent unmet need, all six programs have been granted “orphan drug” designation in the United States. Orphan drug designation provides incentives to encourage development of therapies for rare and serious diseases.

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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.

ANNUAL SHAREHOLDERS' MEETING

30 May 2022

neuren pharmaceuticals

IMPROVING THE LIVES OF PEOPLE WITH NEURODEVELOPMENTAL DISABILITIES

Annual Shareholders' Meeting 30 May 2022

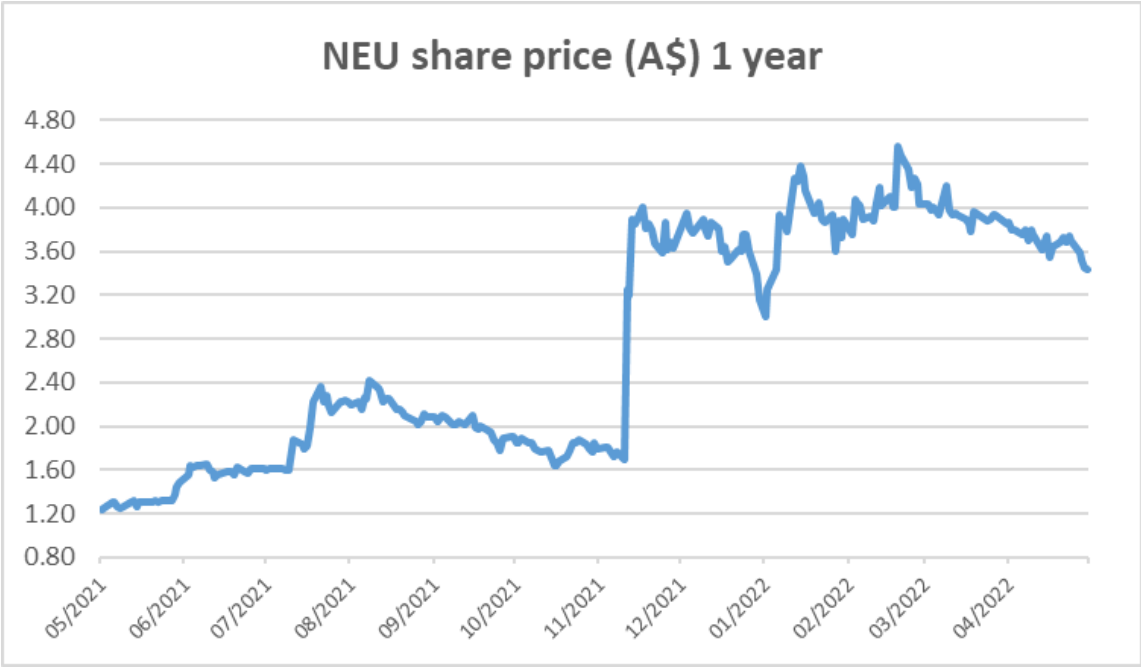
FORWARD LOOKING STATEMENTS

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.

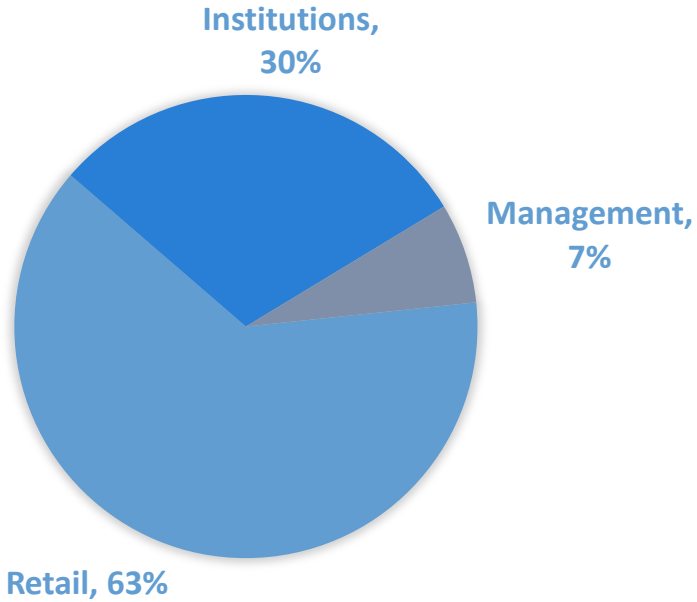
STOCK INFORMATION (ASX: NEU)

