neuren

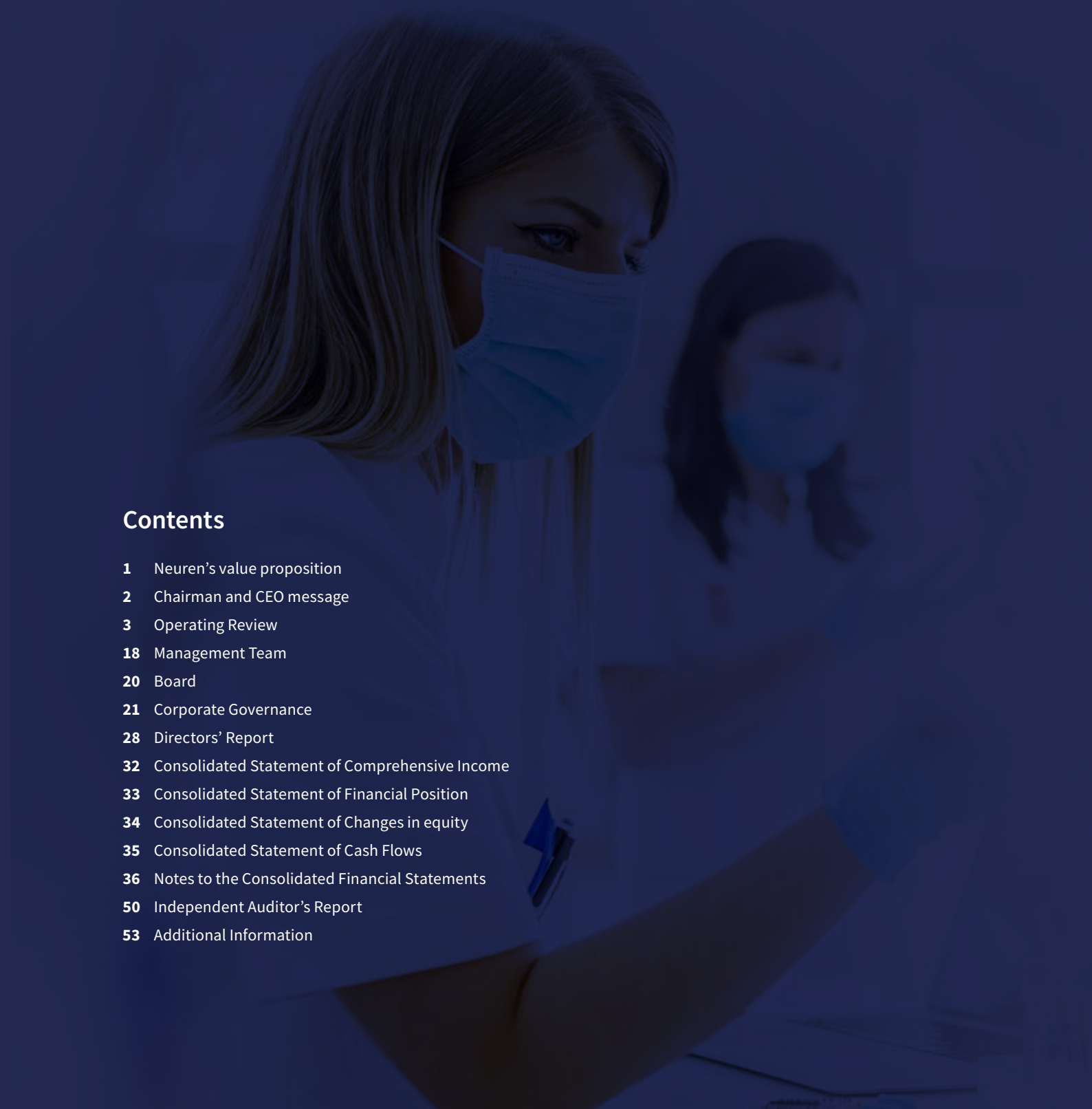
pharmaceuticals

Fighting neurodevelopmental disorders

Neuren Pharmaceuticals Limited

ANNUAL REPORT 2020

Neuren Pharmaceuticals is developing new therapies for debilitating neurodevelopmental disorders that emerge in early childhood and are characterised by impaired connections and signalling between brain cells. Incorporated in New Zealand and based in Melbourne, Australia, Neuren is listed on the ASX under the code NEU.



Contents

NEUREN'S VALUE PROPOSITION

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 2021***		
	Angelman syndrome[2]			***Commence 2021***		
	Pitt Hopkins syndrome[2]			***Commence 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

Three key drivers of future value

1. Realise Neuren's share of trofinetide value in the US through ACADIA's Phase 3 results and New Drug Application
   - Phase 3 results Q4 2021
   - Potential US approval 2022
2. Implement commercial strategy for trofinetide ex-North America, using US data for registration
   - EMA interactions 2021
   - Execute commercial strategy in Europe and Asia 2021/22
3. Confirm efficacy of NNZ-2591 in Phase 2 trials for 3 valuable indications
   - Submit IND H1 2021
   - Start Phase 2 2021
   - Phase 2 results 2022

2021 Milestones

- ✓ 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
- Submit NNZ-2591 INDs to FDA
- Complete 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 results

CHAIRMAN AND CEO MESSAGE

PATRICK DAVIES & JON PILCHER

Dear Shareholders,

2021 is potentially a transforming year for Neuren. We ended 2020 in a very strong position, having achieved all our targeted milestones. The further announcements since the end of the year of a successful Phase 1 trial and addition of Prader-Willi syndrome to the pipeline each added significantly to the underlying value of NNZ-2591, both from risk reduction and increasing the upside. For the remainder of 2021 we are focused on the results of the trofinetide Phase 3 trial in Rett syndrome in Q4 2021, obtaining FDA clearance before commencing the NNZ-2591 Phase 2 trials and progressing the optimum commercial strategy for our products in Europe and Asia. These approaching events have the potential to transform Neuren's corporate profile.

Despite the many challenges of covid-19 in the United States, our US partner Acadia has done a very good job keeping the Rett syndrome Phase 3 trial on track to report top-line results in Q4 2021. This also reflects the support and determination of the Rett community. We look forward to the completion of enrolment into the trial in the near term. Acadia is fully funding the Phase 3 program and its very substantial commitment to our partnership is illustrated by its recent 10k Annual Report, which detailed expenditure to date on trofinetide of approximately A$100 million for external service providers only.

In parallel with the Rett syndrome trial, Neuren's rapid advancement of NNZ-2591 into Phase 2 trials in multiple indications has transformed the potential upside in the value of our business, as well as improving the risk profile. The Neuren team has achieved this in a remarkably short time frame, leveraging all the knowledge and experience they have gained from the Rett syndrome program. We believe that the breadth and late stage of Neuren's pipeline now places us in a world-leading position in the fight against neurodevelopmental disorders.

The United States and Europe remain key markets for trofinetide and NNZ-2591. However, Asia has emerged as a third commercial opportunity that may rival the other two, with potentially a higher number of patients. Established Orphan Drug markets such as Japan and Korea are now joined by large markets such as China and Russia in which rare disease therapies are increasingly being made available. Asia has not been factored into any published valuations of Neuren, so it represents very significant upside.

The capital raising that we executed in June 2020 was important to enable our ambitions for NNZ-2591 and we are grateful to all who participated. We are fully funded to execute the currently planned NNZ-2591 Phase 2 trials, while Acadia continues to fund the trofinetide program.

The Neuren management and board are determined and highly motivated to improve the lives of so many families impacted by these debilitating disorders, whilst appropriately rewarding our shareholders for participating in that mission. We would like to thank all stakeholders for their support and look forward to providing further updates as we achieve the important approaching milestones.

Neuren's Values

- We are passionate about making a difference to the lives of patients and their families
- We aim to earn the respect of everyone we deal with
- We are determined and creative to break through barriers
- We harness the power of collaboration and different perspectives
- We recognise the importance of all stakeholders and endeavour to use financial resources efficiently

Patrick Davies
Chairman

Jon Pilcher
CEO

OPERATING REVIEW

NEUREN'S NOVEL THERAPIES FIGHTING NEURODEVELOPMENTAL DISORDERS

Neuren has two novel patented drugs, trofinetide and NNZ-2591, which potentially have broad utility in the treatment of neurological disorders. Both drugs can be administered orally in a patient-friendly liquid dose. Each drug is in clinical development to treat debilitating neurodevelopmental disorders that emerge in early childhood, for which there are currently no approved drug therapies. The disorders stem from problems in brain development which lead to a wide range of serious issues, which place a severe life-long burden on the patients and their families.

Each neurodevelopmental disorder is caused by a different genetic mutation, but in many cases they share similar symptoms and the common characteristic of impaired connections and signalling between brain cells. Neuren's drugs, which are synthetic analogues of important molecules that occur naturally in the brain, induce improvements in the impaired connections and signalling, which means that the target is a broad impact on the disorder rather than aiming to treat one symptom.

A critical feature of Neuren's work to develop therapies for these disorders is close collaboration with the leading specialist physicians and with the well-organised patient advocacy organisations.

THE IMPORTANCE OF ORPHAN DRUG DESIGNATION

Neuren has received Orphan Drug designation from both the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for trofinetide to treat Rett syndrome and Fragile X syndrome and for NNZ-2591 to treat Phelan-McDermid syndrome, Angelman syndrome and Pitt Hopkins syndrome. Applications for Prader-Willi syndrome will be submitted in the near term.

Orphan Drug designation is a special status that the regulators may grant to a drug to treat a rare disease or condition. Amongst other incentives, Orphan Drug designation qualifies the sponsor of the drug for exclusivity periods during which the regulators will not approve a generic competitor product. These marketing exclusivity periods are extremely valuable for the commercialisation of Orphan Drugs. They provide additional protection, along with patents, against generic competitors and potentially can continue to provide protection after patent expiry. The exclusivity periods after marketing authorisation of products approved for pediatric use are 7.5 years in the US and 12 years in the EU.

OPERATING REVIEW

CONTINUED

As well as the exclusivity periods, Orphan Drugs have many other commercial advantages compared with existing markets that have apparently attractive large sales in which established products and companies have to be displaced. Orphan Drugs typically secure significantly higher pricing. The serious and urgent unmet need results in a more supportive regulatory environment and strong support from patient community and leading physicians. Historical data indicates a higher probability of achieving regulatory approval and the potential for immediate access to known patients means that a large sales organisation is less important.

In short, the Orphan Drug business model targets a leadership position in markets with urgent need, at a favourable price with little competition, and with a higher probability of getting to market.

TARGET MARKETS

The neurodevelopmental disorders that Neuren is aiming to treat are technically "rare diseases", however they are not "ultra-rare" and in each there are tens of thousands of potential patients. Estimates of potential patient numbers in the US, Europe and Asia are shown in the table below. Asia has emerged as an important market for Neuren. There are established Orphan Drug programs in Japan, Korea, Taiwan and Israel, whilst in China and Russia increasing numbers of rare disease treatments are being introduced. To date published analyst valuations of Neuren's business have not included Asia, which means that it represents very significant upside.

Estimates of target patient populations

Disorder	Gene mutation	Published prevalence estimates	Potential patients US[1]	Potential patients Europe[1]	Potential patients 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

COMMERCIAL EXCLUSIVITY

In addition to the primary protection of the important exclusivity periods from Orphan Drug designation explained above, Neuren has additional commercial protection from issued patents, which extend as far as 2032 for trofinetide and 2034 for NNZ-2591. Further international patent applications have been filed for both drugs, which if granted will extend to 2040. Since trofinetide and NNZ-2591 are new chemical entities, following the first marketing authorisation for each drug, one patent may potentially be extended by up to 5 years in the United States, Europe and Japan.

OPERATING REVIEW

CONTINUED

TROFINETIDE FOR RETT SYNDROME

Neuren's lead program for Rett syndrome is approaching the end of the development journey, with top-line results from the Phase 3 clinical trial ("LAVENDER") in the US expected in Q4 2021. As an Orphan Drug, the marketing application will qualify for an expedited Priority Review period of 6 months, which means that there is the potential for marketing approval in 2022.

The Phase 3 program is being executed and fully funded by Neuren's US partner Acadia Pharmaceuticals (Nasdaq: ACAD). Acadia has exclusive rights to trofinetide in all indications for the United States, Canada and Mexico. Neuren retained all rights to trofinetide for countries outside North America with free and full access to utilise the US regulatory package for registration in those countries.

Important factors for Neuren when partnering with Acadia in 2018 were the proven capabilities within the Acadia team in the development and commercialisation of novel neurology therapies in the US, their strong commitment to achieve a treatment option for Rett syndrome patients, and the strategic importance that Acadia attaches to trofinetide. Acadia's substantial commitment to trofinetide is illustrated by its 2020 10-K Annual Report, which detailed expenditure to date of US$78 million (approximately A$100 million) on external service providers only.

A redacted version of the licence agreement between Neuren and Acadia was filed with the US Securities and Exchange Commission as a material contract exhibit to Acadia's 2018 10-K Annual Report, which is available to view via the SEC Filings section of Acadia's website.

As well as Acadia fully funding the Phase 3 development program and commercialisation, Neuren will receive significant participation in the future value of trofinetide in the US, through the following payments from Acadia:

- Double digit percentage royalties on sales of trofinetide in all indications. The annual sales are recorded in tiers and an escalating percentage is applied to each successive tier. Acadia has stated the peak annual sales potential for Rett syndrome alone in the US as being more than US$500m.
- Payments of up to US$455 million (approximately A$760 million) on achievement of development and annual sales milestones. US$105 million is to be paid on achievement of development milestones, split between Rett and Fragile X. The remaining US$350 million, is to be paid on achievement of a series of 4 thresholds of total annual sales for all indications.
- One third of the market value of any Rare Pediatric Disease Priority Review Voucher, if awarded to Acadia by the US Food and Drug Administration upon approval of a New Drug Application for trofinetide. These vouchers are tradeable and published sales in 2019 fetched between US$95 million and US$105 million. Acadia's eligibility for a voucher was confirmed by receiving Rare Pediatric Disease Designation from the FDA for the Rett syndrome program.

About Rett syndrome

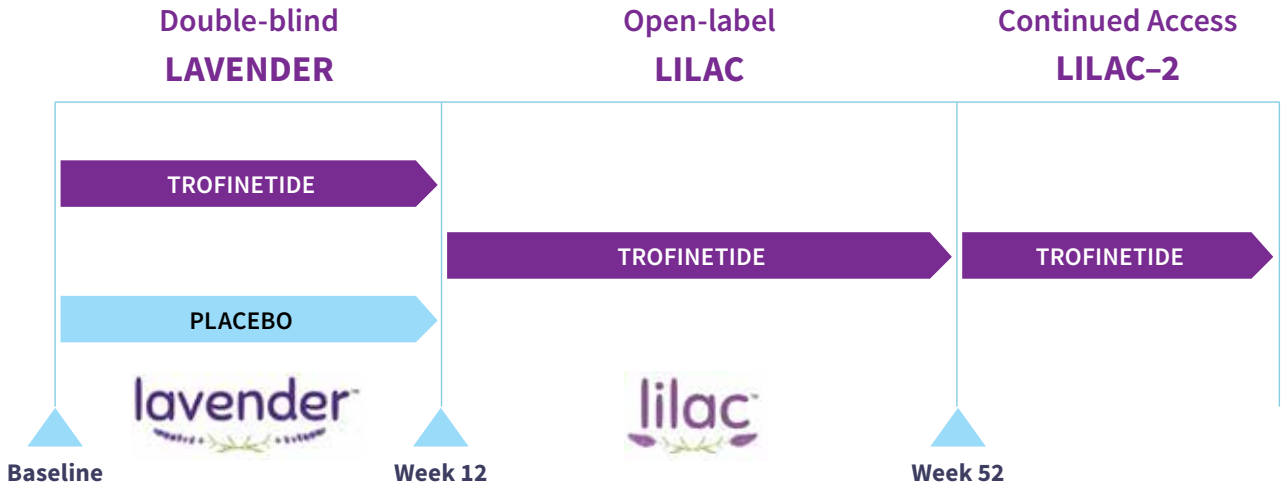
Rett syndrome is a seriously debilitating and life-threatening neurological disorder, for which there are no approved medicines. It is first recognized in infancy and seen predominantly in girls, but can occur very rarely in boys. At diagnosis, Rett syndrome has often been misdiagnosed as autism, cerebral palsy, or non-specific developmental delay. Most cases of Rett syndrome are caused by mutations on the X chromosome on a gene called *MECP2*. Rett syndrome strikes all racial and ethnic groups and has been estimated to occur worldwide in 1 of every 10,000 to 15,000 female births, causing problems in brain function that are responsible for cognitive, sensory, emotional, motor and autonomic function. These problems can include learning, speech, sensory sensations, mood, movement, breathing, cardiac function, and even chewing, swallowing, and digestion. Rett syndrome symptoms appear after an early period of apparently normal or near normal development until six to eighteen months of life, when there is a slowing down or stagnation of skills. A period of regression then follows, with loss of communication skills and purposeful hand use, loss or impairment of walking, and the onset of stereotypic hand movements. Other problems frequently include seizures and erratic breathing patterns, an abnormal side-to-side curvature of the spine (scoliosis), and sleep disturbances.

OPERATING REVIEW

CONTINUED

The Phase 3 program

The Phase 3 program was agreed with the FDA Division of Neurology. Recognising the urgent unmet need and the small population, it involves a single trial rather than the standard two trials and provision for a smaller than standard safety database. The program has continuing strong support from leading Rett syndrome physicians and the largest advocacy group (rettsyndrome.org).



A randomised double-blind placebo-controlled study for 12 weeks (LAVENDER) is followed by an open label extension study (LILAC) in which all participants, including those on placebo in LAVENDER, are eligible to receive trofinetide. In LILAC, all participants are be followed to evaluate long term tolerability and safety of trofinetide. A continued access program (LILAC 2) enables participants to continue to receive trofinetide during the period before marketing approval.

Approximately 180 females with Rett syndrome aged 5 to 20 years are being enrolled at US sites, randomised into one active group and a placebo group. Change after 12 weeks measured by each of the Rett Syndrome Behaviour Questionnaire (RSBQ) and the Clinical Global Impression – Improvement scale (CGI-I) are the co-primary efficacy endpoints. RSBQ is an assessment by the caregiver and CGI-I is an assessment by the physician.

Acadia is nearing the end of enrolment into the LAVENDER study. The first subjects enrolled have now completed LAVENDER and LILAC and commenced LILAC 2.

