Neuren (NEU) - ASX Announcement **22 June 2021**

Chairman's Address at 2021 Annual Meeting of Shareholders

There is no doubt that Neuren has never been in a better position to deliver substantial value for our shareholders. Our lead drug trofinetide is in the last stages of enrolment of its Phase 3 trial in the USA, led by our partner Acadia Pharmaceuticals and we expect enrolments in the trial to close in the coming weeks followed by announcement of the trial results later this year. Our commercial partnership with Acadia put in place three years ago has a number of very attractive components to it and I'll expand on these shortly. The journey of our second product NNZ-2591 has advanced materially in last 12 months and we are increasingly confident in the commercial potential of this product, which is set to be a much larger source of value than trofinetide. We are exploring commercialization options with potential partners for our products in Asia including China, which is not reflected in any external valuation of Neuren to date. Our cash reserves at the end of March 2021 were $22.6 million and we are well resourced to progress our immediate development plans with our experienced and talented management team.

Despite all this, 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. There's no hiding that investing in Neuren has its risks, that's the nature of drug development, but external analyst valuations of the business today are multiples of the current share price with one at $3.93 and our internal modelling is higher again. Our highest priority is to expedite the development of our products, which is the key to unleashing the full value of our company for our shareholders, but we are also running an extensive investor relations program, communicating with existing shareholders and potential new investors at every opportunity possible.

As mentioned earlier our lead product trofinetide is at an advanced stage of its phase 3 trial for Rett syndrome patients in the United States. Neuren could not have funded this on our own, the size of the investment and human resources required to complete the manufacturing scale-up and then execute the trial was simply beyond our reach. To underline this point Acadia to date has invested over $100M just on external parties and has deployed vast internal resources to support the development and commercialization of trofinetide. Our partnership agreement allows us to receive very substantial milestone payments, of up to US$455M as various hurdles are met and we will be paid double digit percentage royalties on sales. Trofinetide has also been awarded Rare Pediatric Designation by the United States FDA, which opens up an additional milestone payment estimated at US$33M for our share of the value of a Priority Review Voucher. And of course, a large additional component of value to Neuren is free and full access to the US data to support the registration of trofinetide in markets outside North America, for which we retain all rights.

We are delighted with the recent public messages by Acadia that the phase 3 trial remains on track for Q4 results and that there has been no change since our partnership began in their expectation of trofinetide being able to generate peak annual sales in North America of at least US$500 million. This is indeed a very exciting time for us with further announcements from Acadia to come in the near term.

Turning now to our second product NNZ-2591, our confidence in the future of this drug continues to grow. At this stage we have identified 4 neurodevelopmental disorders as the first indications for NNZ-2591, namely Angelman syndrome, Phelan-McDermid syndrome, Pitt Hopkins syndrome and Prader-Willi syndrome. The sum of the estimated patient populations for these disorders are 5 to 6 times greater than for Rett syndrome, which gives us very sizeable commercial opportunities to pursue. The Phase 1 trial confirmed the safety and tolerability profile of the product at the dose to be used in Phase 2. We have held very successful pre-IND meetings with the FDA and we are working diligently now to complete IND applications and the many preparatory activities for our Phase 2 trials. We are looking forward to the Angelman trial being run here in Australia, with the Phelan-McDermid and Pitt Hopkins trials to be conducted in the United States. The Neuren team has established excellent engagement with the patient organisations and key physicians associated with these particular disorders. Prader-Willi syndrome has more recently been added to the pipeline on the back of compelling pre-clinical model results and there may be broader application in other neurological conditions as we progress further with our evaluation of the potential of this drug. The progress we have made in developing a proprietary process for large scale manufacturing that has given exceptional purity and high yields is very important for the commercial value of this product. This is one of the factors that drive our confidence that NNZ-2591 provides potentially very large upside for Neuren and our shareholders.