Current analyst risk-adjusted valuations per share: A$8.10, A$6.65, A$6.21, A$5.10

52 week price range: A$1.20 - A$4.68



Current share register composition (126 million quoted shares – top 20 hold 52%)



A$34 million cash at 31 March 2022 – well funded to execute NNZ-2591 Phase 2 trials and preparation for Phase 3

THREE KEY DRIVERS TRANSFORMING NEAR TERM VALUE

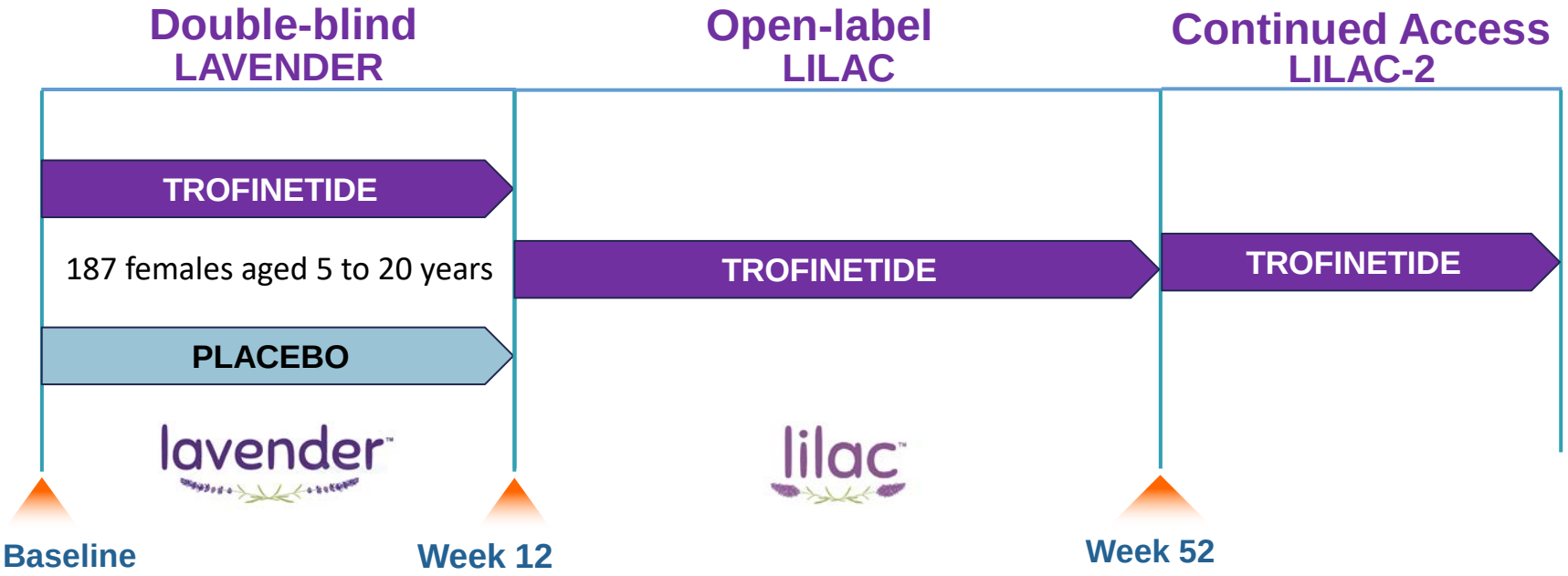
KEY MILESTONES IN NEXT 18 MONTHS

- Prader-Willi syndrome Phase 2 trial results (H2 2023)
- Phase 2 trial results in Angelman, Phelan-McDermid and Pitt Hopkins syndromes (H1 2023)
- Approval of NDA for Rett syndrome (Q1 2023)
- Commercial partnerships ex-North America for Rett syndrome
- Commence Prader-Willi syndrome Phase 2 trial (H2 2022)
- Acadia New Drug Application (NDA) for Rett syndrome (mid-2022)
- Commence Phase 2 trials in Angelman, Phelan-McDermid and Pitt Hopkins syndromes (Q2 2022)