Results of Neuren's Phase 2 paediatric trial highly relevant for Phase 3

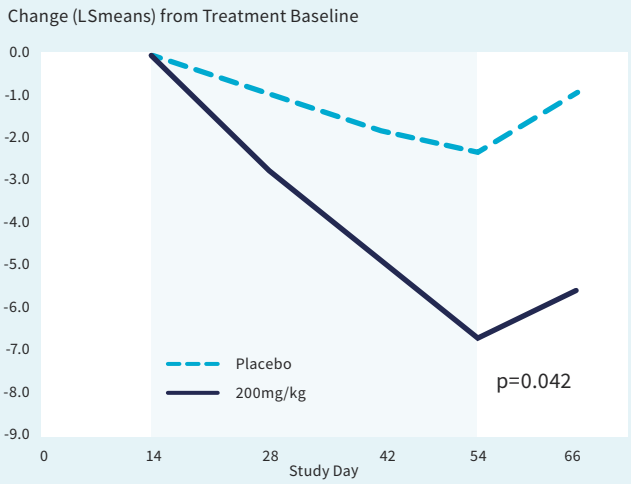
Neuren's Phase 2 trial was a double-blind, randomized, placebo-controlled study that tested three doses of trofinetide compared with placebo in 82 girls with Rett syndrome aged 5 to 15. Trofinetide was well tolerated and had a good safety profile in these younger subjects, with no dose-limiting effects observed. The highest dose achieved statistically significant and clinically relevant benefit compared with placebo measured by each of RSBQ and CGI-I. The improvement increased through to the time that treatment ceased after 6 weeks, suggesting that further benefit may be achieved with a longer treatment duration.

OPERATING REVIEW

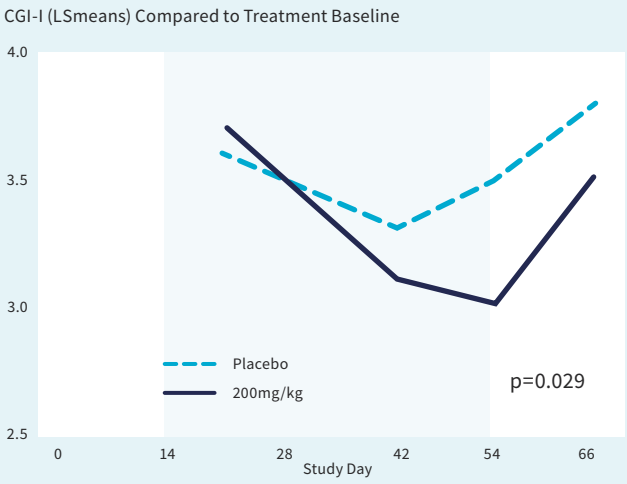
CONTINUED

These efficacy results are illustrated in the following charts, in which a downward movement represents an improvement from day 14 baseline and study day 54 to 66 is the period after treatment ceased:

Clinical improvement measured by RSBQ



Clinical improvement measured by CGI-I



In 2019 the Phase 2 trial was published in Neurology®, the Medical Journal of the American Academy of Neurology, which is the most widely read and highly cited peer-reviewed neurology journal providing strong validation of the results from Neuren's ground-breaking work in Rett syndrome.

The Phase 3 trial design maximises the 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 treatment 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 and therefore has 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 at US sites only, with most Phase 2 sites participating in Phase 3

OPERATING REVIEW

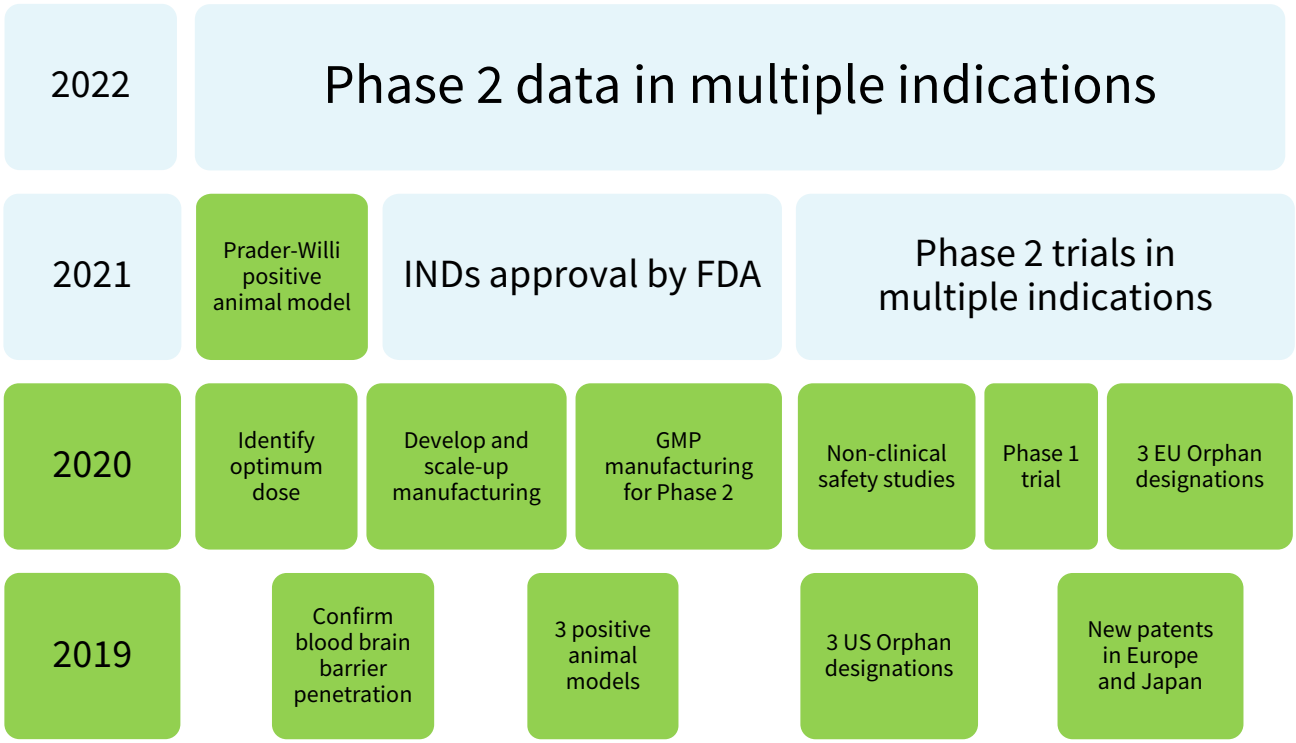
CONTINUED

NNZ-2591 FOR MULTIPLE NEURODEVELOPMENTAL DISORDERS

Neuren is preparing to start Phase 2 clinical trials of NNZ-2591 for Phelan-McDermid, Angelman and Pitt Hopkins syndromes, each of which currently has no approved therapy. A fourth disorder, Prader-Willi syndrome was also recently added to the development pipeline. Each syndrome is caused by a different genetic mutation, however they share the feature of impaired signalling between neurons, with abnormal length and density of the dendritic spines that connect the neurons via synapses. In turn this means that they share many common clinical characteristics.

In designing and executing the NNZ-2591 development program, Neuren has been able to leverage the extensive and highly relevant experience gained from the trofinetide Rett syndrome and Fragile X syndrome programs across manufacturing, non-clinical, clinical and regulatory. Neuren has spent the last two years meticulously building strong foundations in each of these areas to enable Phase 2 trials in multiple indications.

NNZ-2591 Foundations in place to realise value



Clear and consistent efficacy in mouse models of all four disorders

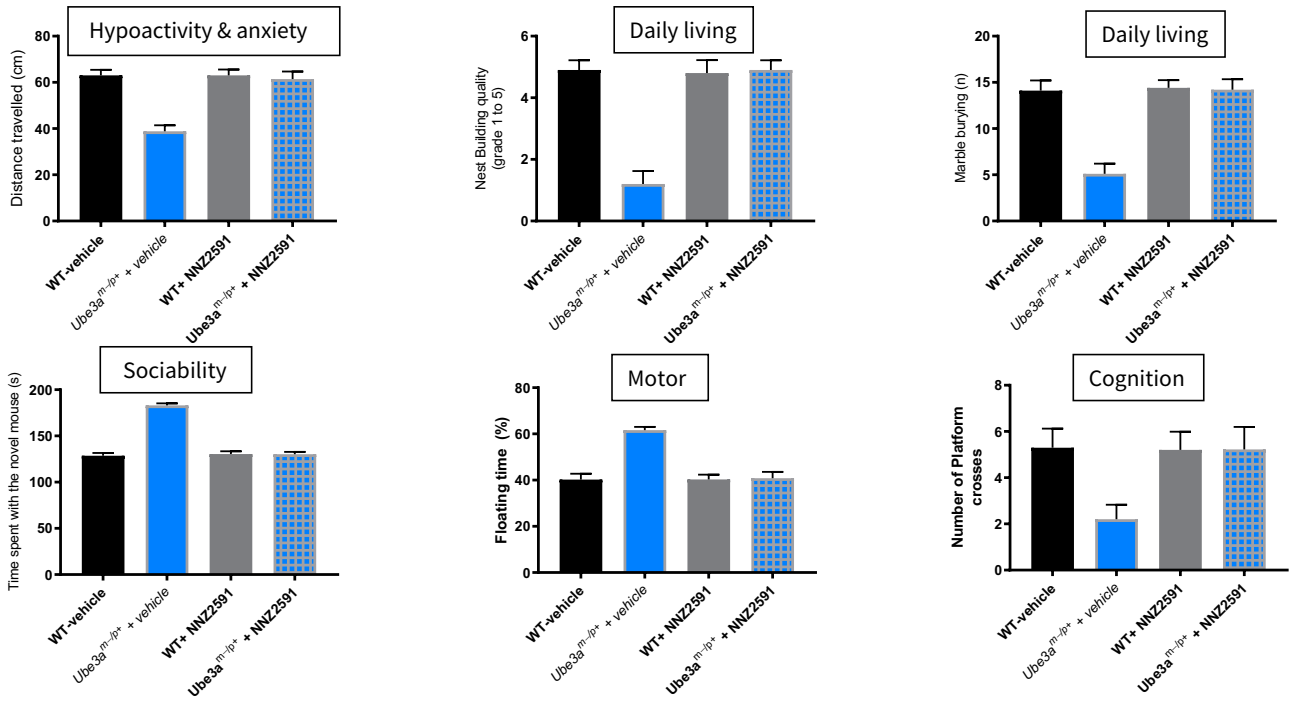
The studies in these models compared normal mice (“wild type” or “WT”) and mice with a disrupted gene (“knockout”). The knockout mice exhibit behavioural and biochemical deficits that mimic each disorder in humans. The wild type mice and the knockout mice were each treated with placebo (vehicle) and NNZ-2591. In all four models treatment with NNZ-2591 for 6 weeks eliminated all the deficits so that the knockout mice were indistinguishable from the wild type mice. Treatment had no impact on the wild type mice, which is important from a safety point of view.

OPERATING REVIEW

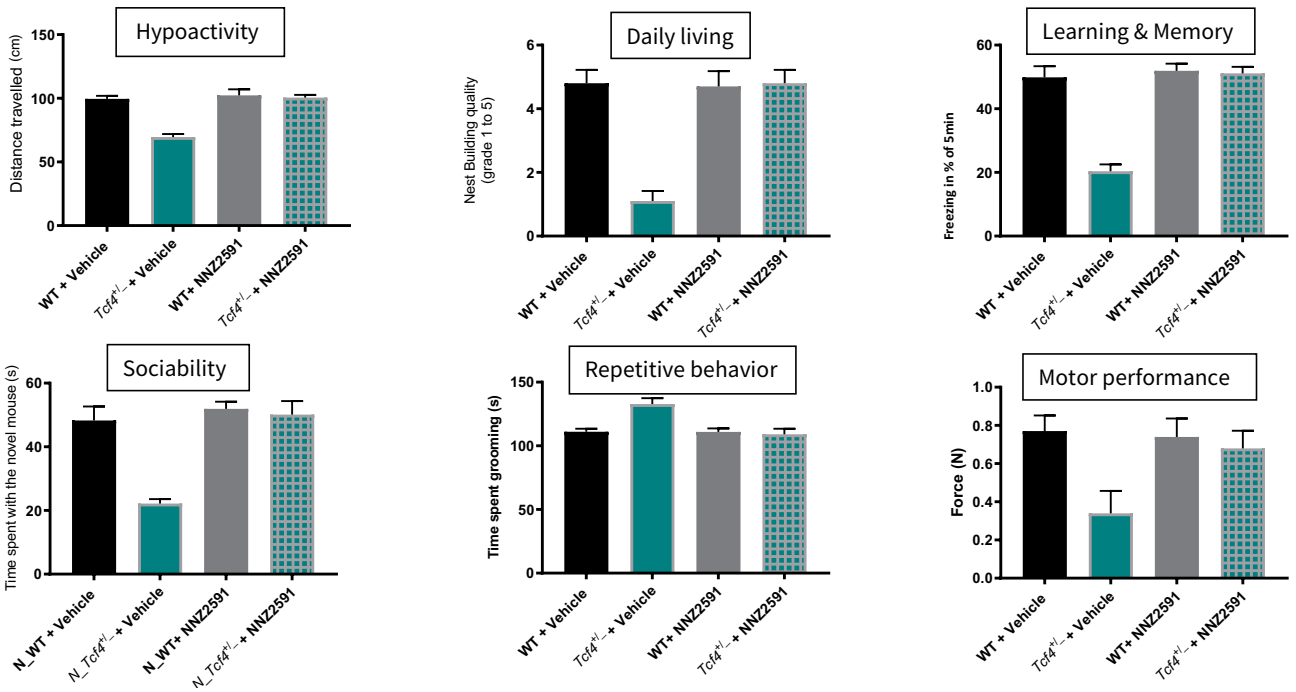
CONTINUED

The charts below show the results in the Angelman syndrome, Pitt Hopkins and Prader-Willi syndrome models. In the Angelman model, treatment also eliminated seizures in the knockout mice.

Efficacy in mouse model of Angelman (*Ube3a*)



Efficacy in mouse model of Pitt Hopkins (*Tcf4*)



OPERATING REVIEW

CONTINUED

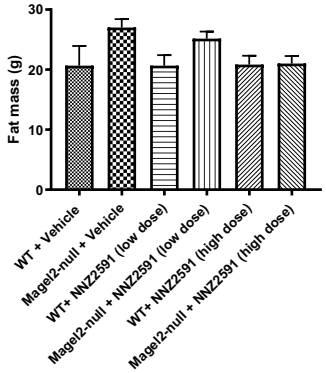
Efficacy in mouse model of Prader-Willi (*Magel2*-null)

Prader-Willi is caused by mutations in the *15q11-q13* region of chromosome 15. In the *Magel2*-null mouse model, which exhibits features of Prader-Willi in humans, wild type mice and knockout mice were treated with placebo (vehicle) or NNZ-2591 for 6 weeks. Treatment with NNZ-2591 normalized fat mass (obesity) insulin levels, IGF-1 levels and all the behavioral deficits in the knockout mice and had no effect on the wild type mice.

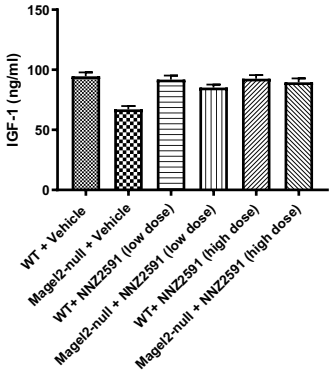
Insulin levels (pM)

WT plus vehicle	*Magel2*-null plus vehicle	WT plus NNZ-2591 low dose	*Magel2*-null plus NNZ-2591 low dose	WT plus NNZ-2591 high dose	*Magel2*-null plus NNZ-2591 high dose
110	173	112	143	115	119

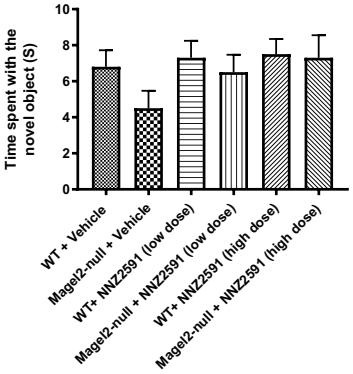
Obesity



Circulating IGF-1 levels

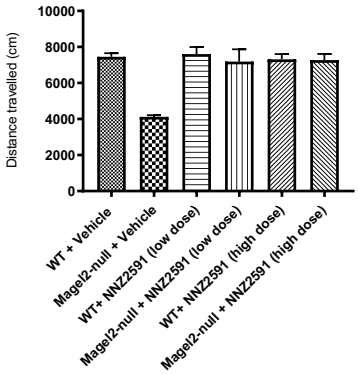


Cognition



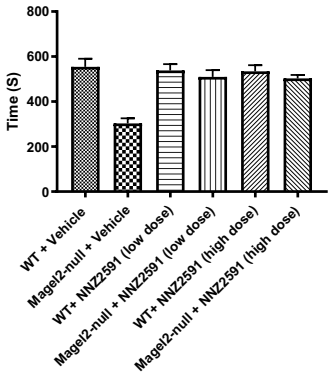
Hypoactivity

(Open Field distance travelled)

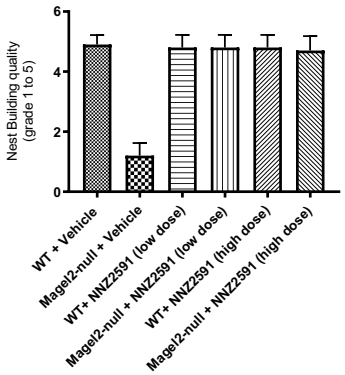


Hypoactivity

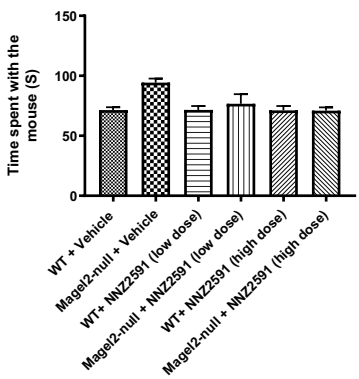
(Open Field time spent active)