The progress on NNZ-2591 over the last 12 months has been rapid and substantial. We are progressing through the development pathway as swiftly as possible without compromising quality as we strive to bring this product to market much faster than trofinetide and maximise the commercial benefit for our shareholders. Most importantly we look forward to giving a better future to the patients and families suffering from these terrible illnesses. For a multitude of reasons we are excited about the work done to date on NNZ-2591 and the next 12 months is pivotal for the development of this product and for the evolution of Neuren.

On behalf of the Board I'd like to acknowledge the team at Neuren who have achieved a great deal in the last 12 months under difficult circumstances. We are fortunate to have excellent people working at Neuren and I'd like to thank Jon, his team and my fellow directors for their efforts over the last year. In recognition of Jon's leadership since his appointment as Chief Executive Officer just over a year ago, he has recently joined the Board, which was a logical extension of his role with the company and we look forward to working together in the pivotal year ahead.

I'll now invite Jon to make his presentation to the meeting.

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 drug compound, trofinetide, is currently in a Phase 3 clinical trial for Rett syndrome with top-line results expected in Q4 2021 and has completed a Phase 2 clinical trial in Fragile X syndrome. Both programs have been granted Fast Track designation by 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 and Pitt Hopkins syndrome in H2 2021. Neuren is also planning a Phase 2 trial in Prader-Willi syndrome.

Because of the urgent unmet need, five programs have been granted "orphan drug" designation in both the United States and the European Union, a designation that provides incentives to encourage therapies for rare and serious diseases.

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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.

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

ANNUAL SHAREHOLDERS' MEETING

22 June 2021

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 pharmaceuticals

FIGHTING NEURODEVELOPMENTAL DISORDERS

22 June 2021

2021 IS A PIVOTAL YEAR FOR NEUREN

- 2 drugs in clinical development for **6 Orphan Drug indications**:
  - All serious neurological disorders in children, no approved therapies
  - Orphan drugs have higher probability of approval and significant commercial advantages
- **Results in Q4 2021 for trofinetide Phase 3 trial in Rett syndrome**
- **Phase 2 trials commencing in H2 2021 for NNZ-2591 in 3 disorders**
- Trofinetide partnered with ACADIA (NASDAQ:ACAD) for North America
  - Up to US$455m milestone payments
  - Double digit % royalties
  - One third of RPD Priority Review Voucher value
  - ACADIA funds all development
  - **Neuren has free access to US data for ex-North America registration**
- **NNZ-2591 provides large potential upside -** multiple indications and global rights retained

PRODUCT PIPELINE

Compound	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Commercial Partner
Trofinetide	Rett syndrome[1]				***Results Q4 2021***	ACADIA *(North America)*
	Fragile X syndrome[1]					ACADIA *(North America)*
NNZ-2591	Phelan-McDermid syndrome[2]			***Commence H2 2021***		
	Angelman syndrome[2]			***Commence H2 2021***		
	Pitt Hopkins syndrome[2]			***Commence H2 2021***		
	Prader-Willi syndrome			***TBA***		