TROFINETIDE FOR RETT SYNDROME - ANTICIPATING LARGE NEAR-TERM CASH FLOWS

RETT SYNDROME PHASE 3 AND NDA

- Acadia plans to submit NDA mid-2022; Orphan Drug qualifies for 6 months Priority Review, which means potential for approval in Q1 2023
- NDA based on pivotal efficacy from positive Phase 3 trial, supportive efficacy from Neuren's positive Phase 2 trial, safety data from completed and ongoing studies
- Robustly positive results in LAVENDER trial
  - Statistically significant improvement over placebo for both co-primary efficacy endpoints: RSBQ (p=0.0175) and CGI-I (p=0.0030)
  - Co-primary endpoints pre-specified and agreed with FDA



RETT SYNDROME OPPORTUNITY

Estimates	US	Europe	Japan	China urban	Other Asia
Potential patients[1]	10,000	13,000	3,000	28,000	6,000
Patients currently identified	5,000	4,000	1,000	2,000	'00s

[1] Potential patient estimates derived by applying the mid-point of the published prevalence estimate range to the populations under 60 years

North America

- Neuren potential revenue from Acadia:
  - US$10 million in 2022 following acceptance of NDA for review
  - US$40 million in 2023 following first commercial sale in the US
  - US$33 million in 2023 one third share of Priority Review Voucher estimated value[1]
  - Up to US$350 million on achievement of thresholds of annual net sales
  - Tiered, escalating double digit percentage royalties on net sales
- Peak annual sales potential in US at least US$500m[2]
- Orphan exclusivity plus patent to 2035

Ex-North America

- Partnering interest from multiple companies for individual countries and broader regions
- Neuren has full access to US data for registration ex-North America
- Strong interest from families, advocacy groups and physicians
- Lower diagnosis rates expected to increase with awareness and accelerate with availability of a treatment

[1] Assuming Rare Pediatric Disease Priority Review Voucher is awarded upon approval of a NDA and has a market value of US$100m

[2] Acadia 2Q18 Earnings Call presentation and Jefferies Healthcare Conference 2 June 2021

NNZ-2591 PROVIDES VERY LARGE POTENTIAL UPSIDE LEVERAGING THE TROFINETIDE EXPERIENCE

FIVE TIMES LARGER OPPORTUNITY FOR NNZ-2591

Disorder	Gene mutation	Published prevalence estimates	Potential patients		
			US[1]	Europe[1]	Asia[1, 2]
Phelan-McDermid	*SHANK3*	1/8,000 to 1/15,000 males and females	22,000	28,000	81,000
Angelman	*UBE3A*	1/12,000 to 1/24,000 males and females	14,000	18,000	52,000
Pitt Hopkins	*TCF4*	1/34,000 to 1/41,000 males and females	7,000	9,000	25,000
Prader-Willi	*15q11-q13*	1/10,000 to 1/30,000 males and females	13,000	16,000	47,000
			56,000	**71,000**	**205,000**

- **Current opportunity for NNZ-2591 is more than 5 times the Rett Syndrome opportunity[3]**
- **There are many other neurodevelopmental disorders potentially relevant for NNZ-2591 mechanism of action**
- **Neuren retains global rights**

[1] Estimates derived by applying the mid-point of the prevalence estimate range to the populations under 60 years
[2] Asia comprises Japan, Korea, Taiwan, Israel and urban populations of China and Russia
[3] Based on number of addressable patients globally