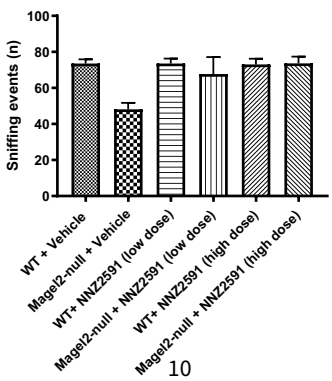
Daily Living



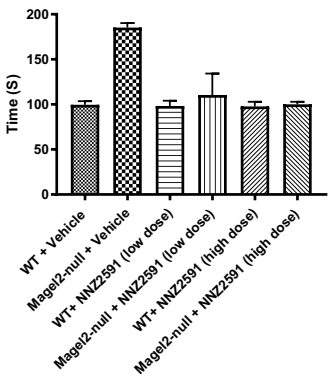
Social preference



Social interaction



Anxiety



OPERATING REVIEW

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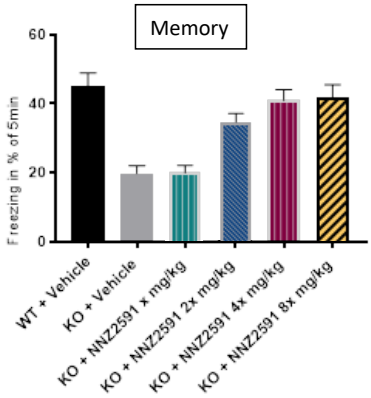
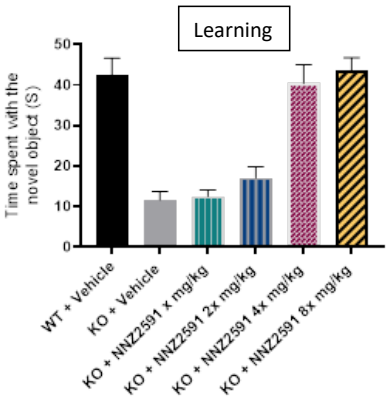
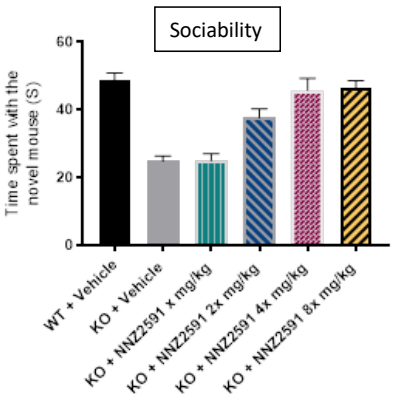
Optimum dose identified

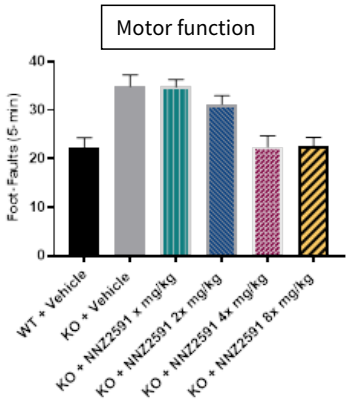
In the Phelan-McDermid syndrome model, the effect of four escalating dose levels was investigated. The results of this dose ranging study are shown in the charts below. They were consistent across all eight behavioral tests and the incidence of seizures, demonstrating that the second highest dose was the optimum dose level in the mouse model. Comparison with human pharmacokinetic data from the Phase 1 clinical trial has informed the equivalent human dose for the Phase 2 trials in patients.

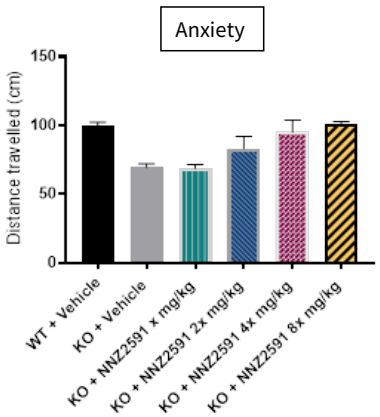
A further observation was that the optimum dose in this 6 weeks study showed better efficacy than the same dose in an earlier 3 weeks study, indicating that efficacy increases with treatment duration. Neuren plans to test treatment with NNZ-2591 for 12 weeks in the Phase 2 trials.

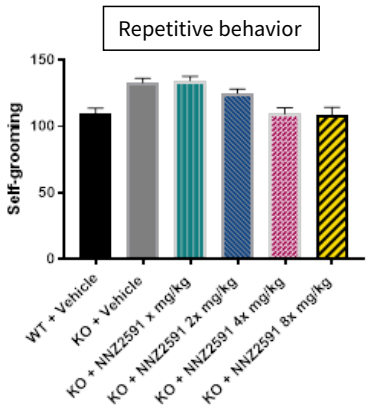


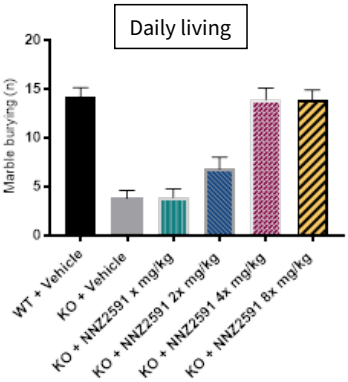


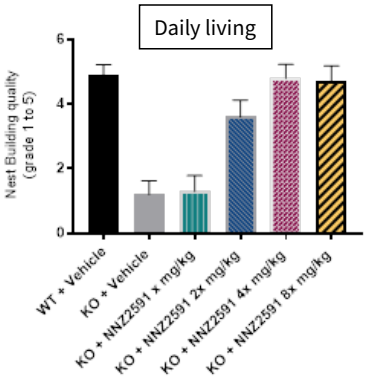












Incidence of seizures

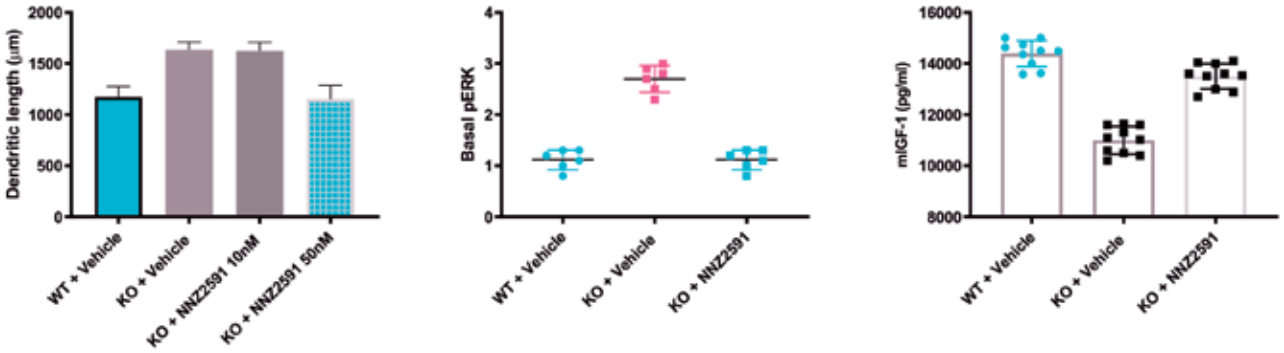
WT + vehicle	KO + vehicle	KO + x mg/kg
0%	60%	50%
KO + 2x mg/kg	**KO + 4x mg/kg**	**KO + 8x mg/kg**
30%	10%	10%

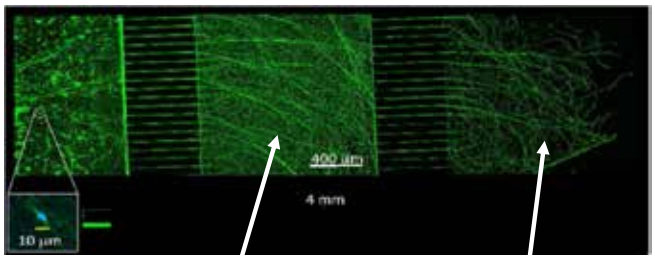
OPERATING REVIEW

CONTINUED

Effects on biochemistry and brain cell structure confirmed

Biochemical testing in the Phelan-McDermid mouse model showed that the abnormal length of dendritic spines between brain cells, the excess activated ERK protein (pERK) and the depressed level of IGF-1 in the knockout mice were all normalised after treatment with NNZ-2591, as shown in the charts below.





Abnormal dendrites in shank3 knockout mice

Normalisation after treatment with NNZ-2591

Blood-brain barrier penetration confirmed

As well as high oral bioavailability, very good penetration of the blood-brain barrier by NNZ-2591 has been demonstrated in a rodent study. A single dose was administered at two dose levels, with the high dose twice the low dose. The concentration of NNZ-2591 was measured in the blood and cerebrospinal fluid after 1.5 hours and again after 4 hours. The amount in the brain was also measured after 4 hours. In each case the amount was approximately proportional to the dose and after 4 hours the concentration in blood and brain tissue was approximately equivalent.

	Mean exposure to NNZ-2591		
Dose	**"A"mg/kg**	**2A mg/kg**	**Ratio of 2A mg/kg: A mg/kg**
1.5 hours post-dose:			
Cerebrospinal fluid (µg/ml)	40.4	82.2	2.03 : 1
Blood (µg/ml)	58.5	116.0	1.98 : 1
4 hours post-dose:			
Cerebrospinal fluid (µg/ml)	11.0	24.7	2.25 : 1
Blood (µg/ml)	15.6	34.2	2.19 : 1
Brain (µg/g)	22.6	37.0	1.63 : 1

OPERATING REVIEW

CONTINUED

Large scale manufacturing process developed

Neuren recently announced that manufacturing of the drug substance for Phase 2 trials of NNZ-2591 had been completed on schedule. This confirmed the successful development of a proprietary process for large scale manufacturing with exceptional purity and high yield. As well as supplying the planned trials in Phelan-McDermid, Angelman and Pitt Hopkins syndromes, the manufacturing campaign produced enough drug substance at no extra cost to supply a Phase 2 trial in Prader-Willi syndrome.

Positive Phase 1 clinical trial results

Neuren recently completed a Phase 1 clinical trial in Australia, in which twice daily oral dosing of NNZ-2591 for seven days was safe and well tolerated in healthy volunteers at doses expected to be within the effective therapeutic range. This was an important milestone for NNZ-2591 to be able to move forward to Phase 2 clinical trials in patients.

The primary objective was to evaluate safety and tolerability, with a secondary objective to evaluate pharmacokinetic parameters. Two double-blind placebo-controlled cohorts of eight healthy adult volunteers were dosed orally twice per day for seven days. Each cohort was titrated up to the target dose, with the target dose in the second cohort double the target dose in the first cohort. These two cohorts were preceded by preliminary testing of single doses of NNZ-2591, which enabled modelling of potential multiple dosing regimens.

No Serious Adverse Events (SAEs) were reported. All reported Adverse Events (AEs) were mild or moderate and resolved during the trial. There were no clinically significant findings from safety laboratory tests, vital signs, or cardiac tests. In the seven days' dosing cohorts, the most common AE reported was drowsiness. In the higher dose cohort only one of the reported AEs was moderate, the remainder were mild. All subjects completed the scheduled dosing, apart from one of the eight subjects in the lower dose cohort, who ceased dosing after receiving the first starting dose following moderate drowsiness and incoordination.

Preparing for Investigational New Drug (IND) applications to commence Phase 2 trials

An extensive program of non-clinical toxicology and manufacturing studies required to open an IND in the United States and enable clinical trials for 12 weeks in pediatric patients has been completed. Neuren plans to submit IND applications to the FDA by 30 June 2021 and commence the Phase 2 trials as soon as possible after receiving clearance.

To find out more about these disorders:

pmsf PHELAN-McDERMID SYNDROME FOUNDATION

www.pmsf.org

angelman SYNDROME FOUNDATION | FAMILIES. RESEARCH. CLINICS. COMMUNITY. WITH YOU FOR THE JOURNEY.

www.angelman.org

fast

www.cureangelman.org

PITT HOPKINS RESEARCH FOUNDATION

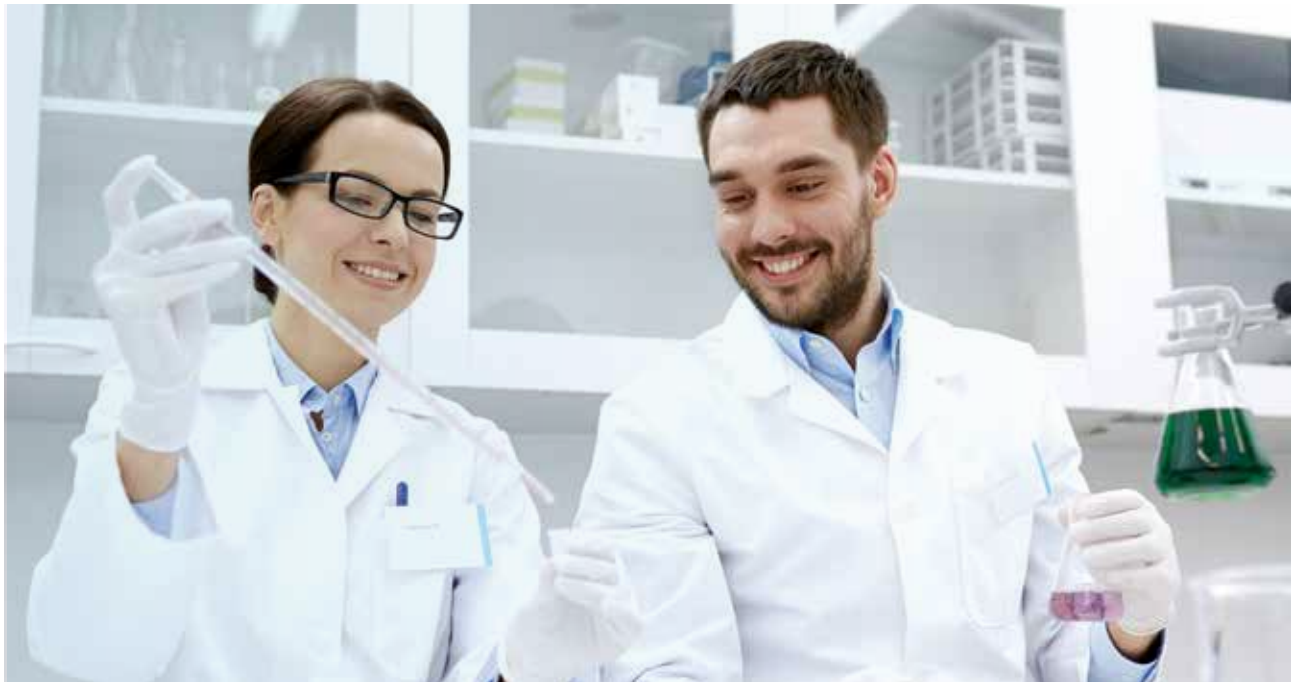
www.pitthopkins.org

FOUNDATION FOR PRADER-WILLI RESEARCH

www.fpwr.org

OPERATING REVIEW

CONTINUED



THE SCIENCE BEHIND NEUREN'S PRODUCTS

Trofinetide (also known as NNZ-2566) and NNZ-2591 are synthetic analogues of glypromate ("GPE") and cyclic glycine-proline ("cGP") respectively, each of which occurs naturally in the brain and is related to IGF-1, which is a growth factor stimulated by growth hormone. In the central nervous system, IGF-1 is produced by both of the major types of brain cells – neurons and glia. IGF-1 in the brain is critical both for normal development and to maintain or restore the biological balance required for normal functioning. During development, the brain and the cells that comprise it change rapidly and in complex ways. IGF-1 and its metabolism play a significant role in regulating these changes. In the mature brain, it plays an important role in responding to disease, stress and injury.

Trofinetide and NNZ-2591 mimic the function of the natural molecules in the brain, however each drug is designed to have a longer half-life in the circulation, be suitable for use as an oral medication, more readily cross the blood brain barrier and have better stability for longer and easier storage and shipping.

Whereas most drugs typically exert a specific effect on a specific target, trofinetide and NNZ-2591 exert diverse effects which can help to control or normalise abnormal biological processes in the brain.

Many neurological conditions share four common, underlying pathological features. The aim of treatment with Neuren's drugs is to restore the natural balance of brain function by:

- reducing inflammation
- restoring the normal functioning of microglia
- improving the dendritic structure of synapses
- normalising the levels of IGF-1 in the brain

OPERATING REVIEW

CONTINUED

1. Inflammation

Inflammation in the brain (neuroinflammation) is perhaps the most common pathological feature of neurological disorders. Much of it is the result of excess production of molecules called inflammatory cytokines. These are prominent in brain injuries, neurodevelopmental disorders such as Rett syndrome, neurodegenerative diseases like Alzheimer's and even so-called "normal" aging.

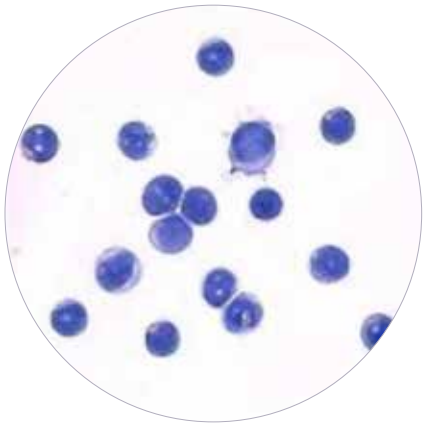
Neuroinflammation places significant stress on brain cells. Stress can disrupt normal cellular processes such as information signalling, increase energy requirements beyond the ability of the cells to meet their metabolic needs and disturb electrical functions which can lead to seizures and other abnormalities and even result in premature cell death.

2. Over-activation of microglia

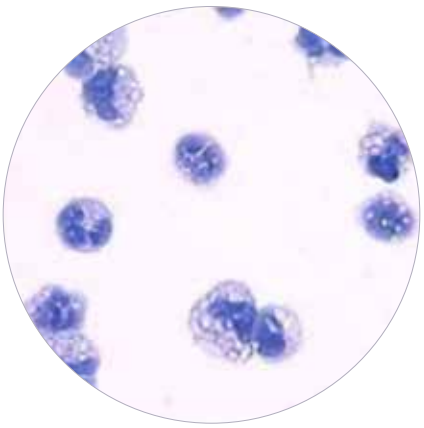
Microglia are the resident immune cells in the brain. Once thought to serve primarily a sentinel function – responding to infection and damaged cells by surrounding and removing them – it is now known that they play a central role in maintaining synapses during development and in mature brains by pruning dendrites, the many small extensions of neurons that form synapses. Microglia are also a key source of IGF-1. Due to this wide-ranging maintenance function, they have appropriately been referred to as the "constant gardeners" of the brain.