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

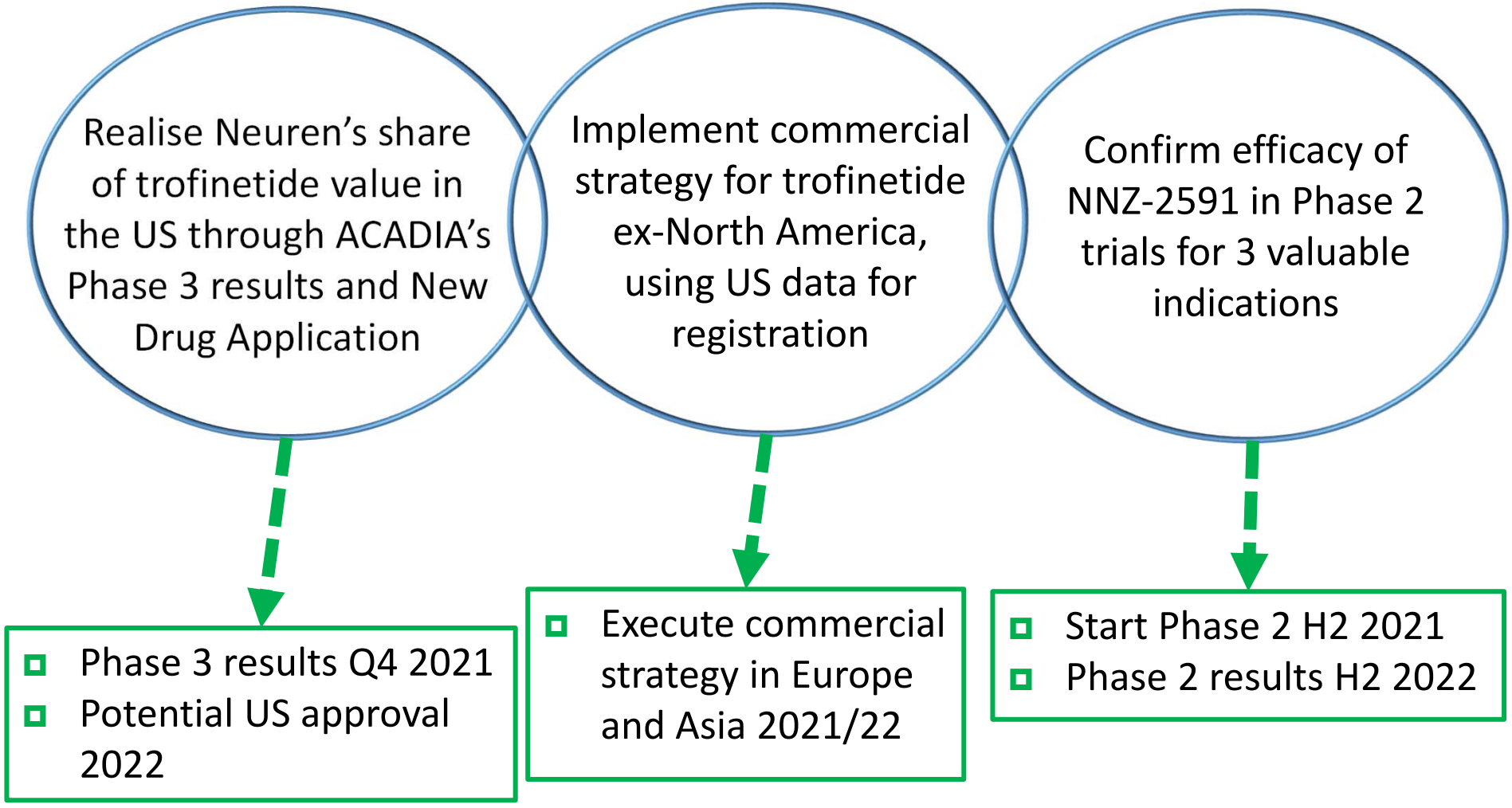
[2] Orphan Drug designation in US and EU

ESTIMATES OF TARGET PATIENT POPULATIONS

Disorder	Gene mutation	Published prevalence estimates	Potential patients		
			US[1]	Europe[1]	Asia[1, 2]
Trofinetide:					
Rett	*MECP2*	1/10,000 to 1/15,000 females	10,000	13,000	37,000
Fragile X	*FMR1*	1/4,000 to 1/7,000 males 1/12,000 to 1/22,000 females	30,000	38,000	112,000
NNZ-2591:					
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

[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

THREE KEY DRIVERS OF FUTURE VALUE



TEN CATALYSTS IN 2021 DRIVING LONG TERM VALUE

- ✓ EU Orphan designations for Phelan-McDermid, Angelman, and Pitt Hopkins
- ✓ Successful Phase 1 trial results for NNZ-2591
- ✓ Prader-Willi syndrome added to NNZ-2591 pipeline
- ✓ Complete drug substance manufacturing for NNZ-2591 Phase 2
- ✓ Pre-IND meetings with FDA to agree NNZ-2591 Phase 2 plans

