Neuren (NEU) – Q2 Activity Report **30 July 2021**

Neuren on track for Phase 3 trial results in Q4 and three Phase 2 trials in H2

Highlights:

- **LAVENDER Phase 3 trial of trofinetide in Rett syndrome is on track for top-line results in Q4 2021**
- **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**
- **$18.2 million cash at 30 June 2021:**
  - **US partner Acadia is fully funding the trofinetide Phase 3 program**
  - **Neuren is funded to achieve Phase 2 data in 2022 for NNZ-2591 in three indications**
- **Clear and constructive guidance received from pre-IND meetings with the FDA for Phase 2 clinical trials of NNZ-2591 in Phelan-McDermid, Angelman and Pitt Hopkins syndromes**
- **Phase 2 trials are all on track to commence in H2 2021, with top-line results in H2 2022**
- **Currently targeted markets for NNZ-2591, for which Neuren retains global rights, are estimated to be more than five times the Rett syndrome market**
- **Published analyst risk-adjusted valuations of Neuren pre-Phase 3 results are A$368 million to A$450 million - versus Neuren's current market capitalisation of A$185 million**

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today filed its quarterly activity and cash flow report for Q2 2021.

Neuren CEO Jon Pilcher commented: "In Q2 Neuren continued to drive towards three critical milestones expected over the remainder of 2021 - completion of enrolment in the Rett syndrome Phase 3 trial, commencement of three Phase 2 trials for NNZ-2591, followed by the top-line results of the Phase 3 trial. We are very excited to be advancing into this transformational period for the business, pursuing both the near-term revenue opportunity in Rett syndrome and the large potential upside in value from global rights to NNZ-2591 in multiple indications."

Commentary on Q2 events and outlook

Rett syndrome Phase 3 trial

During Q2 Neuren's US partner for trofinetide, Acadia Pharmaceuticals (Nasdaq: ACAD), advanced further towards completion of enrolment in the LAVENDER Phase 3 trial of trofinetide in Rett syndrome, remaining on track for top-line results from the 12 weeks trial in Q4 2021. The 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. Positive results from the Phase 3 trial should enable Neuren to commercialise trofinetide in Europe and Asia, as well as enabling a New Drug Application in the US.

Phase 2 trials in Phelan-McDermid, Angelman and Pitt Hopkins syndromes

In Q2 Neuren conducted three pre-IND meetings with the FDA Office of Neuroscience to discuss the proposed Phase 2 clinical trials for NNZ-2591 in patients with each of Phelan-McDermid syndrome, Angelman syndrome and Pitt Hopkins syndrome. The clear and constructive guidance from the FDA has enabled Neuren to proceed with preparing Investigational New Drug (IND) applications for clearance to start the trials. Subject to that clearance, the trials will commence as planned in H2 2021. In parallel with the IND applications, across all three disorders Neuren is completing the preparations for the trials with the patient communities, the clinical trial sites and CROs. Neuren aims to obtain top-line results from the trials in H2 2022.

The number of potential patients across the disorders currently targeted by NNZ-2591 is estimated to be more than five times the number of potential patients with Rett syndrome. Neuren retains full global rights to NNZ-2591.

Financials

Cash reserves at 30 June 2021 were $18.2 million, funding Neuren through to achieving Phase 2 data for NNZ-2591 in three indications while Acadia fully funds the trofinetide Phase 3 program.

In Q2 net cash of $4.4 million was used in operating activities, with R&D payments of $3.8 million mainly comprising the NNZ-2591 Phase 1 clinical trial, manufacture of drug for clinical trials and non-clinical studies. Payments to Related Parties of approximately $80,000 comprised non-executive directors' fees.

If the results of the Rett syndrome Phase 3 trial are positive, a New Drug Application is approved by the FDA and trofinetide is launched in the US, 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. 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. There is no cost associated with this revenue.

The currently published analysts' risk-adjusted discounted cash flow valuations of Neuren before the Phase 3 results range from A$368 million to A$450 million. Neuren's current market capitalisation of A$185 million is between 40% and 50% of those valuations.

2021 milestones progress

- ✓ EU Orphan designations for Phelan-McDermid, Angelman, and Pitt Hopkins
- ✓ Successful Phase 1 trial results for NNZ-2591
- ✓ Prader-Willi syndrome added to NNZ-2591 pipeline
- ✓ Complete drug substance manufacturing for NNZ-2591 Phase 2
- ✓ Pre-IND meetings with FDA to agree NNZ-2591 Phase 2 plans
- **Acadia completes enrolment in trofinetide Rett syndrome Phase 3**
- **Submit NNZ-2591 INDs to FDA**
- **Commence NNZ-2591 Phase 2 trials**
- **Orphan designation for Prader-Willi syndrome**
- **Trofinetide Rett syndrome Phase 3 top-line results**

About Neuren

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

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

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

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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 June 2021

Consolidated statement of cash flows		**Current quarter $A'000**	**Year to date (6 months) $A'000**
1.	**Cash flows from operating activities**		
1.1	Receipts from customers	-	-
1.2	Payments for		
	(a) research and development	(3,803)	(4,970)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	-	-
	(d) leased assets	-	-
	(e) staff costs	(422)	(784)
	(f) administration and corporate costs	(186)	(424)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	12	33
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**	**(4,399)**	**(6,145)**

2.	**Cash flows from investing activities**		
2.1	Payments to acquire or for:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	(4)	(8)
	(d) investments	-	-
	(e) intellectual property	-	-
	(f) other non-current assets	-	-

Consolidated statement of cash flows		Current quarter $A'000	Year to date (6 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**	**(4)**	**(8)**

3.	**Cash flows from financing activities**		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	-	-
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	-	-
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**	**-**	**-**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	22,554	24,188
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(4,399)	(6,145)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	(4)	(8)

Consolidated statement of cash flows		Current quarter $A'000	Year to date (6 months) $A'000
4.4	Net cash from / (used in) financing activities (item 3.10 above)	-	-
4.5	Effect of movement in exchange rates on cash held	69	185
4.6	**Cash and cash equivalents at end of period**	**18,220**	**18,220**

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	392	759
5.2	Call deposits	17,828	21,795
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)**	**18,220**	**22,554**

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	80
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)	(4,399)
8.2	Cash and cash equivalents at quarter end (item 4.6)	18,220
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	18,220
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	4.1

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: 29 July 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.