Neuren (NEU) – Q4 Activity Report **31 January 2022**

Positive Phase 3 trial results transforming event for Neuren

Highlights:

- **Robustly positive results in the Lavender™ Phase 3 trial of Trofinetide in Rett syndrome:**
  - **Both co-primary efficacy endpoints and key secondary endpoint demonstrated statistically significant improvement over placebo**
  - **Acadia plans to submit New Drug Application (NDA) to the US Food and Drug Administration (FDA) mid-year 2022, following a pre-NDA meeting in Q1 2022**
  - **NDA with Orphan Drug designation is eligible for Priority Review in 6 months**
- **Neuren expects to receive revenue over 2022 and 2023 for Rett syndrome in the US alone of A$111 million plus double-digit percentage royalties on net sales:**
  - **Two milestone payments and one third of the value of a Rare Pediatric Disease Priority Review Voucher**
- **Discussions with potential partners for trofinetide ex-North America progressing, with strong interest received from multiple parties**
- **NNZ-2591 for multiple neurodevelopmental disorders with global rights retained provides large potential upside:**
  - **Commencement of Phase 2 trials in Phelan-McDermid, Angelman and Pitt Hopkins syndromes pending FDA approval of amended protocols**
  - **Revised Angelman syndrome protocol has been submitted to FDA, Phelan-McDermid and Pitt Hopkins protocols to be submitted shortly**
  - **Prader-Willi Phase 2 trial planned for mid-2022**
- **$36.8 million cash at 31 December 2021 – well funded to execute NNZ-2591 trials and foundational work for Phase 3 across all indications**

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today filed its quarterly activity and cash flow report for Q4 2021.

Neuren CEO Jon Pilcher commented: “The robustly positive Phase 3 results for Rett syndrome ended a very successful year and have positioned Neuren for a much larger step-change in 2022. We expect material cash flows to commence from trofinetide in the US as the NDA process unfolds. In the meantime, I am highly encouraged by the level of interest from

potential partners for trofinetide outside North America, which has increased significantly following the Phase 3 results a month ago. Discussions are progressing as we work towards securing the best outcome for shareholders and for patients around the world."

Commentary on Q4 events and outlook

Trofinetide for Rett syndrome in North America

In December Neuren's partner for trofinetide in North America, Acadia Pharmaceuticals (Nasdaq: ACAD), announced positive top-line results from the pivotal, Phase 3 Lavender™ study evaluating the efficacy and safety of trofinetide in 187 girls and young women aged 5-20 years with Rett syndrome. The 12-week placebo-controlled study demonstrated a statistically significant improvement over placebo for both co-primary endpoints. On the Rett Syndrome Behaviour Questionnaire (RSBQ), change from baseline to week 12 was -5.1 vs. -1.7 (p=0.0175; effect size=0.37). The Clinical Global Impression–Improvement (CGI-I) score at week 12 was 3.5 vs. 3.8 (p=0.0030; effect size=0.47). The RSBQ is a caregiver assessment of the core symptoms of Rett syndrome and the CGI-I is a global physician assessment of worsening or improving of Rett syndrome. Additionally, trofinetide demonstrated a statistically significant separation over placebo on the key secondary endpoint, the Communication and Symbolic Behavior Scales Developmental Profile™ Infant-Toddler Checklist–Social composite score (CSBS-DP-IT–Social) change from baseline to week 12 was -0.1 vs. -1.1 (p=0.0064; effect size=0.43).

The trofinetide program has Orphan Drug, Fast Track and Rare Pediatric Disease designations from the FDA. Acadia is preparing for a pre-NDA meeting with the FDA in the first quarter of 2022 and plans to submit the NDA around mid-year 2022. A NDA with Orphan Drug Designation is eligible for Priority Review in 6 months, compared with the standard review period of 10 months.

The development and commercialisation of trofinetide in North America is fully funded by Acadia and Neuren is eligible to receive potential milestone payments of up to US$455 million, plus tiered escalating double-digit percentage royalties on net sales of trofinetide in North America, plus one third of the market value of a Rare Pediatric Disease Priority Review Voucher if awarded by the FDA upon approval of a NDA for trofinetide.

Neuren expects to receive revenue over 2022 and 2023 for Rett syndrome in the US alone of A$111 million, comprising two milestone payments and Neuren's share of a Rare Pediatric Disease Priority Review Voucher, as well as receiving double-digit percentage royalties on net

sales. This assumes a USD/AUD exchange rate of 0.75, launch of trofinetide in the US and that Neuren receives US$33 million as its share of the market value of the Priority Review Voucher.