Submit NNZ-2591 INDs to FDA

Acadia completes enrolment in trofinetide Rett syndrome Phase 3

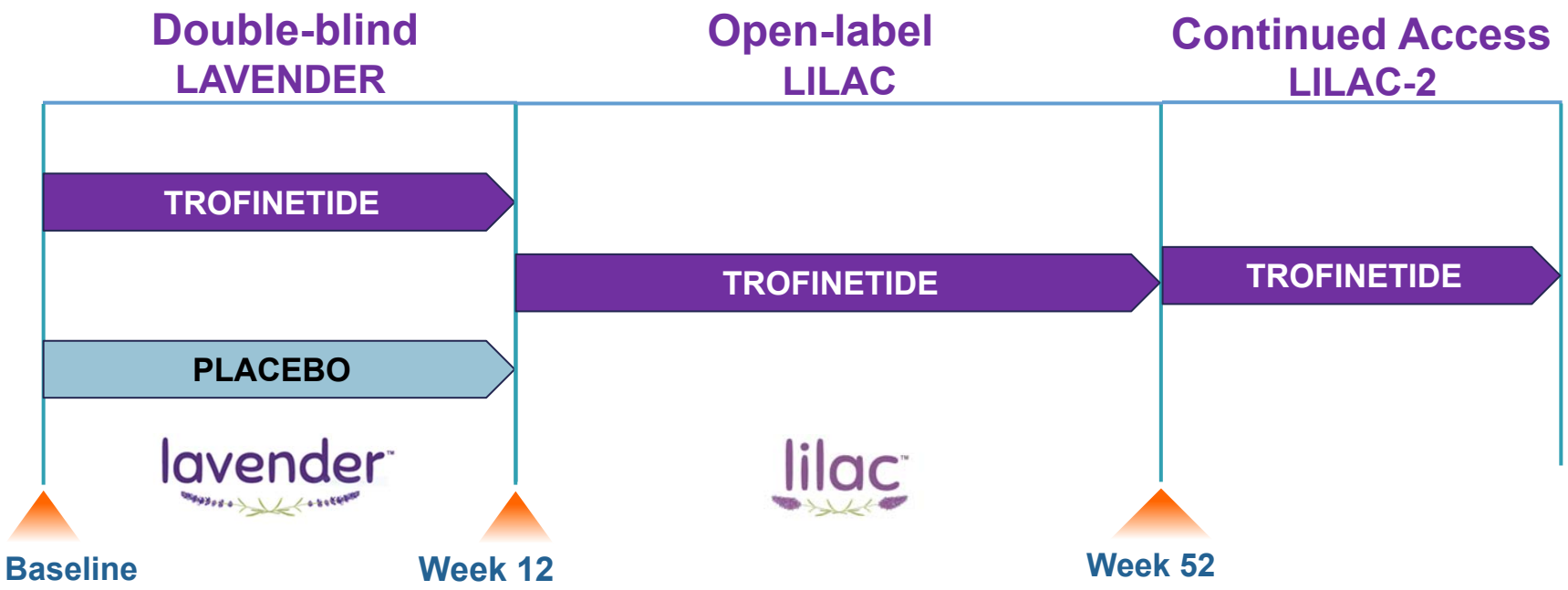
Commence NNZ-2591 Phase 2 trials

Orphan designation in US and EU for Prader-Willi syndrome

Trofinetide Rett syndrome Phase 3 top-line results

TROFINETIDE FOR RETT SYNDROME

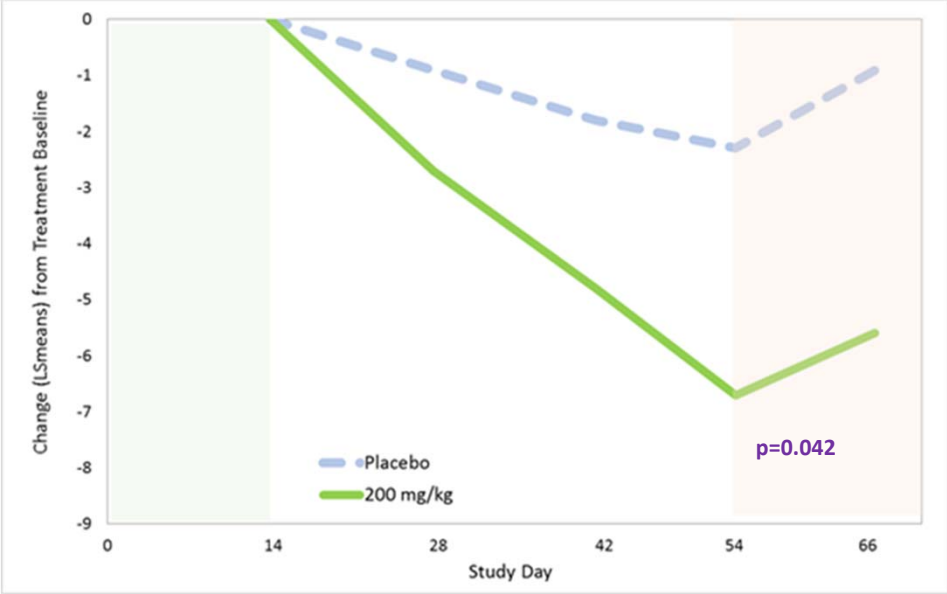
RETT SYNDROME PHASE 3 PROGRAM