Microglia are not only activated in response to infection and injury, they also are activated by inflammation. In this activated state, they lose their ability to effectively perform their normal function in synaptic maintenance and also produce more inflammatory cytokines which can further compound the damage to neurons and other brain cells.

Resting Microglial Cells



Activated Microglial Cells



3. Dysfunction of synapses

Neurons communicate with each other by chemical and electrical signals transmitted via synapses. Normal synaptic function is essential for healthy brain function and underlies memory, cognition, behaviour and other brain activities. Normal synaptic function requires that the dendrites (the branches on the neurons) which form synapses are appropriately formed as well as that excitatory and inhibitory signals are kept in balance.

When dendritic structure and synaptic signalling are abnormal, virtually all brain activities can be negatively impacted. Synaptic dysfunction has been identified as a core feature of many conditions including acute brain injury, neurodevelopmental disorders and neurodegenerative diseases.

4. Reduced levels of IGF-1

IGF-1 levels in the brain have been reported to be depressed in a number of conditions, which means that the critical role of IGF-1 in maintaining and repairing brain cells and synapses is impaired.

OPERATING REVIEW

CONTINUED

FINANCE

	2020 $'m	2019 $'m
R&D Tax Incentive	0.7	0.5
Interest income	0.1	0.4
Other income (Government cash-flow boost)	0.1	–
Foreign exchange gain	–	0.1
Total income	**0.9**	**1.0**
Research & Development	(7.8)	(9.9)
Corporate & Administration	(1.7)	(1.7)
Foreign exchange loss	(0.6)	–
Loss in fair value of Lanstead settlements	–	(0.2)
(Loss)/Profit after tax	**(9.2)**	**(10.8)**
Cash flow from operations	(8.1)	(11.7)
Cash flow from financing	19.1	1.9
Effect of exchange rates on cash balances	(0.7)	0.1
Cash at 31 December	**24.2**	**13.8**

The loss after tax for 2020 was $9.2 million compared with $10.8 million in 2019. Research and development costs were $2.1 million lower, due to lower expenditure relating to the Rett syndrome Phase 3 trial, partially offset by an increase in expenditure for the NNZ-2591 non-clinical studies, Phase 1 trial and manufacture of the required drug for these and for the planned Phase 2 clinical trials. In addition, foreign exchange losses were $0.6 million compared with a foreign exchange gain of $0.1 million in 2019. This is due to the carrying value in AUD of USD cash held to eliminate exchange risk for USD expenditure falling, as a result of the weakening of the USD against the AUD.

Cash reserves at 31 December 2020 were $24.2 million (2019: $13.8 million), funding Neuren through to achieving Phase 2 results for NNZ-2591 in three indications, while ACADIA fully funds the trofinetide Phase 3 program. Net cash used in operating activities was $8.1 million, compared with $11.7 million in 2019. The decrease of $3.6 million was mainly in payments to other suppliers, due to lower research and development expenditure. Financing provided cash of $19.1 million, received for the issue of new ordinary shares in the capital raise, compared with $1.9 million in 2019 received in the final settlements from the Sharing Agreement with Lanstead Capital.

MANAGEMENT TEAM

Neuren's management team has been together since 2013/14, designing and executing all Neuren's product development programs for Orphan neurodevelopmental disorders, commencing with Rett syndrome.

1. JON PILCHER

Chief Executive Officer

BSc (Hons), FCA

Jon joined Neuren in August 2013 as CFO and was appointed CEO in May 2020. He has played a central role in all aspects of Neuren's R&D, commercial and corporate activities. Before joining Neuren he was a member of the leadership team at Acrux (ASX: ACR) throughout a period that included Acrux's IPO and listing on the ASX, the development and FDA approval of three novel pharmaceutical products and a transforming licensing deal with Eli Lilly in 2010. He formerly spent seven years in a series of executive positions in the R&D and corporate functions of international pharmaceutical groups Medeva and Celltech, which are now part of UCB. Jon is a Chartered Accountant and holds a degree in Biotechnology from the University of Reading in the UK. He is a non-executive director of BTC Health Limited (ASX: BTC).

2. LARRY GLASS

Chief Science Officer

BA (Biology)

Larry joined Neuren in 2004 and was an Executive Director from 2012 to 2018. He directs Neuren's scientific and non-clinical development, as well as playing a leading role in clinical and regulatory strategy. Larry has more than 30 years' experience in the life sciences industry, including clinical trials, basic and applied research, epidemiologic studies, diagnostics and pharmaceutical product development. Before he joined Neuren, he worked as an independent consultant for a number of biotech companies in the US and internationally provided management, strategic and business development services. Prior to that, he was CEO of a contract research organisation that provided preclinical research and clinical trials support for major pharmaceutical and biotechnology companies and the US government. For a number of years, the CRO operated as a subsidiary of a NYSE-listed company and was subsequently sold to a European biopharmaceutical enterprise which was then acquired by Johnson & Johnson. Larry is a biologist with additional graduate training in epidemiology and biostatistics.

3. DR CLIVE BLOWER

Vice President, Product Development

BSc (Hons), PhD

Clive joined Neuren in August 2014, bringing over twenty years of global drug development experience. He has led all aspects of CMC (Chemistry, Manufacturing and Controls) development of both trofinetide and NNZ-2591. Before joining Neuren, Clive was at Acrux (ASX: ACR) for seven years as Director of Product Development and Technical Affairs and then Chief Operating Officer. During this period he led the CMC development of the company's lead product through Phase 3 clinical trials, FDA approval and commercial launch. Clive formerly served in senior management positions at Hospira Inc. (previously Faulding Pharmaceuticals, then Mayne Pharma), including leading the Injectable Drug Development Group. He earned a Doctorate in Chemistry from Monash University in 1992 and has experience in all stages of drug development, from concept to commercialisation, having contributed to the development and launch of more than 25 pharmaceutical products.

MANAGEMENT TEAM

CONTINUED

4. DR NANCY JONES

Vice President, Clinical Development

PhD

Nancy joined Neuren in January 2013. She leads the design and implementation of Neuren's clinical studies in neurodevelopmental disorders. Prior to joining Neuren, Nancy held a senior position at Autism Speaks, the largest science and advocacy organization in the US focused on autism spectrum and related disorders. She was at Autism Speaks for 6 years, directing the overall operations of the Autism Treatment Network, a network of hospitals and medical centers dedicated to improving access to comprehensive, coordinated medical care for individuals with ASD. She also oversaw the Autism Clinical Trials Network, a network developed to promote and expedite clinical trials in ASD, and played a lead role in an initiative to enhance the development of syndrome-specific outcome measures for treatment trials in ASD. Nancy received her Ph.D. in Applied Linguistics from the University of California, Los Angeles where she focused on the neurobiology of language and developmental disorders.

5. JAMES SHAW

Vice President, Clinical & Regulatory Operations

BSc (Hons), MBA

James joined Neuren in August 2013, bringing twenty years of development and commercialisation experience in the Pharmaceutical Industry, having worked for both large Pharma and Clinical Research Organisations. He leads the clinical and regulatory execution of Neuren's programs. Before joining Neuren, James was CEO of a Clinical Research and Site Management Organisation providing full service clinical trial support in ANZ. Prior to that he spent seven years with Quintiles in Sydney and Singapore working across Business Development and Operational leadership roles. James brings a global focus to drug development, having led product teams from Phase 2 through to FDA submission and commercialisation during six years with AstraZeneca at their Global headquarters in the UK.

6. LAUREN FRAZER

Chief Financial Officer & Company Secretary

BBus (Acc), CA

Lauren joined Neuren in March 2020 and brings over fifteen years of experience in accounting and finance. Prior to joining Neuren, Lauren was at Boundary Bend, one of Australia's leading agribusinesses and owner of Australian olive oil brands Cobram Estate and Red Island. Lauren was at Boundary Bend for ten years as Financial Controller and then Senior Manager of Accounting & Tax. Lauren is a Chartered Accountant and began her career with Pitcher Partners.

BOARD

1. PATRICK DAVIES

Non-Executive Chair

B EC, MBA

Patrick joined the Neuren Board in July 2018. He has held executive management roles in the Australian and New Zealand healthcare industry for over twenty five years having performed successfully in senior roles across many industry sectors including pharmacy, primary care, pharmaceutical and consumer products. During his ten year period as Chief Executive Officer of EBOS Group Limited (and previously Symbion), the enterprise value of the group achieved compound annual growth in enterprise value of +20% (from circa $450M to in excess of $3.1B). He is a director on other corporate boards and provides strategic advice to a range of healthcare businesses and investors.

2. DR TREVOR SCOTT

Non-Executive Director

MNZM, LLD (Hon), BCom, FCA, FNZIM, DF Inst D

Trevor joined the Neuren Board in March 2002. He is the founder of T.D. Scott and Co., an accountancy and consulting firm, which he formed in 1988. He is an experienced advisor to companies across a variety of industries. Trevor serves on numerous corporate boards and is chairman of several.

3. DIANNE ANGUS

Non-Executive Director

BSc (Hons), Master of Biotechnology, IPTA

Dianne joined the Neuren Board in July 2018. She has worked as a senior executive and non-executive director within the biotechnology, biopharmaceutical and agritech industries for over twenty-five years. She has created numerous global industry partnerships which include Prana Biotechnology, Gerolymatos International, Florigene, Suntory & Monsanto to yield novel and competitive medical, pharmaceutical and agricultural products. Dianne has successfully forged strong partnerships with key medical opinion leaders to create innovative clinical research programs and driven the development path for novel neurological pre-clinical agents to late-stage clinical assets before the FDA and European regulators. With over fifteen years' experience in an ASX and NASDAQ listed company, she has expertise in business development, capital raising, investor relations, regulatory affairs and intellectual property, together with corporate governance and compliance capabilities. Dianne holds a Masters degree in biotechnology and is a registered patent attorney.

4. DR JENNY HARRY

Non-Executive Director

BSc (Hons), PhD

Jenny joined the Neuren Board in 2018. She has 20 years' experience in executive management of companies in the biotechnology and biopharmaceutical sectors. As CEO and Managing Director of Tyrian Diagnostics, Jenny transformed the company from an R&D business to a diagnostics company and oversaw development of the company's first products through to commercialisation and early revenue generation. She is a graduate of the Harvard Business School General Manager Program and the Australian Institute of Company Directors. Jenny is currently a Non-Executive Director on the boards of Aeris Environmental Ltd (ASX:AEI) and Ondek Pty Ltd.

CORPORATE GOVERNANCE

Neuren's board of directors ("Board") aims to ensure that the Company and its subsidiaries (the "Group") operates with a corporate governance framework and practices that promote an appropriate governance culture throughout the organisation and that are relevant, practical and cost-effective for the current size and stage of development of the business.

This Statement provides a description of the framework and practices, laid out under the structure of the ASX Listing Rules and the Corporate Governance Principles (the "Principles") and Recommendations (the "Recommendations") 4th Edition. This edition takes effect for the Group's full financial year commencing on 1 January 2020.

PRINCIPLE 1. LAY SOLID FOUNDATIONS FOR MANAGEMENT AND OVERSIGHT

The Board is responsible for the overall corporate governance of the Group. The Board acts on behalf of and is accountable to the shareholders. The Board seeks to identify the expectations of shareholders as well as other regulatory and ethical expectations and obligations. The Board is responsible for identifying areas of significant business risk and ensuring mechanisms are in place to manage those risks adequately. In addition, the Board sets the overall strategic goals and objectives, and monitors achievement of goals.

The Board appoints the principal executive officer, currently the Chief Executive Officer. The Board has delegated the responsibility for the operation and administration of the Group to the Chief Executive Officer and senior management. The Board ensures that the management team is appropriately qualified to discharge its responsibilities.

The Board ensures management's objectives and activities are aligned with the expectations and risks identified by the Board through a number of mechanisms including the following:

- establishment of the overall strategic direction and leadership of the Group;
- approving and monitoring the implementation by management of the Group's strategic plan to achieve those objectives;
- reviewing performance against its stated objectives, by receiving regular management reports on business situation, opportunities and risks;
- monitoring and review of the Group's controls and systems including those concerned with regulatory matters to ensure statutory compliance and the highest ethical standards; and
- review and adoption of budgets and forecasts and monitoring the results against stated targets.

The Board sets the corporate strategy and financial targets with the aim of creating long-term value for shareholders.

In accordance with Recommendation 1.2, the Board undertakes appropriate checks before appointing a new director, or putting forward to shareholders a candidate for election and provides shareholders with all material information in its possession relevant to a decision on whether or not to elect or re-elect a director.

The Group has a written agreement with each director and senior executive, setting out the terms of their appointment, in accordance with Recommendation 1.3. The Company Secretary is accountable directly to the Board on all matters to do with the proper functioning of the Board, in accordance with Recommendation 1.4.

At this stage of the Group's development, considering the very small size of the workforce and the specialist nature of most positions, the Board has chosen not to establish a formal diversity policy or formal objectives for gender diversity, as recommended in Recommendation 1.5. The Group does not discriminate on the basis of age, ethnicity, religion, gender or sexuality and when a position becomes vacant the Group seeks to employ the best candidate available for the position. Currently there are two male and two female directors. Two of the six senior executives are female. The Group currently has seven employees and consultants, of which three are female.

In accordance with Recommendation 1.6, there is a process to evaluate periodically the performance of the Board, its committees and individual directors. Each director completes a quantitative evaluation questionnaire and is able to provide qualitative comments. The Company Secretary collates the responses and reports back to the board for discussion. A performance evaluation was undertaken during 2020.

In accordance with Recommendation 1.7, there is a process for the Board to evaluate periodically the performance of the Chief Executive Officer and for the Chief Executive Officer to evaluate periodically the performance of senior executives. The evaluation of the Non-Executive Chair is part of the board performance evaluation process. For the evaluation of senior executives, an individual discussion is held after each senior executive complete a qualitative questionnaire, covering past individual and team achievements and challenges, as well as forward-looking outcomes and areas of personal focus. Performance evaluations were not undertaken during 2020, however have been undertaken since the end of the financial year.

CORPORATE GOVERNANCE

CONTINUED

PRINCIPLE 2. STRUCTURE THE BOARD TO BE EFFECTIVE AND ADD VALUE

The Board has not considered it necessary or value-adding to establish a separate Nomination Committee (Recommendation 2.1). The selection, appointment and retirement of directors is considered by the full Board, within the framework of the skills matrix described below. The Board may also engage an external consultant where appropriate to identify and assess suitable candidates who meet the Board's specifications. The composition of the board is discussed regularly and each director may propose changes for discussion.

In accordance with Recommendation 2.2, the Company has a skills matrix setting out the mix of skills that the Board is looking to achieve in its membership. The matrix is summarised in the table below.

Skill	Requirements Overview
Professional Director Skills	
Risk & Compliance	Identify key risks to the organisation related to each key area of operations. Ability to monitor risk and compliance and knowledge of legal and regulatory requirements.
Financial & Audit	Experience in accounting and finance to analyze statements, assess financial viability, contribute to financial planning, oversee budgets and oversee funding arrangements.
Strategy	Ability to identify and critically assess strategic opportunities and threats to the organization. Develop strategies in context to our policies and business objectives.
Policy Development	Ability to identify key issues for the organisation and develop appropriate policy parameters within which the organization should operate.
Executive Management	Experience in evaluating performance of senior management, and oversee strategic human capital planning.
Previous Board Experience	The board's directors should have director experience and have completed formal training in governance and risk.
Industry Specific Skills	
Pharmaceutical product development	Experience in and/or understanding of the issues in clinical development, interactions with international regulators and/or CMC development.
International pharmaceutical commercialisation	Experience in and/or understanding of the issues in entering international pharmaceutical markets, including pricing, distribution and exclusivity.
Pharmaceutical partnering	Experience in and/or understanding of the issues in partnering transactions and/or relevant contacts in international pharma companies.
Risk capital management	Experience in raising funding from equity markets and/or relevant contacts in relevant funds and/or investment banks.
Intellectual property	Understanding of the importance and value of market exclusivity and the various ways of protecting it across different jurisdictions, including patents and data exclusivity.
Interpersonal Skills	
Leadership	Make decisions and take necessary actions in the best interest of the organisation, and represent the organisation favorably. Analyze issues and contribute at board level to solutions. Recognise the role of the board versus the role of management.
Ethics and Integrity	Understand role as director and continue to self educate on legal responsibility, ability to maintain board confidentiality, declare any conflicts.
Contribution	Ability to constructively contribute to board discussions and communicate effectively with management and other directors.
Crisis Management	Ability to constructively manage crises, provide leadership around solutions and contribute to communications strategy with stakeholders.

CORPORATE GOVERNANCE

CONTINUED

The Board is highly engaged in the oversight and direction of the business. Five members served during the year to 31 December 2020, as set out in the table below. Details of the relevant skills, experience and expertise of each Board member are set out on page 20 of this report.

	Appointment	Retirement	Role	Independent	Committees
Patrick Davies	Appointment as director: 2018 Appointment as Chair: 26 May 2020		Non-executive chair	Yes	Member of Audit Committee and Remuneration Committee
Trevor Scott[1]	2002		Non-executive director	Yes	Chair of Audit Committee and member of Remuneration Committee
Dianne Angus	2018		Non-executive director	Yes	Member of Audit Committee and Remuneration Committee
Jenny Harry[1]	2018		Non-executive director	Yes	Member of Audit Committee and Chair of Remuneration Committee
Richard Treagus	2013	26 May 2020	Executive Chairman	No[2]	

[1] Jenny Harry replaced Trevor Scott as Chair of Remuneration Committee effective 1 December 2020.
[2] Richard Treagus was not considered independent due to his executive role.

There is a majority of independent directors in accordance with Recommendation 2.4. The chair has been independent and the chair and chief executive officer roles have been separate (Recommendation 2.5) since the appointment of Patrick Davies as Non-Executive Chair and Jon Pilcher as CEO on 26 May 2020 following Richard Treagus' retirement from the Board. The directors believe that the structure and membership profile of the Board has provided and continues to provide the maximum value to the business at its stage of its development.

In accordance with Recommendation 2.6, the Company has a program for inducting new directors and provides appropriate professional development opportunities for directors to develop and maintain the skills and knowledge needed to perform their role as directors effectively.