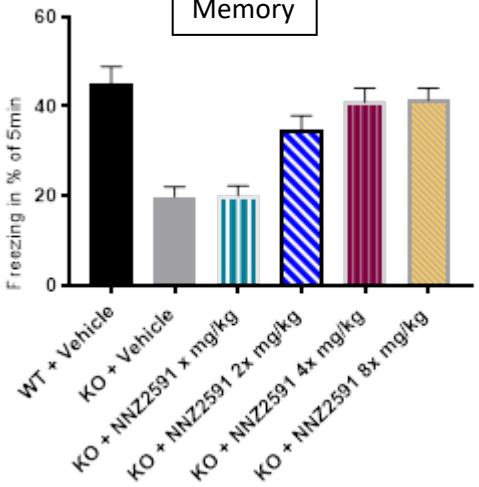
NNZ-2591 HAS IDEAL ATTRIBUTES LEADING INTO PHASE 2

- ✓ Novel mechanism of action
- ✓ Clear and consistent efficacy in mouse models of each syndrome
- ✓ Biochemical effects in the brain and optimum dose confirmed
- ✓ Demonstrated high oral bioavailability and blood-brain barrier penetration
- ✓ IND-enabling program of non-clinical toxicology and CMC studies completed
- ✓ Proprietary drug substance manufacturing process with exceptional purity and high yield, administered as patient-friendly liquid dose
- ✓ Safe and well tolerated in Phase 1 trial
- ✓ Orphan designations from FDA and EMA

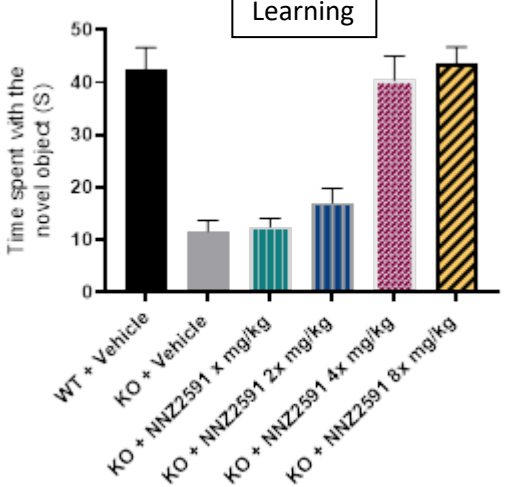
CONSISTENT EFFICACY AND DOSE RESPONSE IN PHELAN-MCDERMID MODEL

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.