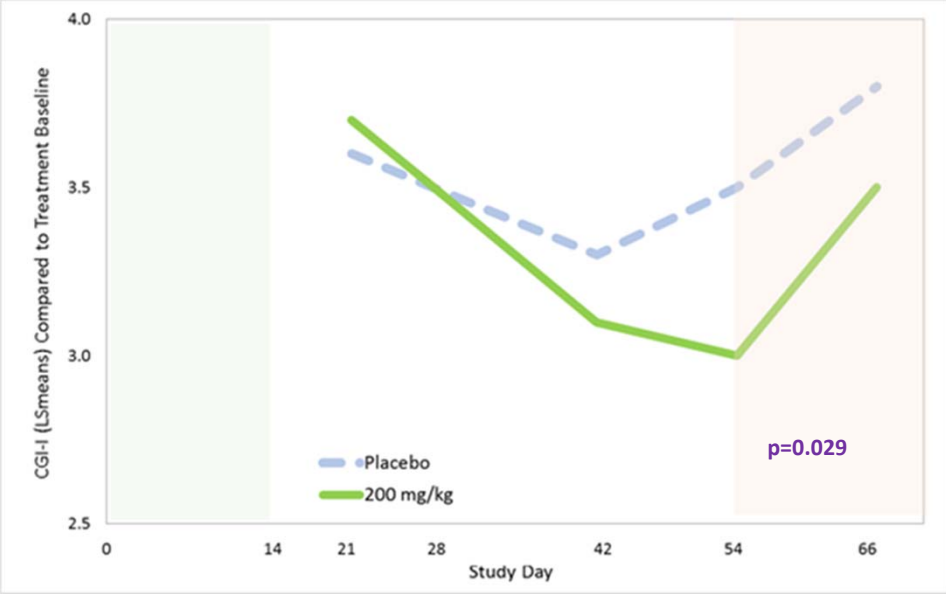
- 180 females aged 5 to 20 years
- RSBQ (caregiver) and CGI-I (physician) at 12 weeks are co-primary efficacy endpoints - both were positive in the Phase 2 trial
- Continuing strong support from leading physicians and Rettsyndrome.org
- Lavender results expected in Q4 2021, potential marketing approval in 2022