PRINCIPLE 3. INSTIL A CULTURE OF ACTING LAWFULLY, ETHICALLY AND RESPONSIBLYG

In accordance with Recommendation 3.1, the Group has articulated its values, which are disclosed on the Company website

- We are passionate about making a difference to the lives of patients and their families
- We aim to earn the respect of everyone we deal with
- We are determined and creative to break through barriers
- We harness the power of collaboration and different perspectives
- We recognise the importance of all stakeholders and endeavour to use financial resources efficiently

The Board has established a Code of Conduct (Recommendation 3.2), which requires that Board members and executives:

- will act honestly, in good faith and in the best interests of the whole Company
- owe a fiduciary duty to the Company as a whole
- have a duty to use due care and diligence in fulfilling the functions of office and exercising the powers attached to that office
- will undertake diligent analysis of all proposals placed before the Board
- will act with a level of skill expected from Directors and key executives of a publicly listed Company
- will use the powers of office for a proper purpose, in the best interests of the Company as a whole
- will demonstrate commercial reasonableness in decision-making
- will not make improper use of information acquired as Directors and key executives

CORPORATE GOVERNANCE

CONTINUED

- will not disclose non-public information except where disclosure is authorised or legally mandated
- will keep confidential information received in the course of the exercise of their duties and such information remains the property of the Company from which it was obtained and it is improper to disclose it, or allow it to be disclosed, unless that disclosure has been authorised by the person from whom the information is provided, or required by law
- will not take improper advantage of the position of Director or use the position for personal gain or to compete with the Company
- will not take advantage of Company property or use such property for personal gain or to compete with the Company
- will protect and ensure the efficient use of the Company's assets for legitimate business purposes
- will not allow personal interests, or the interest of any associated person, to conflict with the interests of the Company
- have an obligation to be independent in judgement and actions and Directors will take all reasonable steps to be satisfied as to the soundness of all decisions of the Board
- will make reasonable enquiries to ensure that the Company is operating efficiently, effectively and legally, towards achieving its goals
- will not engage in conduct likely to bring discredit upon the Company
- will encourage fair dealing by all employees with the Company's customers, suppliers, competitors and other employees
- will encourage the reporting of unlawful/unethical behaviour and actively promote ethical behaviour and protection for those who report violations in good faith
- will give their specific expertise generously to the Company
- have an obligation, at all times, to comply with the spirit, as well as the letter of the law and with the principles of this Code of Conduct

Neuren is committed to the highest standards of conduct and ethical behaviour in all business activities. The Group's Whistleblower Policy was approved by the Board in October 2020, and is available on the Company webiste (Recommendation 3.3). Any material breaches of the Whistleblower Policy are to be reported to the Board.

The Group's Anti-bribery and Corruption Policy was approved by the Board in October 2020, and is available on the Company website (Recommendation 3.4). Any material breaches of the Anti-bribery and Corruption Policy are to be reported to the Board.

PRINCIPLE 4. SAFEGUARD INTEGRITY OF CORPORATE REPORTS

The Board has an Audit Committee, which consists of only independent non-executive directors, has at least 3 members and is chaired by an independent director as suggested in Recommendation 4.1. The Committee met twice during 2020, attended by all members.

The Committee operates under a charter approved by the Board, a summary of which is available on the Neuren website. It is responsible for undertaking a broad review of, ensuring compliance with, and making recommendations in respect of, the Group's internal financial controls and legal compliance obligations. In respect of financial reporting, it is also responsible for:

- review of audit assessment of the adequacy and effectiveness of internal controls over the Company's accounting and financial reporting systems, including controls over computerised systems;
- review of the audit plans and recommendations of the external auditors;
- evaluating the extent to which the planned scope of the audit can be relied upon to detect weaknesses in internal control, fraud and other illegal acts;
- review of the results of audits, any changes in accounting practices or policies and subsequent effects on the financial statements and make recommendations to management where necessary and appropriate;
- review of the performance and fees of the external auditor;
- audit of legal compliance including trade practices, corporations law, occupational health and safety and environmental statutory compliance , and compliance with the Listing Rules of the ASX;
- supervision of special investigations when requested by the Board;

In undertaking these tasks the Audit Committee meets separately with management and external auditors where required.

In accordance with Recommendation 4.2, the Board also, before it approves the entity's financial statements for a financial period, receives a declaration in writing from the Chief Executive Officer and the Chief Financial Officer that the financial records of the company have been properly maintained and that the financial statements are in accordance with New Zealand Equivalents to International

CORPORATE GOVERNANCE

CONTINUED

Financial Reporting Standards (NZ FRS) and present a true and fair view, in all material respects, of the Group's financial position and performance and that this opinion is founded on a sound system of risk management and internal control that is operating effectively in all material respects with regard to business and financial reporting risks. The Board received those assurances for the annual financial statements on 23 February 2021.

For other periodic corporate reports released to the market that are not audited or reviewed by an external auditor, processes are in place to ensure that the reports are materially accurate, balanced and provide investors with appropriate information to make informed investment decisions (Recommendation 4.3). Reports are prepared by the Chief Financial Officer and reviewed by the Chief Executive Officer, or are prepared by the Chief Executive Officer and reviewed by the Board. The Board receives a declaration in writing from the Chief Financial Officer and Chief Executive Officer regarding the quarterly cash flow reports.

PRINCIPLE 5. MAKE TIMELY AND BALANCED DISCLOSURE

Neuren is required to comply with the continuous disclosure requirements as set out in the ASX Listing Rules, disclosing to the ASX any information that a reasonable person would expect to have a material effect on the price or value of Neuren's securities, unless certain exemptions from the obligation to disclose apply.

In accordance with Recommendation 5.1, the Board has approved policies and procedures to ensure that it complies with its disclosure obligations and that disclosure is timely, factual, clear and objective. The Board has designated the company secretary as the person primarily responsible for implementing and monitoring those policies and procedures. A summary of the policies and procedures is available on the Neuren website. All information disclosed to the ASX is placed on the Neuren website after it has been published by the ASX, and the Board receives copies of all material market announcements promptly after they have been made (Recommendation 5.2).

All substantive investor or analyst presentation are released on the ASX Market Announcements Platform ahead of such presentations, in accordance with Recommendation 5.3.

PRINCIPLE 6. RESPECT THE RIGHTS OF SECURITY HOLDERS

The Board strives to communicate effectively with shareholders, give them ready access to balanced and understandable information about the business and make it easy for them to participate in shareholder meetings.

In accordance with Recommendation 6.1, comprehensive information about the Company and its governance is provided via the website www.neurenpharma.com. This includes information about the Board and senior executives, as well as corporate governance policies. All announcements, presentations, financial information and meetings materials disclosed to the ASX are placed on the website, so that current and historical information can be accessed readily.

The Company's investor relations program facilitates effective two-way communication with investors (Recommendation 6.2). Supported by the Non-Executive Chair, the Chief Executive Officer interacts with institutional investors, private investors, analysts and media on an ad hoc basis, conducting meetings in person or by teleconference and responding personally to enquiries.

The Board seeks practical and cost-effective ways to promote informed participation at shareholder meetings (Recommendation 6.3). This includes providing access to clear and comprehensive meeting materials and electronic proxy voting. The Annual Shareholders' Meeting in 2020 was conducted as a virtual meeting, with participation by electronic means.

All resolutions at the Company's Annual Shareholders' Meeting in 2020 were decided by a poll (Recommendation 6.4)

In accordance with Recommendation 6.5, shareholders are provided with and encouraged to use electronic methods to communicate with the Company and with the share registry.

PRINCIPLE 7. RECOGNISE AND MANAGE RISK

The Board has established policies for the oversight and management of material business risks, a summary of which is available on the Neuren website. The Board does not have a separate committee to oversee risk, judging that the whole Board is better able to conduct that function efficiently and effectively, given the small size of the Board and the specialised nature of the business (Recommendation 7.1).

CORPORATE GOVERNANCE

CONTINUED

In accordance with Recommendation 7.2, the Board reviews the Group's risk management framework at least annually to satisfy itself that it continues to be sound. A review was conducted in 2020.

The size and complexity of the Group's business is not sufficient to warrant an internal audit function (Recommendation 7.3). The risk management policy is designed to involve the entire organisation in risk management and to ensure that the effectiveness of the risk management and internal control processes are continually improved.

The Group does not have a material exposure to economic, environmental or social sustainability risks (Recommendation 7.4).

PRINCIPLE 8. REMUNERATE FAIRLY AND RESPONSIBLY

Neuren believes having highly skilled and motivated people will allow the organisation to best pursue its mission and achieve its goals for the benefit of shareholders and stakeholders more broadly. The ability to attract and retain the best people is critical to the Company's future success. The Board believes remuneration policies are a key part of ensuring this success.

The Board has a Remuneration Committee, which consists of only independent non-executive directors, has at least three members and is chaired by an independent director as suggested in Recommendation 8.1. The Committee met once during 2020.

The Committee operates under a charter approved by the Board, a summary of which is available on the Neuren website. It is responsible for undertaking a broad review of, ensuring compliance with, and making recommendations in respect of, the Group's remuneration policies. It is also responsible for:

- setting and reviewing compensation policies and practices of the Company;
- setting and reviewing all elements of remuneration of the directors and members of the executive team; and
- setting and reviewing long term incentive plans for employees and/or directors.

In undertaking these tasks the Remuneration Committee meets separately with management where required.

The Group's remuneration policies and practices are summarised below, in accordance with Recommendation 8.2.

The Remuneration Committee assesses the appropriateness of the nature and amount of remuneration of executive directors and senior executives on a regular basis by reference to relevant employment market conditions, with the overall objective of ensuring maximum shareholder benefit from the retention of a high quality executive team. To assist in achieving these objectives, the nature and amount of executive remuneration is linked to the Company's performance. Remuneration consists of fixed cash remuneration, including superannuation contributions required by law, and equity-based remuneration. Fixed cash remuneration takes into account labour market conditions, as well as the scale and nature of the Group's business. Equity-based remuneration is provided by participation in a share option plan, a loan funded share plan and equity performance rights. These are designed to ensure that key executives are aligned with shareholders through an interest in the long-term growth and value of the Company. Senior executive service agreements generally include a requirement for 3 months' notice of termination by the executive or the Group. There are no other termination payments. Termination for misconduct does not require notice or payment.

Remuneration of non-executive directors comprises fixed cash fees only. The fees are determined by the Board within the aggregate limit for directors' fees approved by shareholders. Non-executive directors on payroll receive retirement benefits as part of their fixed fee. All other non-executive directors receive no retirement benefits.

Participants in equity based remuneration schemes are not permitted to enter into transactions which limit the economic risk of participating in the scheme (Recommendation 8.3).

PRINCIPLE 9. ADDITIONAL RECOMMENDATIONS

Neuren is incorporated in New Zealand and ensures meetings of security holders are held at a reasonable place and time (Recommendation 9.2).

Since Neuren is incorporated in New Zealand and applies New Zealand financial reporting standards, its auditor is located in New Zealand. The Board has considered it impractical and an unnecessary expense for the auditor to travel to Australia to attend the annual general meeting, as suggested in Recommendation 9.3. The Company's constitution enables the Board to convene virtual shareholder meetings, with participation by electronic means.

FINANCIAL REPORT

FOR THE YEAR ENDED 31 DECEMBER 2020

DIRECTORS' REPORT

PRINCIPAL ACTIVITIES

Neuren Pharmaceuticals Limited (Neuren or the Company, and its subsidiaries, or the Group) is a publicly listed biopharmaceutical company developing drugs for neurological disorders.

REVIEW OF OPERATIONS

Neuren is developing two new therapies to treat multiple neurodevelopmental disorders that emerge in early childhood and are characterized by impaired connection and signalling between brain cells. No approved therapies are currently available for these seriously debilitating disorders. Neuren's potential therapies utilize synthetic analogs of peptides that occur naturally in the brain.

Trofinetide is currently in a Phase 3 clinical trial in the United States 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 (FDA) and Orphan Drug designation in both the United States and the European Union. Neuren has granted an exclusive license to ACADIA Pharmaceuticals Inc. (ACADIA) for the development and commercialization of trofinetide in North America, whilst retaining all rights outside North America. ACADIA is a NASDAQ listed company (ACAD) that specialises in commercialising and developing breakthroughs in neuroscience.

Neuren is preparing for Phase 2 clinical trials of its second drug candidate NNZ-2591 for Phelan-McDermid syndrome, Angelman syndrome and Pitt Hopkins syndrome. Based on its mechanism of action and positive results in animal models, NNZ-2591 has received Orphan Drug designation in both the United States and the European Union for each of these disorders. Neuren also recently announced that Prader-Willi syndrome has been added to the NNZ-2591 development pipeline following highly encouraging results in a pre-clinical model of the syndrome.

During the year ended 31 December 2020, significant progress was made in the development programs.

ACADIA commenced the Rett syndrome Phase 3 program in October 2019. The program involves treatment of approximately 180 females aged 5 to 20 with trofinetide or placebo for 12 weeks to evaluate efficacy and safety (the "LAVENDER" study), following which patients are eligible to continue treatment with trofinetide for 40 weeks to provide longer-term safety data (the "LILAC" study). Top-line results from the LAVENDER study are expected in the second half of 2021. Positive results potentially will enable a New Drug Application, which should be eligible for "Priority Review" by the FDA in an abbreviated period of 6 months. ACADIA has also established "LILAC-2" under which eligible patients who complete LAVENDER and LILAC will be able to continue to receive trofinetide during the period before marketing approval. Enrolment of new patients in LAVENDER was paused temporarily from March 2020 to June 2020, due to the initial measures taken in the US to combat the COVID-19 pandemic.

In March 2020, the FDA granted Rare Pediatric Disease (RPD) designation to trofinetide for the treatment of Rett syndrome. Upon FDA approval of a product with RPD designation, the sponsor may be eligible to receive a Priority Review Voucher, which can be used to obtain FDA review of a New Drug Application for another product in an expedited period of six months. The voucher may also be sold for use by another company. Under the terms of the Licence Agreement between Neuren and ACADIA, Neuren will receive from ACADIA one third of the market value of a Priority Review Voucher. In January 2021, a voucher was sold for US$100 million.

In April 2020 a new patent was granted by the Israel Patent Office covering trofinetide to treat Rett syndrome, Fragile X syndrome and autism. This first patent for trofinetide in Israel expires in 2032, with the potential for patent term extension of up to 5 years.

Neuren commenced its first clinical trial of NNZ-2591 in May 2020. The Phase 1 trial, conducted in Australia, generated information on the safety, tolerability and pharmacokinetics in healthy adult volunteers to inform the safety and efficacy assessment in patients for the Phase 2 trials. Twice daily oral dosing for 7 days was safe and well tolerated at all dose levels tested. There were no Serious Adverse Events or clinically significant findings from safety lab tests, vital signs or cardiac tests.

In parallel with completing the Phase 1 trial, Neuren initiated the manufacture of NNZ-2591 to supply the planned Phase 2 clinical trials, whilst also completing a program of non-clinical studies for NNZ-2591. Neuren is preparing to meet with the US Food and Drug Administration (FDA) and then submit Investigational New Drug (IND) applications in the first half of 2021. The IND's will incorporate data from manufacturing, non-clinical studies and the Phase 1 clinical trial, as well as the Phase 2 trial protocols.

In December 2020, Neuren received notice from the European Medicines Agency (EMA) of positive opinions for all three Orphan designation applications that were submitted for NNZ-2591 in Phelan-McDermid syndrome, Angelman syndrome and Pitt Hopkins syndrome. Orphan designation in the EU enables sponsors to benefit from incentives including free protocol assistance, fee reductions and 10 years of market exclusivity plus two additional years if approved for paediatric use.

In May 2020 Neuren announced the appointment of Jon Pilcher and Patrick Davies as Chief Executive Officer and non-executive Chair respectively, with Richard Treagus standing down after more than 7 years as Executive

DIRECTORS' REPORT

CONTINUED

Chairman to enable him to focus on his other business interests.

There are three large value-drivers for Neuren that may potentially crystallise in 2021 and 2022:

- ACADIA's Rett syndrome Phase 3 results and New Drug Application for trofinetide in the US;
- Selecting the optimum commercial outcome for trofinetide in Europe and Asia using the US regulatory package; and
- Phase 2 clinical results for NNZ-2591 to confirm the positive effects seen in the animal models of all three indications.

The consolidated financial statements are presented on pages 32 to 35. All amounts in the Financial Statements are shown in Australian dollars unless otherwise stated.

The Group's loss after tax attributable to equity holders of the Company for the year ended 31 December 2020 was $9.2 million compared with the Group's loss after tax of $10.8 million in 2019. This was mainly due to research and development costs which were $2.1 million lower, due to lower expenditure for manufacturing and non-clinical activities relating to the Rett Phase 3 trial, partially offset by an increase in expenditure in 2020 for the NNZ-2591 non-clinical studies, Phase 1 trial and manufacture of the required drug for these and for the planned Phase 2 clinical trials. In addition, foreign exchange losses were $0.6 million compared with a foreign exchange gain of $0.1 million in 2019. This is due to the carrying value in AUD of USD cash held to eliminate exchange risk for USD expenditure falling, as a result of the weakening of the USD against the AUD. Prudent control of expenditure continues to be an important principle in the Group's operations and financing.

The basic loss per share for 2020 was $0.086 (2019: earnings of $0.108 per share), based on a weighted average number of shares outstanding of 107,057,317 (2019: 100,168,413).

Cash reserves at 31 December 2020 were $24.2 million (2019: $13.8 million). Net cash used in operating activities was $8.1 million (2019: $11.7 million). The decrease of $3.6 million was mainly in payments to other suppliers, due to lower research and development expenditure. Financing provided cash of $19.1 million, received for the issue of new ordinary shares in the capital raise, compared with $1.9 million in 2019 received in the final settlements from the Sharing Agreement with Lanstead Capital.

On 29 June 2020, the Group announced the successful completion of a capital raise of $20 million, with $19 million net of costs received after 30 June 2020. On 6 July 2020, the Group issued 14,285,723 fully paid ordinary shares at an issue price of $1.40 per share to institutional and sophisticated investors in Australia, New Zealand, Hong Kong and the United Kingdom. The funds raised enabled the Group to fund plans to generate valuable Phase 2 clinical trial data for NNZ-2591.

No dividends were paid in the year, or in the prior year and the Directors recommend none for the year.

DIRECTORS

Patrick Davies B EC, MBA (Non-Executive Chair)

Patrick joined the Neuren Board in July 2018. He has held executive management roles in the Australian and New Zealand healthcare industry for over twenty five years having performed successfully in senior roles across many industry sectors including pharmacy, primary care, pharmaceutical and consumer products. During his ten year period as Chief Executive Officer of EBOS Group Limited (and previously Symbion), the enterprise value of the group achieved compound annual growth in enterprise value of +20% (from circa $450M to in excess of $3.1B). He is a director on other corporate boards and provides strategic advice to a range of healthcare businesses and investors.