Trofinetide for Rett syndrome ex-North America

Under the licence agreement with Acadia, Neuren retained all rights to trofinetide outside North America and has free and full access to all data for use in those countries. There is urgent unmet need for a treatment for Rett syndrome around the world. Neuren has received strong interest for potential commercial partnerships and the number of interested parties has increased significantly since the Phase 3 results were announced last month. Discussions are now in progress under a process to secure the best outcome for shareholders and for patients.

NNZ-2591 for multiple neurodevelopmental disorders

Neuren is preparing to commence Phase 2 trials in children and adolescents with each of Phelan-McDermid syndrome, Angelman syndrome and Pitt Hopkins syndrome, subject to approval by the FDA of amended trial protocols. Neuren has worked with expert clinical advisors to address all the detailed feedback that was received from the FDA following its review of the three Investigational New Drug (IND) Applications. The amended protocol for the Angelman syndrome trial has been submitted to the FDA, with the similarly amended Phelan-McDermid and Pitt Hopkins protocols to follow shortly. Neuren hopes to receive clearance from the FDA after 30-day reviews of each submission. All three programs are supervised by the FDA Office of Neuroscience, with Phelan-McDermid and Pitt Hopkins reviewed by the Division of Neurology 1 and Angelman reviewed by the Division of Psychiatry.

Neuren is also planning to commence Phase 2 clinical trial in Prader-Willi syndrome in mid-2022, as well as executing the foundational work to prepare for Phase 3 development of NNZ-2591 across all four syndromes. Neuren is well funded from current cash reserves to execute the Phase 2 trials and Phase 3 preparation.

Neuren has Orphan Drug designation from the FDA for NNZ-2591 in all four syndromes, which are serious neurodevelopmental disorders with no approved medicines. The number of potential patients across these syndromes is estimated to be more than five times the number of potential patients with Rett syndrome. Neuren retains full global rights to NNZ-2591.

Analyst valuations

Following the positive Phase 3 trial results in December, the analysts covering Neuren significantly increased their current risk-adjusted valuations, with the range now $5.05 to $7.70 per share. In addition, Neuren was selected by Bioshares as one of the “Top 6 Picks for 2022” and was added to its model portfolio.

Financials

Cash reserves increased to $36.8 million at 31 December 2021, from $33.6 million at 30 September 2021. In Q4 the receipt of $2.5 million under the R&D Tax Incentive program matched cash of $2.5 million used in operating activities. $3.3 million was received from the Share Purchase Plan. Payments to Related Parties of approximately $173,000 comprised the Managing Director's executive remuneration and non-executive directors' fees.

About Neuren

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

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

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

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

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ASX Listing Rules information

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

Forward-looking Statements

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

Appendix 4C

Quarterly cash flow report for entities subject to Listing Rule 4.7B

Name of entity	
Neuren Pharmaceuticals Limited	
ABN	**Quarter ended ("current quarter")**
72 111 496 130	31 December 2021

Consolidated statement of cash flows		**Current quarter $A'000**	**Year to date (12 months) $A'000**
1.	**Cash flows from operating activities**		
1.1	Receipts from customers	-	-
1.2	Payments for		
	(a) research and development	(1,731)	(9,799)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	-	-
	(d) leased assets	-	-
	(e) staff costs	(486)	(1,756)
	(f) administration and corporate costs	(364)	(990)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	8	54
1.5	Interest and other costs of finance paid	-	-
1.6	Income taxes paid	-	-
1.7	Government grants and tax incentives	2,521	2,521
1.8	Other (provide details if material)	-	-
1.9	**Net cash from / (used in) operating activities**	**(52)**	**(9,970)**

2.	**Cash flows from investing activities**		
2.1	Payments to acquire or for:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	(2)	(10)
	(d) investments	-	-
	(e) intellectual property	-	-
	(f) other non-current assets	-	-

Consolidated statement of cash flows		Current quarter $A'000	Year to date (12 months) $A'000
2.2	Proceeds from disposal of:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	-	-
	(d) investments	-	-
	(e) intellectual property	-	-
	(f) other non-current assets	-	-
2.3	Cash flows from loans to other entities	-	-
2.4	Dividends received (see note 3)	-	-
2.5	Other (provide details if material)	-	-
2.6	**Net cash from / (used in) investing activities**	**(2)**	**(10)**

3.	**Cash flows from financing activities**		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	3,281	23,281
3.2	Proceeds from issue of convertible debt securities	-	-
3.3	Proceeds from exercise of options	-	-
3.4	Transaction costs related to issues of equity securities or convertible debt securities	(51)	(1,106)
3.5	Proceeds from borrowings	-	-
3.6	Repayment of borrowings	-	-
3.7	Transaction costs related to loans and borrowings	-	-
3.8	Dividends paid	-	-
3.9	Other (provide details if material)	-	-
3.10	**Net cash from / (used in) financing activities**	**3,230**	**22,175**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	33,596	24,188
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(52)	(9,970)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	(2)	(10)