RETT SYNDROME PHASE 2 - RSBQ AND CGI-I

Clinical improvement measured by RSBQ



Clinical improvement measured by CGI-I



RSBQ is a caregiver rating, reflecting the severity of the syndrome. Mean improvements for trofinetide and placebo were, respectively, 16% and 6%

CGI-I is a clinician rating of how much the subject's overall illness has improved or worsened. 22% of subjects on trofinetide received a score of 2 ("much improved") compared with 4% of subjects on placebo

RSBQ and CGI-I measure overall syndrome rather than a particular symptom, reflecting heterogeneity of symptoms and disease-modifying action of trofinetide

Publication: https://n.neurology.org/content/early/2019/03/27/WNL.0000000000007316

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 MULTIPLE NEURODEVELOPMENTAL DISORDERS

FOUNDATIONS IN PLACE FOR MULTIPLE INDICATIONS

Neuren is leveraging experience from Rett syndrome program across all areas to execute much faster development for NNZ-2591

2022

Phase 2 data in multiple indications

2021

INDs approval by FDA

Commence Phase 2 trials in multiple indications

2020

- **Identify optimum dose**
- **Develop and scale-up manufacturing**
- **Initiate GMP manufacturing for Phase 2**
- **Non-clinical safety studies**
- **Phase 1 trial**
- **3 EU Orphan designations**

2019

- **Confirm blood brain barrier penetration**
- **3 positive animal models**
- **3 US Orphan designations**
- **New patents in Europe and Japan**

IDEAL ATTRIBUTES LEADING INTO PHASE 2

- ✓ Unique 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
- ✓ Orphan designation from FDA and EMA
- ✓ 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
- ✓ 7 days dosing safe and well tolerated in Phase 1 trial
- ✓ Phase 2 plans confirmed at pre-IND meetings with FDA

KEY FEATURES OF PHASE 2 TRIALS COMMENCING H2 2021

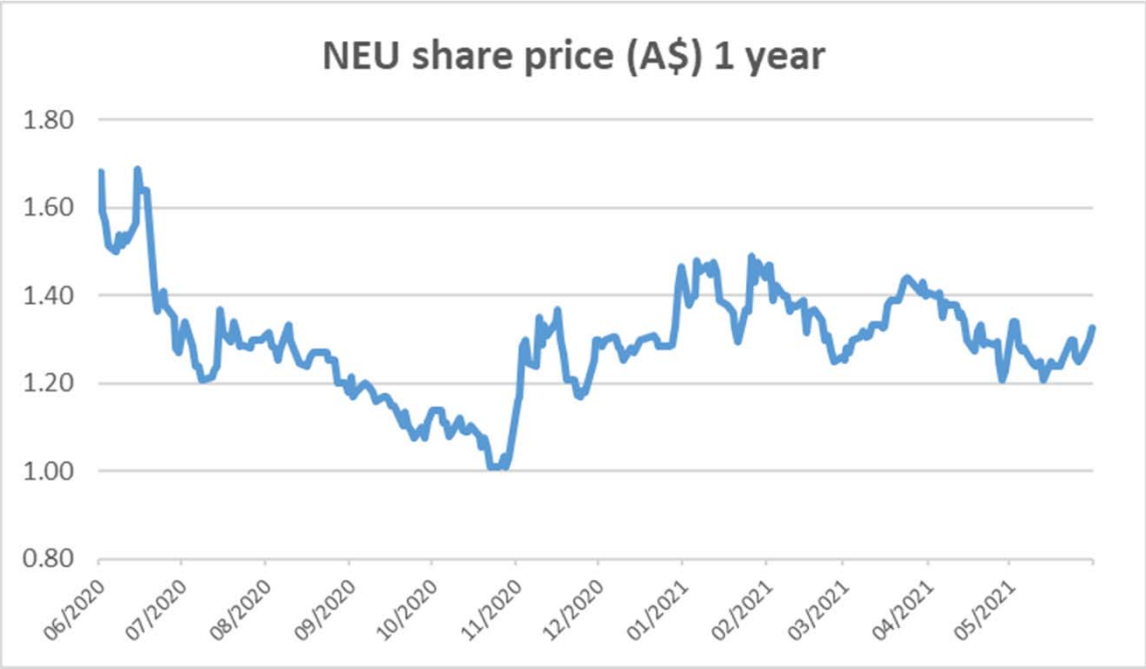
- Prioritising speed to data – results in H2 2022:
  - Angelman syndrome trial in Australia
  - Phelan-McDermid and Pitt Hopkins trials in US
  - 10-20 patients in each trial
- Maximising opportunity to demonstrate effects:
  - Pediatric patients
  - 13 weeks' treatment
- Confirm safety and PK in pediatric patients
- Assess treatment impact across multiple efficacy measures