Dr Trevor Scott, MNZM, LLD (Hon), BCom, FCA, FNZIM, DF Inst D (Non-Executive Director)

Trevor joined the Neuren Board in March 2002. He is the founder of T.D. Scott and Co., an accountancy and consulting firm, which he formed in 1988. He is an experienced advisor to companies across a variety of industries. Trevor serves on numerous corporate boards and is chairman of several.

Dianne Angus BSc (Hons), Master of Biotechnology, IPTA (Non-Executive Director)

Dianne joined the Neuren Board in July 2018. She has worked as a senior executive and non-executive director within the biotechnology, biopharmaceutical and agritech industries for over twenty-five years. She has created numerous global industry partnerships which include Prana Biotechnology, Gerolymatos International, Florigene, Suntory & Monsanto to yield novel and competitive medical, pharmaceutical and agricultural products. Dianne has successfully forged strong partnerships with key medical opinion leaders to create innovative clinical research programs and driven the development path for novel neurological pre-clinical agents to late-stage clinical assets before the FDA and European regulators. With over fifteen years' experience in an ASX and NASDAQ listed company, she has expertise in business development, capital raising, investor relations, regulatory affairs and intellectual property, together with corporate governance and compliance capabilities. Dianne holds a Masters degree in biotechnology and is a registered patent attorney.

DIRECTORS' REPORT

CONTINUED

Dr Jenny Harry BSc (Hons), PhD (Non-Executive Director)

Jenny joined the Neuren Board in 2018. She has 20 years' experience in executive management of companies in the biotechnology and biopharmaceutical sectors. As CEO and Managing Director of Tyrian Diagnostics, Jenny transformed the company from an R&D business to a diagnostics company and oversaw development of the company's first products through to commercialisation and early revenue generation. She is a graduate of the Harvard Business School General Manager Program and the Australian Institute of Company Directors. Jenny is currently Chair of QUT Enterprise Holdings and a non-executive director on the boards of Ondek Pty Ltd, QUTbluebox and Creative Enterprise Australia.

INTERESTS REGISTER

The Company is required to maintain an interests register in which particulars of certain transactions and matters involving Directors must be recorded. Details of the entries in this register for each of the Directors during and since the end of 2020 are as follows:

Director	Ordinary Shares Purchased/(Sold)	Consideration Paid/(Received)	Date of Transaction
Dr Trevor Scott	(400,000)[1]	Nil	11 Aug 2020
Patrick Davies	5,911	$6,560	19 Mar 2020
Patrick Davies	45,455	$52,046	25 Mar 2020
Patrick Davies	28,655	$50,719	28 May 2020
Patrick Davies	21,428	$30,000	07 Aug 2020
Patrick Davies	35,211	$50,175	17 Feb 2021
Dr Jenny Harry	5,823	$9,955	29 May 2020

1 Off-market distribution of shares from family trust at nil consideration to adult beneficiaries of the trust, who still hold those shares.

INFORMATION USED BY DIRECTORS

During the year the Board received no notices from Directors of the Company requesting to use Company information received in their capacity as Directors, which would not otherwise have been available to them.

INDEMNIFICATION AND INSURANCE OF DIRECTORS AND OFFICERS

Neuren has entered into a deed of indemnity, insurance and access with Directors and Officers, which provides that Directors and Officers generally will incur no monetary loss as a result of actions undertaken by them as Directors and Officers. The indemnity does not cover criminal liability or liability in respect of a breach of a director's duty to act in good faith and in what the director believes to be the best interests of the Company or a breach of any fiduciary duty owed to the Company or a subsidiary.

DONATIONS

No donations were made by the Company or its subsidiary companies during the year (2019: $nil).

REMUNERATION OF DIRECTORS

Remuneration of the Directors is shown in the table below.

Remuneration of Directors	2020 $'000	2019 $'000
Patrick Davies	95	60
Dr Richard Treagus (resigned May 2020)	146	360
Dr Trevor Scott	72	72
Dianne Angus	60	60
Dr Jenny Harry	60	60

DIRECTORS' REPORT

CONTINUED

EXECUTIVE REMUNERATION

The number of employees, not being directors of the Company, who received remuneration and benefits in their capacity as employees totalling NZ $100,000 or more during the year, shown in bands denominated in Australian dollars, was as follows:

Excluding shared based payments	2020 $'000	2019 $'000
$100,000 – $109,999	1	–
$240,000 – $249,999	–	1
$250,000 – $259,999	1	–
$270,000 – $279,999	–	1
$280,000 – $289,999	1	1
$340,000 – $349,999	1	–

Including shared based payments	2020 $'000	2019 $'000
$100,000 – $109,999	1	–
$240,000 – $249,999	–	1
$270,000 – $279,999	–	1
$280,000 – $289,999	–	1
$350,000 – $359,999	1	–
$380,000 – $389,999	1	–
$540,000 – $549,999	1	–

AUDITORS

Grant Thornton New Zealand Audit Limited ('Grant Thornton') is the independent auditor of the Company. Audit fees in relation to the annual and interim financial statements were $57,759 (2019: $59,649). Grant Thornton did not receive any other fees in relation to other financial advice and services. No amounts were payable to an auditor by subsidiary companies in 2020 or 2019.

For and on behalf of the Board of Directors who authorised the issue of these consolidated financial statements on 23 February 2021.

Patrick Davies
Non-Executive Chair

Dr Trevor Scott
Director

CONSOLIDATED STATEMENT OF COMPREHENSIVE INCOME

FOR THE YEAR ENDED 31 DECEMBER 2020

	Note	2020 $'000	2019 $'000
Interest		147	389
Foreign exchange gain		–	132
Australian R&D Tax Incentive		717	495
Other income		100	–
Total income		964	1,016
Research and development costs		(7,763)	(9,858)
Corporate and administrative costs		(1,763)	(1,713)
Foreign exchange loss		(631)	–
Losses on financial assets measured at fair value through profit or loss		–	(261)
Loss before income tax		(9,193)	(10,816)
Income tax	5	–	–
Loss after income tax		(9,193)	(10,816)
Other comprehensive loss, net of tax			
Amounts which may be subsequently reclassified to profit or loss:			
Exchange differences on translation of foreign operations		11	(6)
Total comprehensive loss for the year		(9,182)	(10,822)
Loss after tax attributable to Equity holders of the Company:		(9,193)	(10,816)
Total comprehensive loss attributable to Equity holders of the Company:		(9,182)	(10,822)
Basic loss per share	6	($0.086)	($0.108)
Diluted loss per share	6	($0.086)	($0.108)

The notes on pages 36 to 49 form part of these consolidated financial statements

CONSOLIDATED STATEMENT OF FINANCIAL POSITION

AS AT 31 DECEMBER 2020

	Note	2020 $'000	2019 $'000
ASSETS			
Current Assets:			
Cash and cash equivalents	7	24,188	13,844
Trade and other receivables	8	755	552
Total current assets		24,943	14,396
Non-current assets:			
Property, plant and equipment		10	10
Total non-current assets		10	10
TOTAL ASSETS		24,953	14,406
LIABILITIES AND EQUITY			
Current liabilities:			
Trade and other payables	9	753	559
Total current liabilities		753	559
Total liabilities		753	559
EQUITY			
Share capital	10	145,567	126,426
Other reserves		(10,284)	(8,503)
Accumulated deficit		(111,083)	(104,076)
Total equity attributable to equity holders		24,200	13,847
TOTAL LIABILITIES AND EQUITY		24,953	14,406

The notes on pages 36 to 49 form part of these consolidated financial statements

CONSOLIDATED STATEMENT OF CHANGES IN EQUITY

FOR THE YEAR ENDED 31 DECEMBER 2020

	Share Capital $'000	Share Option Reserve $'000	Currency Translation Reserve $'000	Accumulated Deficit $'000	Total Equity $'000
Equity as at 1 January 2019	126,426	2,186	(10,683)	(93,260)	24,669
Loss after income tax				(10,816)	(10,816)
Other comprehensive loss			(6)		(6)
Total Comprehensive income for the year	–	–	(6)	(10,816)	(10,822)
Equity as at 31 December 2019	126,426	2,186	(10,689)	(104,076)	13,847
Shares issued in capital raising	20,000				20,000
Shares issued in share purchase plan	216				216
Share issue costs expensed	(1,075)				(1,075)
Transfer on expiry of options		(2,186)		2,186	–
Share based payments		394			394
Transactions with owners	19,141	(1,792)	–	2,186	19,535
Loss after income tax				(9,193)	(9,193)
Other comprehensive loss			11		11
Total Comprehensive loss for the year			11	(9,193)	(9,182)
Equity as at 31 December 2020	145,567	394	(10,678)	(111,083)	24,200

The notes on pages 36 to 49 form part of these consolidated financial statements

CONSOLIDATED STATEMENT OF CASH FLOWS

FOR THE YEAR ENDED 31 DECEMBER 2020

	Note	2020 $'000	2019 $'000
Cash flows from operating activities:			
Receipts from Australian R&D Tax Incentive		491	450
Interest received		164	413
GST refunded		283	102
Receipts from government cash flow boost		100	–
Payments for employees and directors		(1,480)	(1,742)
Payments to other suppliers		(7,636)	(10,942)
Net cash flow used in operating activities		(8,078)	(11,719)
Cash flows from investing activities:			
Purchase of property, plant and equipment		(6)	(12)
Net cash used in investing activities		(6)	(12)
Cash flows from financing activities:			
Proceeds from the issue of shares	10	20,216	1,860
Payment of share issue expenses		(1,075)	–
Net cash provided from financing activities		19,141	1,860
Net increase / (decrease) in cash		11,057	(9,871)
Effect of exchange rate changes on cash balances		(713)	139
Cash and cash equivalents at the beginning of the year		13,844	23,576
Cash and cash equivalents at the end of the year		24,188	13,844
Reconciliation with loss after income tax:			
(Loss) / Profit after income tax		(9,193)	(10,816)
Non-cash items requiring adjustment:			
Depreciation of property, plant and equipment		6	4
Share based payments expense		394	–
Foreign exchange loss/(gain)		724	(144)
Loss on financial assets		–	261
Changes in working capital:			
Trade and other receivables		(203)	390
Trade and other payables		194	(1,414)
Net cash used in operating activities		(8,078)	(11,719)

The notes on pages 36 to 49 form part of these consolidated financial statements

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

FOR THE YEAR ENDED 31 DECEMBER 2020

1. NATURE OF BUSINESS

Neuren Pharmaceuticals Limited (Neuren or the Company, and its subsidiaries, or the Group) is a publicly listed biopharmaceutical company developing drugs for neurological disorders.

The Company is a limited liability company incorporated in New Zealand. The address of its registered office in New Zealand is at the offices of Lowndes Jordan, Level 15 PWC Tower, 188 Quay Street, Auckland 1141. Neuren ordinary shares are listed on the Australian Securities Exchange (ASX code: NEU).

These consolidated financial statements have been approved for issue by the Board of Directors on 23 February 2021.

Material Uncertainties

- The Group's research and development activities involve inherent risks. These risks include, among others: dependence on, and the Group's ability to retain key personnel; the Group's ability to protect its intellectual property and prevent other companies from using the technology; the Group's business is based on novel and yet to be proven technology; the Group's ability to sufficiently complete the clinical trials process; and technological developments by the Group's competitors could render its products obsolete.
- The Group's revenue from licence agreements is contingent on future events and will be intermittent until product sales commence. The business plan therefore may require expenditure in excess of revenue and in the future the Group may need to raise further financing through other public or private equity financings, collaborations or other arrangements with corporate sources, or other sources of financing to fund operations. There can be no assurance that such additional financing, if available, can be obtained on terms reasonable to the Group.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

These general-purpose consolidated financial statements of the Group are for the year ended 31 December 2020 and have been prepared in accordance with and comply with generally accepted accounting practice in New Zealand (GAAP), New Zealand equivalents to International Financial Reporting Standards (NZ IFRS) issued by the New Zealand Accounting Standards Board which comply with International Financial Reporting Standards, the requirements of the Financial Markets Conduct Act 2013, and other applicable Financial Reporting Standards as appropriate for profit-oriented entities that fall into Tier 1 as determined by the New Zealand External Reporting Board.

(a) Basis of preparation

Entities Reporting

The consolidated financial statements incorporate the assets and liabilities of all subsidiaries of the Group as at 31 December 2020 and the results of all subsidiaries for the year then ended. Neuren Pharmaceuticals Limited and its subsidiaries, which are designated as profit-oriented entities for financial reporting purposes, together are referred to in these financial statements as the Group.

Statutory Base

Neuren is registered under the New Zealand Companies Act 1993. Neuren is also registered as a foreign company under the Australian *Corporations Act 2001*.

Historical cost convention

These consolidated financial statements have been prepared under the historical cost convention as modified by certain policies below. Amounts are expressed in Australian Dollars and are rounded to the nearest thousand, except for earnings per share.

Critical accounting estimates

The preparation of financial statements requires the use of certain critical accounting estimates. It also requires the Group to exercise its judgement in the process of applying the Group's accounting policies. Actual results may differ from those estimates. The areas involving a higher degree of judgement or complexity, or areas where assumptions and estimates are significant to the financial statements are disclosed in Note 16.

Going concern basis

The directors monitor the Group's cash position and initiatives to ensure that adequate funding continues to be available for the Group to meet its business objectives. The Group recorded a loss after tax of $9.2 million for the year ending 31 December 2020 and had negative operating cash flows of $8.1 million for the year ended 31 December 2020. The Group had net assets at 31 December 2020 of $24.2 million, including cash balances and receivables of $24.9 million.

On 29 June 2020, the Group announced the successful completion of a capital raise of $20 million, with $19 million net of costs received. On 6 July 2020, the Group issued 14,285,723 fully paid ordinary shares at an issue price of $1.40 per share to institutional and sophisticated investors in Australia, New Zealand, Hong Kong and the United Kingdom. The funds raised will enable the Group to fund plans to generate Phase 2 clinical trial data for NNZ-2591.

It is the considered view of the Directors that the Group will have access to adequate resources to meet its ongoing obligations for at least a period of 12 months from the date of signing these financial statements. On this basis, the Directors have assessed it is appropriate to adopt the going concern basis in preparing its consolidated financial statements. The consolidated financial statements do not include any adjustments that would result if the Group was unable to continue as a going concern.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

CONTINUED

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (CONTINUED)

Impact of COVID-19 on our business

On March 11, 2020 the World Health Organization declared a pandemic resulting from the disease known as COVID-19 caused by a novel strain of coronavirus, SARS-CoV-2. In an effort to contain COVID-19 or slow its spread, state or federal governments around the world have enacted various measures, including orders to close businesses not deemed "essential", isolate residents to their homes or places of residence, and practice social distancing when engaging in essential activities. In certain jurisdictions, such orders have been lifted, although subsequent trends in COVID-19 infections have led to the reinstatement of such orders in various jurisdictions.

To date there has been no financial impact of COVID-19 on the Group. In the United States, enrolment of new patients in the trofinetide Phase 3 LAVENDER study was re-initiated in June 2020 after it was temporarily paused by ACADIA in March 2020 due to COVID-19 restrictions and risks. It is possible that clinical trials or other research and development activities for trofinetide or NNZ-2591 could be impacted in the future by COVID-19 restrictions or risks. The Group is continuing to monitor the situation and may take further actions affecting its business operations as are deemed necessary.

Changes in accounting policies

There is no significant impact of changes in accounting policies for the year ended 31 December 2020.

Standards, interpretations and amendments to published standards that are not yet effective

Certain new standards, amendments and interpretations to existing standards have been published that are mandatory for later periods and which the Group has not adopted early. None are expected to materially impact the Group.

(b) Principles of Consolidation

Subsidiaries

Subsidiaries are all entities (including structured entities) over which the group has control. The group controls an entity when the group is exposed to, or has rights to, variable returns from its involvement with the entity and has the ability to affect those returns through its power over the entity.

Subsidiaries are fully consolidated from the date on which control is transferred to the group. They are deconsolidated from the date that control ceases.

Inter-company transactions, balances and unrealised gains on transactions between group companies are eliminated. Unrealised losses are also eliminated. When necessary, amounts reported by subsidiaries have been adjusted to conform with the group's accounting policies.

(c) Foreign Currency Translation

(i) Functional and Presentation Currency

The functional currency of the Company and the presentation currency of Group is Australian Dollars.

(ii) Transactions and Balances

Foreign currency transactions are translated into the functional currency using the exchange rates prevailing at the dates of the transactions. Foreign exchange gains and losses resulting from the settlement of such transactions and from the translation at year-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recognised in the Statement of Comprehensive Income, except when deferred in equity as qualifying cash flow hedges and qualifying net investment hedges.

(iii) Foreign Operations

The results and financial position of foreign entities (none of which has the currency of a hyperinflationary economy) that have a functional currency different from the presentation currency are translated into the presentation currency as follows:

- assets and liabilities for each statement of financial position presented are translated at the closing rate at the date of that statement of financial position;
- revenue and expenses for each Statement of Comprehensive Income are translated at average exchange rates; and
- all resulting exchange differences are recognised as a separate component of equity.

Exchange differences arising from the translation of any net investment in foreign entities, and of borrowings and other currency instruments designated as hedges of such investments, are taken to shareholders' equity.

Goodwill and fair value adjustments arising on the acquisition of a foreign operation are treated as assets and liabilities of the foreign operation and translated at the closing rate.

(d) Revenue

Revenue arises mainly from grants received and interest. Revenue is recognised either at a point in time or over time, when (or as) the Group satisfies performance obligations by transferring the promised goods or services to its customers.

Grants

Grants received are recognised in profit or loss within the Statement of Comprehensive Income over the periods in which the related costs for which the grants are intended to compensate are recognised as expenses and when the requirements under the grant agreement have been met. Any grants received for which the requirements under the grant agreement have not been completed are carried as liabilities until all the conditions have been fulfilled.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

CONTINUED

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (CONTINUED)

Interest income
Interest income is recognised on a time-proportion basis using the effective interest method.

(e) Research and development

Research costs include direct and directly attributable overhead expenses for drug discovery, research and pre-clinical and clinical trials. Research costs are expensed as incurred.

When a project reaches the stage where it is reasonably certain that future expenditure can be recovered through the process or products produced, development expenditure is recognised as a development asset using the following criteria:

- a product or process is clearly defined and the costs attributable to the product or process can be identified separately and measured reliably;
- the technical feasibility of the product or process can be demonstrated;
- the existence of a market for the product or process can be demonstrated and the Group intends to produce and market the product or process;
- adequate resources exist, or their availability can be reasonably demonstrated to complete the project and market the product or process.