Consolidated statement of cash flows		Current quarter $A'000	Year to date (12 months) $A'000
4.4	Net cash from / (used in) financing activities (item 3.10 above)	3,230	22,175
4.5	Effect of movement in exchange rates on cash held	13	402
4.6	**Cash and cash equivalents at end of period**	**36,785**	**36,785**

5.	Reconciliation of cash and cash equivalents at the end of the quarter (as shown in the consolidated statement of cash flows) to the related items in the accounts	Current quarter $A'000	Previous quarter $A'000
5.1	Bank balances	6,912	19,508
5.2	Call deposits	29,873	14,088
5.3	Bank overdrafts	-	-
5.4	Other (provide details)	-	-
5.5	**Cash and cash equivalents at end of quarter (should equal item 4.6 above)**	**36,785**	**33,596**

6.	Payments to related parties of the entity and their associates	Current quarter $A'000
6.1	Aggregate amount of payments to related parties and their associates included in item 1	173
6.2	Aggregate amount of payments to related parties and their associates included in item 2	-

Note: if any amounts are shown in items 6.1 or 6.2, your quarterly activity report must include a description of, and an explanation for, such payments.

7.	**Financing facilities** *Note: the term "facility' includes all forms of financing arrangements available to the entity.* *Add notes as necessary for an understanding of the sources of finance available to the entity.*	**Total facility amount at quarter end $A'000**	**Amount drawn at quarter end $A'000**
7.1	Loan facilities	-	-
7.2	Credit standby arrangements	-	-
7.3	Other (please specify)	-	-
7.4	**Total financing facilities**	-	-

7.5	**Unused financing facilities available at quarter end**	-
7.6	Include in the box below a description of each facility above, including the lender, interest rate, maturity date and whether it is secured or unsecured. If any additional financing facilities have been entered into or are proposed to be entered into after quarter end, include a note providing details of those facilities as well.	

8.	**Estimated cash available for future operating activities**	**$A'000**
8.1	Net cash from / (used in) operating activities (item 1.9)	(52)
8.2	Cash and cash equivalents at quarter end (item 4.6)	36,785
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	36,785
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	707.4

Note: if the entity has reported positive net operating cash flows in item 1.9, answer item 8.5 as "N/A". Otherwise, a figure for the estimated quarters of funding available must be included in item 8.5.

8.6 If item 8.5 is less than 2 quarters, please provide answers to the following questions:

8.6.1 Does the entity expect that it will continue to have the current level of net operating cash flows for the time being and, if not, why not?

Answer: N/A

8.6.2 Has the entity taken any steps, or does it propose to take any steps, to raise further cash to fund its operations and, if so, what are those steps and how likely does it believe that they will be successful?

Answer: N/A

8.6.3 Does the entity expect to be able to continue its operations and to meet its business objectives and, if so, on what basis?

Answer: N/A

Note: where item 8.5 is less than 2 quarters, all of questions 8.6.1, 8.6.2 and 8.6.3 above must be answered.

Compliance statement

1 This statement has been prepared in accordance with accounting standards and policies which comply with Listing Rule 19.11A.

2 This statement gives a true and fair view of the matters disclosed.

Date: 31 January 2022

Authorised by: The Board
(Name of body or officer authorising release – see note 4)

Notes

1. This quarterly cash flow report and the accompanying activity report provide a basis for informing the market about the entity's activities for the past quarter, how they have been financed and the effect this has had on its cash position. An entity that wishes to disclose additional information over and above the minimum required under the Listing Rules is encouraged to do so.

2. If this quarterly cash flow report has been prepared in accordance with Australian Accounting Standards, the definitions in, and provisions of, *AASB 107: Statement of Cash Flows* apply to this report. If this quarterly cash flow report has been prepared in accordance with other accounting standards agreed by ASX pursuant to Listing Rule 19.11A, the corresponding equivalent standard applies to this report.

3. Dividends received may be classified either as cash flows from operating activities or cash flows from investing activities, depending on the accounting policy of the entity.

4. If this report has been authorised for release to the market by your board of directors, you can insert here: "By the board". If it has been authorised for release to the market by a committee of your board of directors, you can insert here: "By the [*name of board committee – eg Audit and Risk Committee*]". If it has been authorised for release to the market by a disclosure committee, you can insert here: "By the Disclosure Committee".

5. If this report has been authorised for release to the market by your board of directors and you wish to hold yourself out as complying with recommendation 4.2 of the ASX Corporate Governance Council's *Corporate Governance Principles and Recommendations*, the board should have received a declaration from its CEO and CFO that, in their opinion, the financial records of the entity have been properly maintained, that this report complies with the appropriate accounting standards and gives a true and fair view of the cash flows of the entity, and that their opinion has been formed on the basis of a sound system of risk management and internal control which is operating effectively.