Overall aim – expedite data that enables subsequent trials to be designed as registration trials

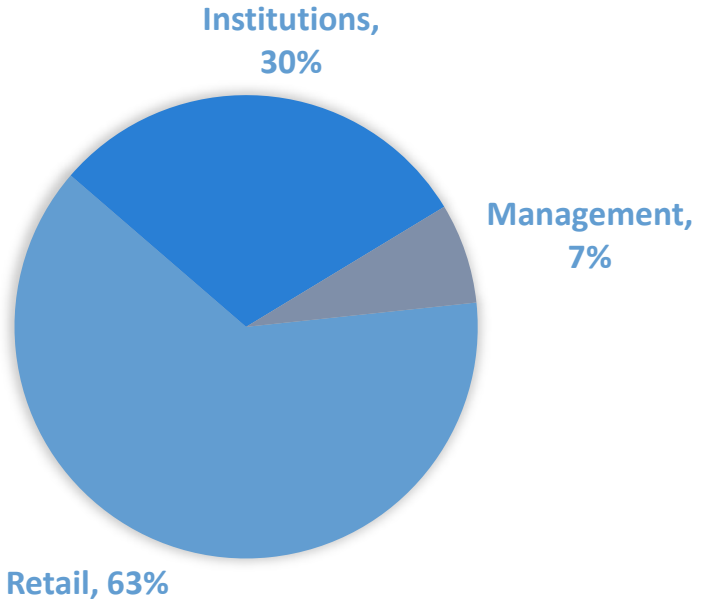
STOCK INFORMATION (ASX: NEU)

Current risk-adjusted valuations:
MST Access - $3.93, Bell Potter - $3.10

52 week price range: A$1.00 - A$1.74



Share register composition
(114 million quoted shares –
top 20 hold 50%)



A$22.6 million cash at 31 March 2021
A$20m placement at $1.40 in June 2020 supported by institutions in Aus, NZ, UK, Hong Kong

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 PATRICK DAVIES AS A DIRECTOR	34,109,026	99.06	321,893	0.93	2,499	0.01	34,433,418	29.28

RESOLUTIONS PROXY VOTES RECEIVED

Resolution 2	Lodged **For**		Lodged **Open**		Lodged **Against**		Total Available Votes	% issued capital
	Votes	%	Votes	%	Votes	%		
AUTHORISATION TO FIX AUDITOR FEES AND EXPENSES	34,153,329	98.59	321,893	0.93	167,002	0.48	34,642,224	29.46

RESOLUTIONS PROXY VOTES RECEIVED

Resolution 3	Lodged **For**		Lodged **Open**		Lodged **Against**		Total Available Votes	% issued capital
	Votes	%	Votes	%	Votes	%		
APPROVAL OF ADDITIONAL 10% PLACEMENT CAPACITY UNDER LISTING RULE 7.1A	33,949,238	98.00	347,143	1.00	344,943	1.00	34,641,324	29.45