In such cases the asset is amortised from the commencement of commercial production of the product to which it relates on a straight-line basis over the years of expected benefit. Research and development costs are otherwise expensed as incurred.

(f) Income tax

The income tax expense for the period is the tax payable on the period's taxable income or loss using tax rates enacted or substantively enacted at the reporting date and adjusted by changes in deferred tax assets and liabilities attributable to temporary differences between the tax bases of assets and liabilities and their carrying amounts in the financial statements, and to unused tax losses.

Deferred tax assets and liabilities are recognised for temporary differences at the tax rates expected to apply when the assets are recovered or liabilities are settled, based on those tax rates which are enacted or substantively enacted at the reporting date. The relevant tax rates are applied to the cumulative amounts of deductible and taxable temporary differences to measure the deferred tax asset or liability. An exception is made for certain temporary differences arising from the initial recognition of an asset or a liability. No deferred tax asset or liability is recognised in relation to these temporary differences if they arose in a transaction, other than a business combination, that at the time of the transaction did not affect either accounting profit or taxable profit or loss.

Deferred tax assets are recognised for deductible temporary differences and unused tax losses only if it is probable that future taxable amounts will be available to utilise those temporary differences and losses.

Current and deferred tax balances attributable to amounts recognised directly in equity are also recognised directly in equity.

(g) Impairment of non-financial assets

Assets that have an indefinite useful life are not subject to amortisation and are tested annually for impairment. All non-financial assets are also reviewed whenever events or changes in circumstances indicate that the carrying amount of the assets may not be recoverable. The carrying amount of a long-lived asset is considered impaired when the recoverable amount from such asset is less than its carrying value. In that event, a loss is recognised in the Statement of Comprehensive Income based on the amount by which the carrying amount exceeds the fair value less costs of disposal and value in use of the long-lived asset. Fair market value is determined using the anticipated cash flows discounted at a rate commensurate with the risk involved.

(h) Goods and services tax (GST)

The financial statements have been prepared so that all components are presented exclusive of GST. All items in the statement of financial position are presented net of GST, with the exception of receivables and payables, which include GST invoiced.

(i) Cash and cash equivalents

Cash and cash equivalents comprises cash and demand deposits held with established financial institutions and highly liquid investments, which have maturities of three months or less that are readily convertible to known amounts of cash and which are subject to an insignificant risk of changes in value.

(j) Trade and other receivables

The Group makes use of a simplified approach in accounting for trade and other receivables and records the loss allowance as lifetime expected credit losses. These are the expected shortfalls in contractual cash flows, considering the potential for default at any point during the life of the financial instrument. In calculating, the Group assesses trade receivables on an individual basis, and uses its historical experience, external indicators and forward-looking information to calculate the expected credit losses.

(k) Property, plant and equipment

Property, plant and equipment are stated at historical cost less depreciation. Historical cost includes expenditure that is directly attributable to the acquisition of the items.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

CONTINUED

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (CONTINUED)

Subsequent costs are included in the asset's carrying amount or recognised as a separate asset, as appropriate, only when it is probable that future economic benefits associated with the item will flow to the Group and the cost of the item can be measured reliably. All other repairs and maintenance are charged to the Statement of Comprehensive Income during the financial period in which they are incurred.

Depreciation is determined principally using the straight-line method to allocate their cost, net of their residual values, over their estimated useful lives, as follows:

Scientific equipment	4 years
Computer equipment	2-10 years
Office furniture, fixtures & fittings	3-4 years

(l) Intangible assets

Intellectual property
Costs in relation to protection and maintenance of intellectual property are expensed as incurred unless the project has yet to be recognised as commenced, in which case the expense is deferred and recognised as contract work in progress until the revenues and costs associated with the project are recognised.

Acquired patents, trademarks and licences have finite useful lives and are carried at cost less accumulated amortisation and impairment losses. Amortisation is calculated using the straight line method to allocate the cost over the anticipated useful lives, which are aligned with the unexpired patent term or agreement over trademarks and licences.

Acquired software
Acquired software licences are capitalised on the basis of the costs incurred to acquire and bring to use the specific software. These costs are amortised over their estimated useful lives.

(m) Employee benefits

Wages and salaries, annual leave, long service leave and superannuation
Liabilities for wages and salaries, bonuses, annual leave, long service leave and superannuation expected to be settled within 12 months of the reporting date are recognised in accrued liabilities in respect of employees' services up to the reporting date and are measured at the amounts expected to be paid when the liabilities are settled. Liabilities for non-accumulating personal leave are recognised when the leave is taken and measured at the rates paid or payable.

Contributions are made by the Group to employee superannuation funds and are charged as expenses when the obligation to pay them arises.

Share-based payments
Neuren has operated a loan funded share plan and equity performance rights plan. Both plans are accounted for as share options. The fair value of the services received in exchange for the grant of the options or shares is recognised as an expense with a corresponding increase in other reserve equity over the vesting period. The total amount to be expensed over the vesting period is determined by reference to the fair value of the options or shares at grant date. At each reporting date, except for options that are subject to a market condition for vesting, the Company revises its estimates of the number of options that are expected to vest and become exercisable. It recognises the impact of the revision of original estimates, if any, in the Statement of Comprehensive Income, and a corresponding adjustment to equity over the remaining vesting period.

When options are exercised, the proceeds received net of any directly attributable transaction costs are credited to share capital.

(n) Share issue costs

Costs associated with the issue of shares which are recognised in shareholders' equity are treated as a reduction of the amount collected per share.

(o) Financial instruments

Recognition and derecognition
Financial assets and financial liabilities are recognised when the Group becomes a party to the contractual provisions of the financial instrument.

Financial assets are derecognised when the contractual rights to the cash flows from the financial asset expire, or when the financial asset and substantially all the risks and rewards are transferred.

A financial liability is derecognised when it is extinguished, discharged, cancelled or expires.

Classification and initial measurement of financial assets
Except for those trade receivables that do not contain a significant financing component and are measured at the transaction price in accordance with NZ IFRS 15 'Revenue from contracts with customers', all financial assets are initially measured at fair value adjusted for transaction costs (where applicable).

Financial assets, other than those designated and effective as hedging instruments, are classified into the following categories:

- amortised cost
- fair value through profit or loss (FVTPL)
- fair value through other comprehensive income (FVOCI).

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

CONTINUED

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (CONTINUED)

In the periods presented the corporation does not have any financial assets categorised as FVTPL or FVOCI.

The classification is determined by both:

- the entity's business model for managing the financial asset
- the contractual cash flow characteristics of the financial asset.

All income and expenses relating to financial assets that are recognised in profit or loss are presented within finance costs, finance income or other financial items, except for impairment of trade receivables which is presented within other expenses.

Subsequent measurement of financial assets

Financial assets at amortised cost

Financial assets are measured at amortised cost if the assets meet the following conditions (and are not designated as FVTPL):

- they are held within a business model whose objective is to hold the financial assets and collect its contractual cash flows
- the contractual terms of the financial assets give rise to cash flows that are solely payments of principal and interest on the principal amount outstanding

After initial recognition, these are measured at amortised cost using the effective interest method.

Discounting is omitted where the effect of discounting is immaterial. The Group's cash and cash equivalents, trade and most other receivables fall into this category of financial instruments.

(p) Financial liabilities

The Group's financial liabilities include trade and other payables. Financial liabilities are initially measured at fair value, and, where applicable, adjusted for transaction costs.

Subsequently, financial liabilities are measured at amortised cost using the effective interest method.

(q) Earnings per share

Basic and diluted earnings per share are calculated by dividing the profit attributable to equity holders of the Company by the weighted average number of ordinary shares outstanding during the period.

3. SEGMENT INFORMATION

The Group operates as a single operating segment and internal management reporting systems present financial information as a single segment. The segment derives its revenue and incurs expenses through the development of pharmaceutical products. Grant income arises from the Australian R&D Tax Incentive and revenue from licence agreements is derived from the United States. The Board of the Company has been identified as the chief operating decision maker. The Board assesses the financial performance and position of the group, and makes strategic decisions.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

CONTINUED

4. EXPENSES

	2020 $'000	2019 $'000
Loss / (Profit) before income tax includes the following expenses:		
Depreciation – property, plant and equipment		
Computer equipment	6	4
Total depreciation	6	4
Remuneration of auditors		
Audit and review of financial statements (Grant Thornton NZ)	58	60
Total remuneration of auditors	58	60
Employee benefits expense		
Short-term benefits	974	754
Post-employment benefits	76	70
Other employee benefits	35	75
Share based payments	394	–
Total employee benefits expenses	1,479	899
Directors' compensation		
Short-term benefits	423	602
Post-employment benefits	10	10
Total Directors' compensation	433	612

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

CONTINUED

5. INCOME TAX

	2020 $'000	2019 $'000
Income tax		
Current tax	–	–
Deferred tax	–	–
	–	–
Numerical reconciliation of income tax to prima facie tax receivable:		
(Loss) / Profit before income tax	(9,193)	(10,816)
Tax at applicable rates 27.5% (2019: 27.5%)	(2,528)	(2,974)
Non-taxable Australian R&D tax incentive income	(197)	(136)
Non deductible expenses for R&D incentive	454	310
Non-taxable loss in fair value of equity derivative	–	72
Taxable (loss) / gain on settlement of equity derivative	–	(268)
Utilisation of previously unrecognised tax losses	–	–
Deductible temporary differences and tax losses for which no deferred tax asset was recognised	2,271	2,996
Income tax	–	–
Gross tax losses for which no deferred tax asset has been recognised[(a)]	107,065	100,883

(a) Of these gross tax losses, $62.9 million (2019: $64.6 million) relates to New Zealand tax losses, which are unlikely to be utilised unless future taxable income is generated in New Zealand. The movement is due to the New Zealand tax losses being translated at the closing foreign exchange rate at each reporting date.

6. EARNINGS PER SHARE

Basic earnings per share is calculated by dividing the profit for the year attributable to the equity holders of the company by the weighted average number of ordinary shares on issue during the year excluding shares held as treasury stock.

Diluted earnings per share is calculated by dividing the profit for the year attributable to the equity holders of the company by the weighted average number of shares outstanding during the year plus the weighted average number of ordinary shares that would be issued on conversion of any dilutive potential ordinary shares into ordinary shares.

The dilutive impact of loan funded shares has not been included in the weighted average number of ordinary shares for the purposes of calculating diluted earnings per share, as it does not meet the requirements for inclusion in NZ IAS 33.

	2020	2019
Loss after income tax attributable to equity holders (basic) - ($'000)	(9,193)	(10,816)
Weighted average shares outstanding (basic) - (No.)	107,057,317	100,168,413
Basic loss per share	($0.086)	($0.108)
Loss after income tax attributable to equity holders (diluted) - ($'000)	(9,193)	(10,816)
Weighted average shares outstanding (diluted) - (No.)	107,057,317	100,168,413
Diluted loss per share	($0.086)	($0.108)

7. CASH AND CASH EQUIVALENTS

	2020 $'000	2019 $'000
Cash	229	820
Demand and short-term deposits	23,959	13,024
	24,188	13,844

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

CONTINUED

8. TRADE AND OTHER RECEIVABLES

	2020 $'000	2019 $'000
Trade receivables	–	13
Other receivables	22	15
Interest receivables	16	33
Australian R&D tax incentive	717	491
	755	552

The Group applies the simplified model of recognising lifetime expected credit losses for all trade receivables as these items do not have a significant financing component.

In measuring the expected credit losses, the trade receivables have been assessed on an individual basis due to the limited number of receivables.

The expected loss rates are based on the payment profile of the individual receivable and other transactions with that debtor over the past 12 months before 31 December 2020 as well as the corresponding historical credit losses during that period.

Trade receivables are written off (i.e. de-recognised) when there is no reasonable expectation of recovery. Failure to make payments within 180 days from the invoice date and failure to engage with the Group on alternative payment arrangements amongst others are considered indicators of no reasonable expectation of recovery. No credit losses have been determined for the current year (2019: nil).

9. TRADE AND OTHER PAYABLES

	2020 $'000	2019 $'000
Trade payables	167	340
Accruals	323	26
Employee Benefits	263	193
	753	559

Trade payables and accruals relate to operating expenses, primarily research and development expenses. Trade payables comprise amounts invoiced prior to the reporting date and accruals comprise the value of work done but not invoiced at each reporting date.

10. SHARE CAPITAL

	2020 Shares	2019 Shares	2020 $'000	2019 $'000
Issued Share Capital				
Ordinary shares on issue at beginning of year	102,668,413	102,668,413	126,426	126,426
Shares issued under Loan Funded Share Plan	3,000,000	–	–	
Shares bought back under Loan Funded Share Plan	(2,500,000)	–	–	–
Shares issued in private placement	14,285,723	–	20,000	–
Share issued in Share Purchase Plan	153,972	–	216	–
Share issue expenses - Cash issue costs	–	–	(1,075)	–
	117,608,108	102,668,413	145,567	126,426

In July 2020, the Group issued 14,285,723 fully paid ordinary shares at an issue price of $1.40 per share in a placement to institutional and sophisticated investors in Australia, New Zealand, Hong Kong and the United Kingdom. In August 2020, the Group issued 153,972 fully paid ordinary shares at an issue price of $1.40 in the Share Purchase Plan (SPP). The issue price of $1.40 per share for the placement and the SPP represented a discount of 10% to the 10-day volume weighted average price of $1.56 and 15% to the last closing price of $1.64.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

CONTINUED

10. SHARE CAPITAL (CONTINUED)

At 31 December 2020 3.0 million ordinary shares (31 December 2019: 2.5 million ordinary shares) were held as treasury stock in respect of the Loan Funded Share Plan described below.

Ordinary Shares

The ordinary shares have no par value and all ordinary shares are fully paid-up and rank equally as to dividends and liquidation, with one vote attached to each fully paid ordinary share.

Share based payments

No securities were issued under any share based payment plans in 2020 or 2019. There were no equity-settled share based payments expensed in the Statement of Comprehensive Income in 2020 or 2019.

Loan funded shares

The Company has a Loan Funded Share Plan to support the achievement of the Company's business strategy by linking executive reward to improvements in the financial performance of the Company and aligning the interests of executives with shareholders. Under the Loan Funded Share Plan, loan funded shares may be offered to employees or consultant ("Participants") by the Remuneration and Audit Committee. The Company issues new ordinary shares, which are placed in a trust to hold the shares on behalf of the Participant. The trustee issues a limited-recourse, interest-free loan to the participant, which is equal to the number of shares multiplied by the issue price. A limited-recourse loan means that the repayment amount will be the lesser of the outstanding loan and the market value of the shares that are subject to the loan. The trustee continues to hold the shares on behalf of the Participant until all vesting conditions have been satisfied and the Participant chooses to settle the loan, at which point ownership of the shares is transferred from the trust to the Participant. Any dividends paid by the Company while the shares are held by the trust are applied as repayment of the loan at the after-tax value of the dividend. On request by the participant, the Company may dispose of, or buy back, vested shares and utilise the proceeds to settle the outstanding loan. The directors may apply vesting conditions to be satisfied before the shares can be transferred to the Participant. Before the loan can be given, the New Zealand Companies Act requires the Company to disclose to shareholders the provision of financial assistance to the Participant. The maximum loan term is 5 years.

All loan funded shares under the plan during the year ended 31 December 2020 were issued subject to the following vesting conditions:

i. 40% of the Loan Funded Shares shall vest on acceptance by the US Food and Drug Administration of the filing of a New Drug Application for Trofinetide; and

ii. 40% of the Loan Funded Shares shall vest when the Company determines to progress NNZ-2591 to a Phase 2b or Phase 3 clinical trial following a positive Phase 2 clinical trial outcome, or executes a partnering transaction for NNZ-2591;

iii. 20% of the Loan Funded Shares shall vest when the Company executes a partnering transaction for trofinetide outside North America, or submits a Marketing Authorisation Application for trofinetide in the European Union, the United Kingdom, or Japan.

Each of these Vesting Conditions shall be tested separately from the other Vesting Conditions.

The estimated fair value of the shares has been determined using the Black-Scholes valuation model. The significant inputs into the model were the share price on date of valuation, the estimated future volatility of the share price, a dividend yield of 0%, an expected life of 5 years, and an annual risk-free interest rate of 0.4%. The estimated future volatility of the share price was derived by analysing the historic volatility of the share price during a relevant period.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

CONTINUED

10. SHARE CAPITAL (CONTINUED)

Details of the shares issued during the year ended 31 December 2020, the estimated fair value and variable inputs into the valuation model are shown in the following table:

Number of shares	3 million
Issue date	13 July 2020
Exercise price per share	$1.84
Share price on date of valuation	$1.28
Fair value per share	$0.70
Estimated future volatility	77.25%

The impact of changes to inputs to the model, holding other assumptions constant, would have affected the fair value of the shares by the amounts below.

	2020	
Expected life	**$'000 Decrease to 3 years**	**$'000 Decrease to 4 years**
Increase/(decrease) in the share based payments expense	(523)	(236)
Share price volatility	**Decrease to 67.25%**	**Increase to 87.25%**
Increase/(decrease) in the share based payments expense	(287)	262

Movements in the number of Loan Funded Shares were as follows:

	Loan Funded Shares	Weighted Average Exercise Price	Exercisable	Weighted Average Exercise Price
Outstanding at 1 January 2019	2,500,000	$1.76	–	–
Expired and bought back	(1,500,000)	$1.84	–	–
Outstanding at 31 December 2019	1,000,000	$1.76	–	–
Expired and bought back	(1,000,000)	$1.76	–	–
Issued	3,000,000	$1.84	–	–
Outstanding at 31 December 2020	3,000,000	$1.84	–	–

The exercise price for 3.0 million unvested Loan Funded Shares is $1.84 per share.

The loans in respect of 1.5 million Loan Funded Shares expired in May 2019, with the share price at that time below the exercise price of $1.84. The loans in respect of 1.0 million Loan Funded Share expired in May 2020, with the share price at that time below the exercise price of $1.76. The Loan Funded Shares were therefore forfeited. On 14 July 2020 the Company bought back 2.5 million ordinary shares from Neuren Trustee Limited. In accordance with the terms of the Loan Funded Share Plan, the consideration for the shares bought back was equal to the outstanding loan balances.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

CONTINUED

11. SUBSIDIARIES

(a) Investment in subsidiaries

The consolidated financial statements incorporate the assets, liabilities and results of the following subsidiaries in accordance with the accounting policy described in Note 2(b).

