Neuren (NEU) – Q3 Activity Report **28 October 2021**

Neuren in strong financial position with Phase 3 trial results imminent

Highlights:

- **$33.6 million cash at 30 September 2021, with $3.3 million from SPP received in October and $2.5 million R&D Tax Incentive expected to be received in November**
- **Successful capital raise has placed Neuren in a very strong financial position to capitalise on a potentially transformative milestone**
- **Top-line results of the LAVENDER Phase 3 trial of trofinetide in Rett syndrome are due before the end of 2021**
- **Positive results could have a large economic impact:**
    - **Potential for Neuren to receive revenue over 2022 and 2023 for Rett syndrome in the US alone of A$111 million plus royalties on net sales**
    - **Expected to enable Neuren to engage commercial partners for Europe and Asia**
- **Large upside of NNZ-2591 for multiple neurodevelopmental disorders with global rights retained:**
    - **Awaiting confirmation of FDA requirements to start Phase 2 trials in Phelan-McDermid, Angelman and Pitt Hopkins syndromes**
    - **FDA granted Orphan Drug designation for Prader-Willi syndrome – Phase 2 trial planned to start mid-2022**
    - **New US patent granted to 2034 for treatment of autism**
    - **Funded to execute foundational work required for Phase 3 across all indications**

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today filed its quarterly activity and cash flow report for Q3 2021.

Neuren CEO Jon Pilcher commented: "We are excited that the last patients are now finishing treatment in the trofinetide Phase 3 trial in Rett syndrome and the top-line results are imminent. As we approach this potentially transformative milestone, the recent successful capital raise has placed Neuren in a very strong financial position to be able to optimize the value of both trofinetide and NNZ-2591. We will work with the FDA to clear the barriers to starting the keenly awaited NNZ-2591 Phase 2 trials as soon as possible."

Commentary on Q3 events and outlook

Rett syndrome Phase 3 trial

In early August Neuren's US partner for trofinetide, Acadia Pharmaceuticals (Nasdaq: ACAD), completed enrolment in the LAVENDER Phase 3 trial of trofinetide in Rett syndrome on schedule to enable top-line results from the trial before the end of 2021. LAVENDER is a 12 week, double-blind, placebo-controlled study in approximately 180 females aged 5 to 20 years. In September Acadia also commenced DAFFODIL, an additional clinical study of trofinetide in approximately 10 girls aged 2 to 5 years. DAFFODIL is a 12-week, open-label, safety, tolerability and pharmacokinetics study in this younger age group. The trofinetide program has Orphan Drug, Fast Track and Rare Pediatric Disease designations from the US Food and Drug Administration (FDA).

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 New Drug Application for trofinetide. In addition, Neuren has free and full access to all data for use in countries outside North America. As well as enabling a New Drug Application in the US, positive results from the Phase 3 trial should enable Neuren to commercialise trofinetide in Europe and Asia. In September the Brazilian patent office issued a notice of allowance for Neuren's first patent in Brazil, which covers the treatment of Rett syndrome using trofinetide until 2032.

Neuren would earn revenue over 2022 and 2023 for Rett syndrome in the US alone of A$111 million plus double-digit percentage royalties on net sales if the results of the LAVENDER Phase 3 trial are positive, a New Drug Application is approved by the FDA and trofinetide is launched in the US. This assumes a USD/AUD exchange rate of 0.75 and that Neuren receives US$33 million as its share of the market value of a Rare Pediatric Disease Priority Review Voucher awarded on approval of a New Drug Application.

NNZ-2591 for multiple neurodevelopmental disorders

In September Neuren submitted to the FDA three Investigational New Drug (IND) applications for clearance to start Phase 2 trials in each of Phelan-McDermid syndrome, Angelman syndrome and Pitt Hopkins syndrome. Following the 30-day review of the first two applications for Angelman and Phelan-McDermid syndromes, the FDA placed those INDs on hold, pending issue

of formal hold letters within 30 days. All three INDs 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. After receiving the formal clinical hold letters, Neuren will work with the Office of Neuroscience to resolve any requirements to proceed with these first trials in patients as quickly as possible.

In September the FDA granted Orphan Drug designation to NNZ-2591 for the treatment of Prader-Willi syndrome (PWS). Neuren previously announced positive results in the *Magel2*-null mouse model of PWS, in which treatment with NNZ-2591 for 6 weeks normalized fat mass, insulin levels, IGF-1 levels and all behavioural deficits. The successful capital raising undertaken following the Orphan Drug designation has enabled Neuren to plan a Phase 2 clinical trial in PWS to commence in mid-2022 and the foundational work to get ready for Phase 3 development of NNZ-2591 across all four syndromes.

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.

In October Neuren received a Notice of Allowance from the US Patent and Trademark Office for a new patent to 2034 that covers NNZ-2591 to treat autism. Similar claims have previously been granted in Europe and Japan.

Financials

Cash reserves at 30 September 2021 were $33.6 million, compared with $18.2 million at 30 June 2021. Subsequently in October $3.3 million was received from the oversubscribed Share Purchase Plan (SPP) and $2.5 million is expected to be received in November under the R&D Tax Incentive program, for eligible expenditure in 2020.

In Q3 net cash of $3.8 million was used in operating activities, with R&D payments of $3.1 million mainly relating to the NNZ-2591 Phase 2 clinical trials. Net proceeds of approximately $19 million were received from the placement of new shares to institutional and sophisticated investors, which was completed in September at A$2.05 per share. 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, is currently in a Phase 3 clinical trial for Rett syndrome with top-line results expected in Q4 2021 and has completed a Phase 2 clinical trial in Fragile X syndrome. Both programs have 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 for 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	30 September 2021

Consolidated statement of cash flows		**Current quarter $A'000**	**Year to date (9 months) $A'000**
1.	**Cash flows from operating activities**		
1.1	Receipts from customers	-	-
1.2	Payments for		
	(a) research and development	(3,098)	(8,068)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	-	-
	(d) leased assets	-	-
	(e) staff costs	(486)	(1,270)
	(f) administration and corporate costs	(202)	(626)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	13	46
1.5	Interest and other costs of finance paid	-	-
1.6	Income taxes paid	-	-
1.7	Government grants and tax incentives	-	-
1.8	Other (provide details if material)	-	-
1.9	**Net cash from / (used in) operating activities**	**(3,773)**	**(9,918)**

2.	**Cash flows from investing activities**		
2.1	Payments to acquire or for:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	-	(8)
	(d) investments	-	-
	(e) intellectual property	-	-
	(f) other non-current assets	-	-

Consolidated statement of cash flows		Current quarter $A'000	Year to date (9 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**	**-**	**(8)**

3.	**Cash flows from financing activities**		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	20,000	20,000
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	(1,055)	(1,055)
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**	**18,945**	**18,945**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	18,220	24,188
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(3,773)	(9,918)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	-	(8)

Consolidated statement of cash flows		Current quarter $A'000	Year to date (9 months) $A'000
4.4	Net cash from / (used in) financing activities (item 3.10 above)	18,945	18,945
4.5	Effect of movement in exchange rates on cash held	204	389
4.6	**Cash and cash equivalents at end of period**	**33,596**	**33,596**

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	19,508	392
5.2	Call deposits	14,088	17,828
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)**	**33,596**	**18,220**

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)	(3,773)
8.2	Cash and cash equivalents at quarter end (item 4.6)	33,596
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	33,596
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	8.9

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: 28 October 2021

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.