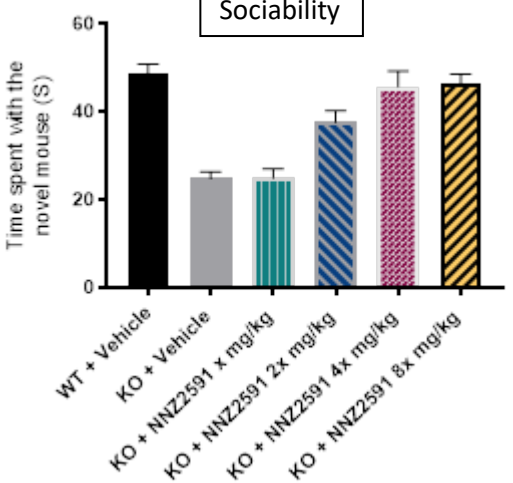
Memory



Learning



Sociability

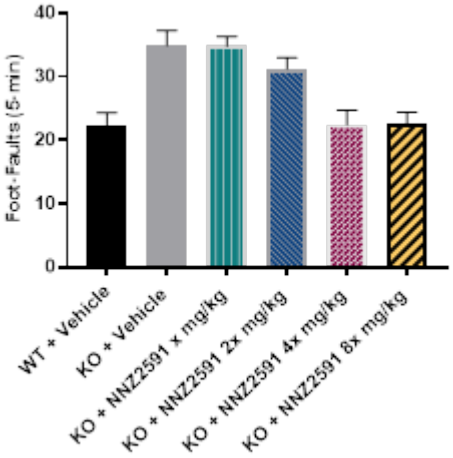


Incidence of seizures

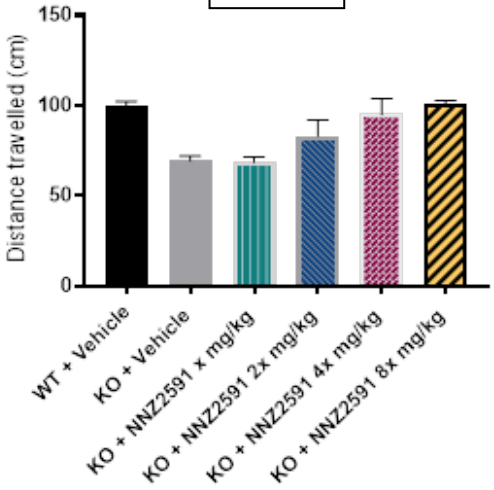
WT + vehicle	KO + vehicle	KO + x mg/kg	KO + 2x mg/kg	KO + 4x mg/kg	KO + 8x mg/kg
0%	60%	50%	30%	10%	10%