Name of entity	Date of incorporation	Principle activities	Interest held	Domicile
Neuren Pharmaceuticals Inc.	20-Aug-02	Development services	100%	USA
Neuren Pharmaceuticals (Australia) Pty Ltd	9-Nov-06	Dormant	100%	AUS
Neuren Trustee Limited	29-May-13	Holds loan funded shares	100%	NZ

All subsidiaries have a reporting date of 31 December.

12. COMMITMENTS AND CONTINGENCIES

(a) Legal claims

The Group had no significant legal matter contingencies as at 31 December 2020 or at 31 December 2019.

(b) Commitments

The Group was not committed to the purchase of any property, plant or equipment or intangible assets as at 31 December 2020 (2019: nil).

At 31 December 2020, the Group had commitments under product development contracts amounting to approximately $5.0 million, comprising approximately US$2.6 million, GBP 0.4 million and AU$0.9 million. At 31 December 2019, the Group had commitments under product development contracts amounting to approximately $6.6 million, comprising approximately US$4.0 million and approximately GBP 0.5 million.

(c) Contingent liabilities

The Group had no contingent liabilities at 31 December 2020 or at 31 December 2019 that require disclosure.

13. RELATED PARTY TRANSACTIONS

(a) Key Management Personnel

The Key Management Personnel of the Group (KMP) include the directors of the Company and direct reports to the Executive Chairman until 26 May 2020, and reporting to the Chief Executive Officer after that date. Compensation for KMP was as follows:

	2020 $'000	2019 $'000
Short-term benefits	1,349	1,345
Post-employment benefits	73	62
Other long-term benefits	35	71
Share based payment compensation	394	–
	1,851	1,478

(b) Subsidiaries

The ultimate parent company in the Group is Neuren Pharmaceuticals Limited ("Parent"). The Parent funds the activities of the subsidiaries throughout the year as needed. Interests in and amounts due from subsidiaries are set out in Note 11. All amounts due between entities in the Group are payable on demand and bear no interest.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

CONTINUED

14. EVENTS AFTER REPORTING DATE

As at the date of these consolidated financial statements authorised for issue, there are no events arising since 31 December 2020 that require disclosure.

15. FINANCIAL INSTRUMENTS AND RISK MANAGEMENT

(a) Categories of financial instruments

		At amortised cost		At fair value through profit or loss	
Financial assets		**Floating Interest Rate $'000**	**Non-Interest Bearing $'000**	**Non-Interest Bearing $'000**	**Total $'000**
2020					
Cash and cash equivalents	7	24,188	–	–	24,188
Trade and other receivables	8	–	37	–	37
Total financial assets		24,188	37	–	24,226
2019					
Cash and cash equivalents	7	13,844	–	–	13,844
Trade and other receivables	8	–	61	–	61
Total financial assets		13,844	61	–	13,906

Financial liabilities		**2020 $'000**	**2019 $'000**
Amortised cost – Non-Interest Bearing:			
Trade and other payables	9	490	366
Total financial liabilities		490	366

At 31 December 2020, the reporting value of all financial instruments approximated to the fair value.

(b) Risk management

The Group is subject to a number of financial risks which arise as a result of its activities.

Market risk

Market risk is the risk that changes in market prices, such as foreign exchange rates and interest rates will affect the Group's income or the value of its holdings of financial instruments. The objective of market risk management is to manage and control market risk exposures within acceptable parameters, while optimising the return.

Currency risk

During the normal course of business the Group enters into contracts with overseas customers or suppliers or consultants that are denominated in foreign currency. As a result of these transactions there is exposure to fluctuations in foreign exchange rates. The Company also has a net investment in a foreign operation, whose net assets are exposed to foreign currency translation risk.

The principle currency risk faced by the business is the exchange rate between the Australian dollar and the US dollar. The Group holds cash denominated in US dollars and Australian dollars and has material expenditure in each of these currencies. Where possible, the Group matches foreign currency income and foreign currency expenditure as a natural hedge, holding foreign currency cash to facilitate this natural hedge. When foreign currency expenditure exceeds foreign currency revenue and foreign currency cash, the group purchases foreign currency to meet anticipated requirements under spot and forward contracts. The Group does not designate formal hedges. At 31 December 2020, there were no forward contracts outstanding (2019: None).

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

CONTINUED

15. FINANCIAL INSTRUMENTS AND RISK MANAGEMENT (CONTINUED)

During the year, the US dollar fluctuated against the Australian dollar. A foreign exchange loss of $631,000 is included in results for the year ended 31 December 2020 (2019: gain $132,000). The majority of the loss relates to losses on the translation for reporting purposes of the Group's US dollar cash reserves into Australian dollars.

The carrying amounts of US dollar denominated financial assets and liabilities are as follows:

	2020 $'000	2019 $'000
Assets		
US dollars	8,686	8,084
Liabilities		
US dollars	46	180

An increase of 10% in the cross rate of the US dollar against the Australian dollar as at the reporting date would have increased the consolidated loss after income tax by $785,000 (2019: $719,000). A decrease of 10% in the cross rate of the US dollar against the Australian dollar as at the reporting date would have decreased the consolidated loss after income tax by $960,000 (2019: $878,000).

Interest rate risk

The Group is exposed to changes in market interest rates as entities in the Group hold cash and cash equivalents.

The effective interest rates on financial assets are as follows:

	2020 $'000	2019 $'000
Financial Assets		
Cash and cash equivalents		
Australian dollar cash deposits	15,502	5,773
Australian dollar interest rate	0.48%	1.54%
US dollar cash deposits	8,686	8,071
US dollar interest rate	0.07%	1.73%

The Company and Group do not have any interest-bearing financial liabilities. Trade and other receivables and payables do not bear interest and are not interest rate sensitive.

A 10% change in average market interest rates would have changed reported loss after tax by approximately $8,000 (2019: $39,000).

Credit risk

The Group incurs credit risk from transactions with financial institutions. The total credit risk on cash and cash equivalents, which have been recognised in the statement of financial position, is the carrying amount. The Company and its subsidiaries do not retain any collateral or security to support transactions with financial institutions. Cash and cash equivalents are held and transacted with National Australia Bank, Western Union and Sonabank.

Liquidity risk

The Group's financial liabilities, comprising trade and other payables, are generally repayable within 1 – 2 months. The maturity and availability of financial assets, comprising cash and cash equivalents and, are monitored and managed to ensure financial liabilities can be repaid when due.

Capital risk

The Group manages its capital, which is its equity, to ensure that the Group entities are able to meet their estimated commitments as they fall due. In this regard, the Company raised additional equity capital during 2020, as described in Note 10. Capital risk is impacted by the material uncertainties described in Note 1.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

CONTINUED

16. CRITICAL ACCOUNTING ESTIMATES AND ASSUMPTIONS

The Group makes estimates and assumptions concerning the future. The resulting accounting estimates will, by definition, seldom equal the related actual results. The estimates and assumptions that have a significant risk of causing material adjustment to the carrying amounts of assets and liabilities within the next financial year are as discussed below.

The Group's research and development activities are eligible under the Australian R&D Tax Incentive. The Group has assessed these activities and expenditure to determine which are likely to be eligible under the incentive scheme. For the period to 31 December 2020 the Group has recorded other revenue of $0.7 million (2019: $0.5 million).

The Group has assessed that all research and development expenditure to date does not meet the requirements for capitalisation as an intangible asset because it is not yet probable that the expected future economic benefits that are attributable to the asset will flow. The Group's current assessment is that future expenditure will not meet that requirement prior to the approval of a New Drug Application by the US Food and Drug Administration.

The Group is subject to income taxes in Australia because it is domiciled in that country. There are transactions and calculations undertaken during the ordinary course of business for which the ultimate tax determination may be uncertain. Where the final tax outcome of these matters is different from the amounts that were initially recorded, such differences will impact the current and deferred tax provisions in the period in which such determination is made.

Loan Funded Shares

The Group measures the fair value of loan funded shares with employees by reference to the fair value of the equity instruments at the date at which they are granted. The estimated fair value of the shares is determined using the Black-Scholes valuation model, taking into account the terms and conditions upon which the instruments were granted. Some judgements are made on the inputs into the valuation model, including the expected life and volatility.

Grant Thornton

Independent Auditor's Report

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To the Shareholders of Neuren Pharmaceuticals Limited

Report on the Audit of the Consolidated Financial Statements

Opinion

We have audited the consolidated financial statements of Neuren Pharmaceuticals Limited (the "Company") and its subsidiaries (the "Group") on pages 32 to 49 which comprise the consolidated statement of financial position as at 31 December 2020, and the consolidated statement of comprehensive income, consolidated statement of changes in equity and consolidated statement of cash flows for the year then ended, and notes to the financial statements, including a summary of significant accounting policies

In our opinion, the accompanying financial statements present fairly, in all material respects, the financial position of the Group as at 31 December 2020 and of its financial performance and cash flows for the year then ended in accordance with New Zealand Equivalents to International Financial Reporting Standards ("NZ IFRS") issued by the New Zealand Accounting Standards Board.

Basis for Opinion

We conducted our audit in accordance with International Standards on Auditing (New Zealand) ("ISAs (NZ)") issued by the New Zealand Audit and Assurance Standards Board. Our responsibilities under those standards are further described in the Auditor's Responsibilities for the Audit of the Consolidated Financial Statements section of our report. We are independent of the Group in accordance with Professional and Ethical Standard 1 (Revised) Code of Ethics for Assurance Practitioners issued by the New Zealand Auditing and Assurance Standards Board, and we have fulfilled our other ethical responsibilities in accordance with these requirements. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Other than in our capacity as auditor we have no relationship with, or interests in, the Group.

Key Audit Matters

Key audit matters are those matters that, in our professional judgement, were of most significance in our audit of the consolidated financial statements of the current period. These matters were addressed in the context of our audit of the consolidated financial statements as a whole, and in forming our opinion thereon, and we do not provide a separate opinion on these matters.

Why matter is significant	How our audit addressed the key audit matter
Loan Funded Shares During the period the entity issued Loan Funded Shares to key employees. The fair value was determined using the Grant-Date Method via a Black-Scholes Model as described in Note 10 in the financial statements. The valuation involved significant judgements and estimates from management, including the estimated future volatility of the share price, an expected life of 5 years and annual risk-free interest rate. We included the valuation of loan funded shares as a key audit matter, due to the high estimation uncertainty within the assumptions and the impact these have on the fair value of the shares.	Our procedures in relation to management's valuation include: • Reviewed the signed contracts to confirm the key inputs used in the valuation were accurate. • Assessed key assumptions for reasonableness and obtained support for assumptions from independent sources where appropriate. • Performed a sensitivity analysis on key inputs to the model and reviewed the impact on the fair value. Based on the audit procedures performed, we obtained sufficient audit evidence to assess that the assumptions made by management in relation to the fair value of the loan funded shares were appropriate.

Other Information

The Directors are responsible for the other information. The other information comprises the information included in the directors' report (but does not include the consolidated financial statements and our auditor's report thereon), which we obtained prior to the date of this auditor's report and the annual report which is expected to be made available to us after that date.

Our opinion on the consolidated financial statements does not cover the other information and we will not express any form of audit opinion or assurance conclusion thereon.

In connection with our audit of the consolidated financial statements, our responsibility is to read the other information identified above when it becomes available and, in doing so, consider whether the other information is materially inconsistent with the consolidated financial statements or our knowledge obtained in the audit, or otherwise appears to be materially misstated. If, based on the work we have performed, we conclude that there is a material misstatement of this other information, we are required to report that fact. We have nothing to report in this regard.

Directors' responsibilities for the Consolidated Financial Statements

The Directors are responsible on behalf of the Group for the preparation and fair presentation of the consolidated financial statements in accordance with New Zealand equivalents to International Financial Reporting Standards issued by the New Zealand Accounting Standards Board, and for such internal control as the Directors determine is necessary to enable the preparation of consolidated financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the consolidated financial statements, the directors are responsible on behalf of the Group for assessing the Group's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless the directors either intend to liquidate the Group or to cease operations, or have no realistic alternative but to do so.

Auditor's responsibilities for the Audit of the Consolidated Financial Statements

Our objectives are to obtain reasonable assurance about whether the consolidated financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditor's report that includes our opinion. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with ISAs (NZ) will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these consolidated financial statements.

A further description of the auditor's responsibilities for the audit of the consolidated financial statements is located on the External Reporting Board's website at https://www.xrb.govt.nz/assurance-standards/auditors-responsibilities/audit-report-1/

Restriction on use of our report

This report is made solely to the Company's shareholders, as a body. Our audit work has been undertaken so that we might state to the Company's shareholders, as a body those matters which we are required to state to them in an auditor's report and for no other purpose. To the fullest extent permitted by law, we do not accept or assume responsibility to anyone other than the Company and its shareholders, as a body, for our audit work, for this report or for the opinion we have formed.

Grant Thornton New Zealand Audit Limited

Grant Thornton

Ryan Campbell
Partner
Auckland

23 February 2021

ADDITIONAL INFORMATION

EQUITY SECURITIES HELD BY DIRECTORS AS AT 23 FEBRUARY 2021

	Interests in Ordinary Shares	
Director	**Direct**	**Indirect**
Trevor Scott	1,000,000	2,589,784
Dianne Angus	–	–
Patrick Davies	–	206,306
Jenny Harry	–	19,907

CEO Jon Pilcher and his Related Parties held 371,851 Ordinary Shares. He also had an interest in 1.5 million Loan Funded Shares held by Neuren Trustee Limited. As detailed in Note 10 to the Financial Statements, the Loan Funded Shares are subject to vesting conditions and repayment of a loan amounting to $1.84 per share before they can be transferred to Jon.

DIRECTORS OF SUBSIDIARY COMPANIES AT 31 DECEMBER 2020

	Jon Pilcher	**Larry Glass**	**Trevor Scott**
Neuren Pharmaceuticals Inc.	√	√	
Neuren Pharmaceuticals (Australia) Pty Ltd	√	√	
Neuren Trustee Limited			√

AUSTRALIAN STOCK EXCHANGE DISCLOSURES

Neuren Pharmaceuticals Limited is incorporated in New Zealand under the Companies Act 1993.

The Company is not subject to Chapters 6, 6A, 6B and 6C of the Corporations Act, Australia, dealing with the acquisition of shares (such as substantial holdings and takeovers).

Limitations on the acquisition of shares are imposed under New Zealand law are as follows:

(a) In general, securities in the Company are freely transferable and the only significant restrictions or limitations in relation to the acquisition of securities are those imposed by New Zealand laws relating to takeovers and overseas investment.

(b) The New Zealand Takeovers Code creates a general rule under which the acquisition of 20% or more of the voting rights in the Company or the increase of an existing holding of 20% or more of the voting rights of the Company can only occur in certain permitted ways. These include a full takeover offer in accordance with the Takeovers Code, a partial takeover in accordance with the Takeovers Code, an acquisition approved by an ordinary resolution, an allotment approved by an ordinary resolution, a creeping acquisition (in certain circumstances), or compulsory acquisition of a shareholder holding 90% or more of the shares.

(c) The New Zealand Overseas Investment Act 2005 and Overseas Investment Regulations 2005 (New Zealand) regulate certain investments in New Zealand by overseas interests. In general terms, the consent of the New Zealand Overseas Investment Office may be required where an 'overseas person' acquires shares in the Company that amount to 25% or more of the shares issued by the Company, or if the overseas person already holds 25% or more, the acquisition increases that holding.

ADDITIONAL INFORMATION

CONTINUED

EQUITY SECURITIES INFORMATION

The Company has only one class of shares, being ordinary shares. Each ordinary share is entitled to one vote when a poll is called; otherwise on a show of hands at a shareholder meeting every member present in person or by proxy has one vote. There are no securities subject to escrow and there is no current on-market buy-back of securities.

The following information is based on share registry information processed up to and including 16 April 2021.

The number of ordinary shareholdings held in less than marketable parcels at 26 April 2021 was 829, holding 128,795 ordinary shares.

DISTRIBUTION OF SECURITY HOLDERS

Ordinary shares

Size of holding	Number of ordinary shares	%	Number of holders	%
100,001 and Over	78,822,914	68.78	137	2.64
10,001 to 100,000	25,953,932	22.65	880	16.93
5,001 to 10,000	4,307,622	3.76	556	10.69
1,001 to 5,000	4,648,248	4.06	1,697	32.64
1 to 1,000	875,392	0.76	1,929	37.10
Total	**114,608,108**	**100.00**	**5,199**	**100.00**

ADDITIONAL INFORMATION

CONTINUED

Twenty largest holders of ordinary shares

	Number of ordinary shares	% of issued share capital
HSBC CUSTODY NOMINEES (AUSTRALIA) LIMITED-GSCO ECA	14,321,650	12.50
CAMERON RICHARD PTY LTD	5,865,240	5.12
CITICORP NOMINEES PTY LIMITED	4,811,785	4.20
STUART ANDREW PTY LTD	2,951,929	2.58
NATIONAL NOMINEES LIMITED	2,951,041	2.57
HSBC CUSTODY NOMINEES (AUSTRALIA) LIMITED	2,948,200	2.57
LINWIERIK SUPER PTY LTD	2,642,143	2.31
BRISPOT NOMINEES PTY LTD	2,482,733	2.17
ESSEX CASTLE LIMITED	2,369,251	2.07
SMITHLEY SUPER PTY LTD	2,140,000	1.87
HOBSON WEALTH CUSTODIANS LTD	1,580,145	1.38
MXB INVESTMENTS LLC	1,330,000	1.16
CS FOURTH NOMINEES PTY LIMITED	1,234,490	1.08
UBS NOMINEES PTY LTD	1,207,722	1.05
FIRST COLBYCO PTY LTD	1,028,520	0.90
DR TREVOR SCOTT	1,000,000	0.87
DR ROBIN LANCE CONGREVE	991,637	0.87
DR RICHARD SPENCER TREAGUS	903,500	0.79
BNP PARIBAS NOMINEES PTY LTD SIX SIS LTD	735,859	0.64
NAMARONG INVESTMENTS PTY LTD	555,556	0.48
Total	**54,051,401**	**47.16**
Balance of share register	60,556,707	52.84
Total ordinary shares quoted on ASX	**114,608,108**	**100.00**
Unquoted loan funded shares held by Neuren Trustee Limited[1]	3,000,000	
Total issued ordinary shares	**117,608,108**	

[1] *Loan Funded Share Plan described in Note 10 to the Financial Statements.*

pharmaceuticals

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