CONSISTENT EFFICACY AND DOSE RESPONSE IN PHELAN-MCDERMID MODEL

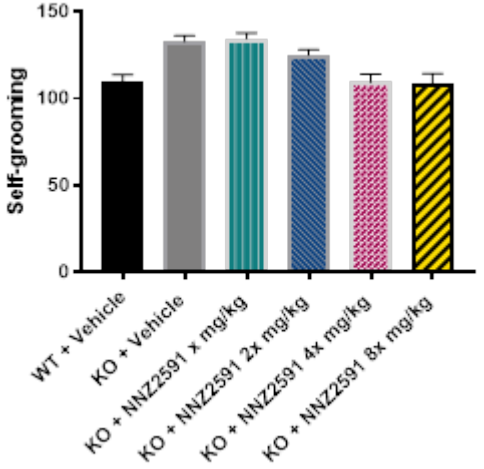
Motor function



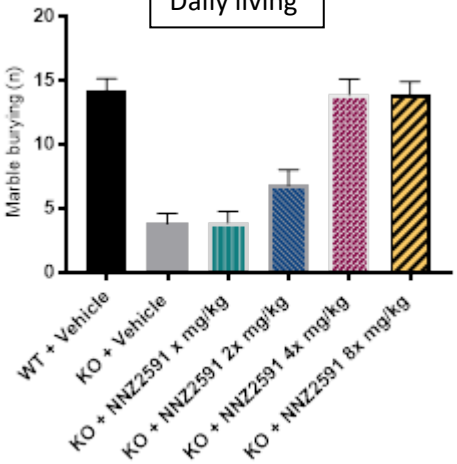
Anxiety



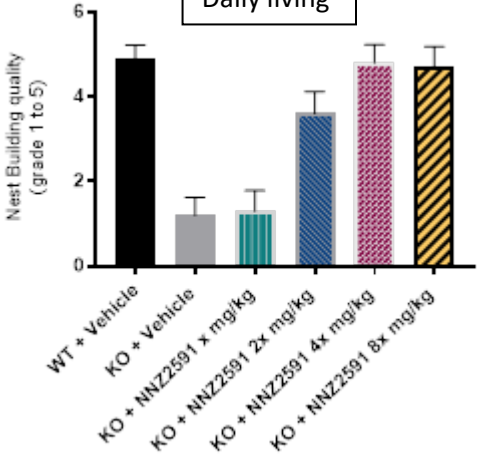
Repetitive behavior



Daily living

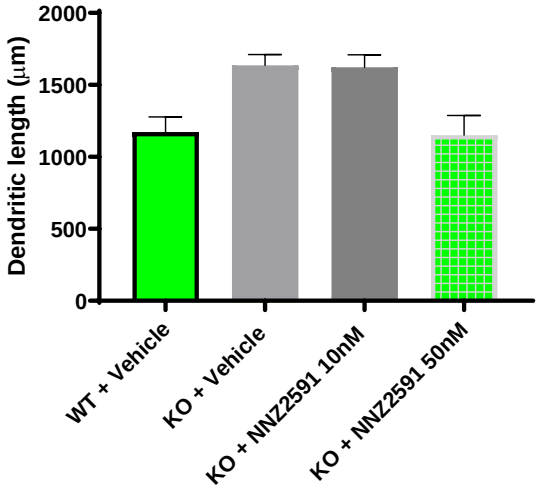


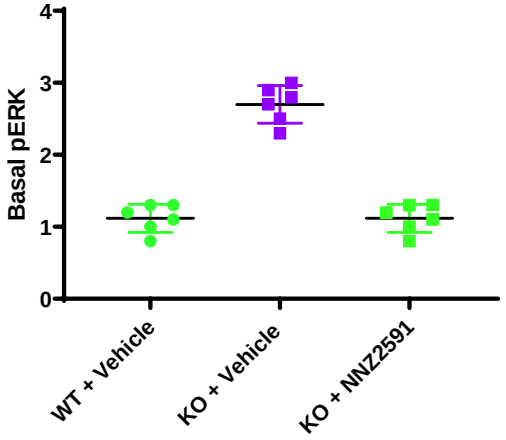
Daily living

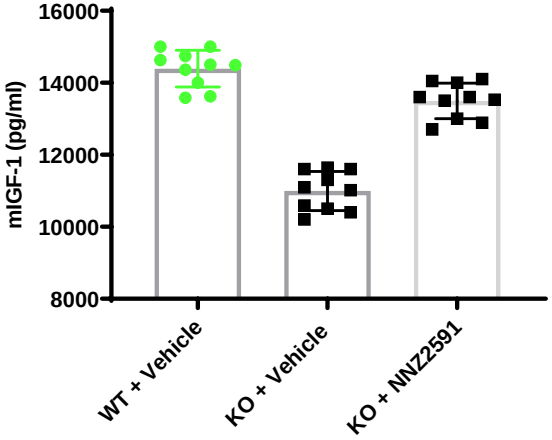


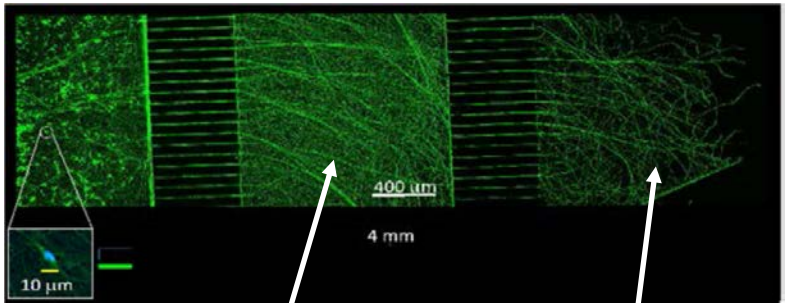
BIOCHEMICAL EFFECTS CONFIRMED IN *SHANK3* MODEL

In 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

KEY FEATURES OF FIRST PHASE 2 TRIALS

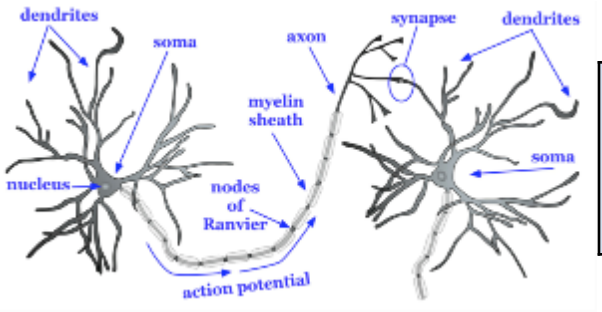
Expedite data across 4 indications that enables subsequent trials to be designed as registration trials and prepare for Phase 3 in parallel

- Prioritising speed to data:
  - Angelman in Australia, Phelan-McDermid and Pitt Hopkins in US
  - Up to 20 patients in each trial, all patients receive drug
- Maximising opportunity to demonstrate effects:
  - Pediatric patients
  - 13 weeks' treatment following well-characterised baseline period
- Confirm safety and PK in pediatric patients
- Assess treatment impact across multiple efficacy measures to select primary endpoint for registration trial
- Three trials commencing imminently, results expected in H1 2023
- Executing foundational preparations for Phase 3 across all indications

CONCLUSION

TREATING NEURODEVELOPMENTAL DISORDERS

Rett	Fragile X	Phelan-McDermid	Angelman	Pitt Hopkins	Prader-Willi
MECP2	*FMR1*	*SHANK3*	*UBE3A*	*TCF4*	*15q11-q13*



Impaired communication between neurons, abnormal formation/pruning of dendrites & chronic inflammation

Neuren's drugs target the critical role of IGF-1 in this upstream process, using analogs of peptides that can be taken orally as liquids

Severe impact on nearly every aspect of life		
walking and balance issues	anxiety and hyperactivity	seizures
speech impairment	intellectual disability	breathing irregularities
impaired hand use	sleep disturbance	gastrointestinal problems

LEADING PIPELINE IN NEURODEVELOPMENTAL DISORDERS

Compound	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Commercial Partner
Trofinetide	Rett syndrome[1]					ACADIA *(North America)*
	Fragile X syndrome[1]					ACADIA *(North America)*
NNZ-2591	Phelan-McDermid syndrome[2]			***Commence H1 2022 Results H1 2023***		
	Angelman syndrome[2]					
	Pitt Hopkins syndrome[2]					
	Prader-Willi syndrome[3]			***Commence H2 2022 Results H2 2023***		

[1] Orphan Drug designation in US and EU, Fast Track designation in US

[2] Orphan Drug designation in US and EU [3] Orphan Drug designation in US

KEY MILESTONES IN NEXT 18 MONTHS

- Acadia New Drug Application (NDA) for Rett syndrome (mid-2022)
- Commence Phase 2 trials in Angelman, Phelan-McDermid and Pitt Hopkins syndromes (Q2 2022)
- Commence Prader-Willi syndrome Phase 2 trial (H2 2022)
- Commercial partnerships ex-North America for Rett syndrome
- Approval of NDA for Rett syndrome (Q1 2023)
- Phase 2 trial results in Angelman, Phelan-McDermid and Pitt Hopkins syndromes (H1 2023)
- Prader-Willi syndrome Phase 2 trial results (H2 2023)

CONTACT

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RESOLUTIONS PROXY VOTES RECEIVED

Resolution 1	Lodged **For**		Lodged **Open**		Lodged **Against**		Total Available Votes	% issued capital
	Votes	%	Votes	%	Votes	%		
RE-ELECTION OF DIANNE ANGUS AS A DIRECTOR	42,542,037	99.62	161,569	0.38	250	0.00	42,703,856	33.11

RESOLUTIONS PROXY VOTES RECEIVED

Resolution 2	Lodged **For**		Lodged **Open**		Lodged **Against**		Total Available Votes	% issued capital
	Votes	%	Votes	%	Votes	%		
RE-ELECTION OF JENNY HARRY AS A DIRECTOR	42,542,037	99.62	161,569	0.38	250	0.00	42,703,856	33.11

RESOLUTIONS PROXY VOTES RECEIVED

Resolution 3	Lodged **For**		Lodged **Open**		Lodged **Against**		Total Available Votes	% issued capital
	Votes	%	Votes	%	Votes	%		
AUTHORISATION TO FIX AUDITOR FEES AND EXPENSES	42,478,671	99.48	161,805	0.38	59,918	0.14	42,700,394	33.11

RESOLUTIONS PROXY VOTES RECEIVED

Resolution 4	Lodged **For**		Lodged **Open**		Lodged **Against**		Total Available Votes	% issued capital
	Votes	%	Votes	%	Votes	%		
INCREASE TO NON-EXECUTIVE DIRECTOR FEE POOL	38,554,653	98.66	140,766	0.36	384,856	0.98	39,080,275	30.30