Neuren (NEU) – ASX Announcement **22 April 2021**

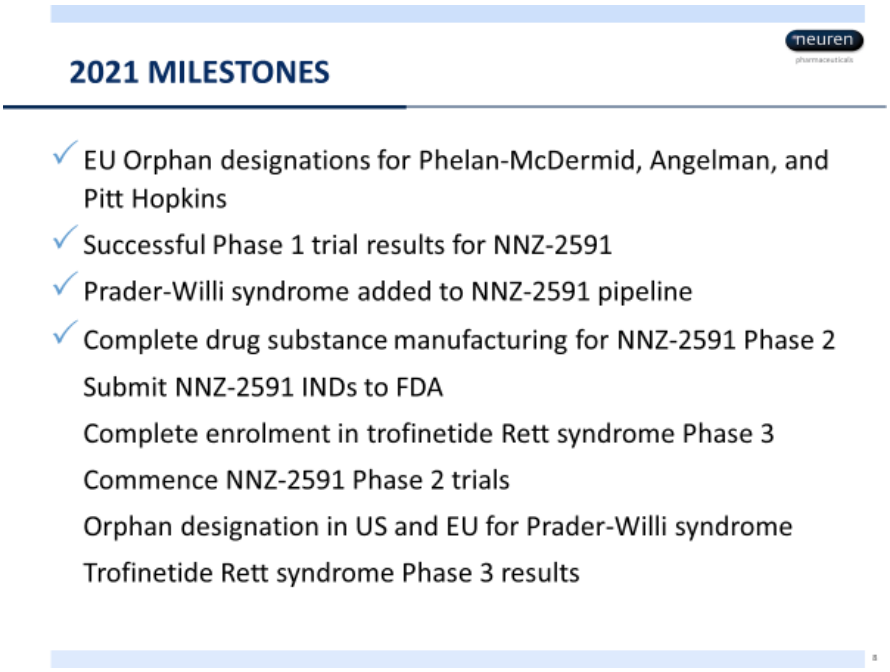
Neuren Q1 update: advancing to Phase 3 trial results and three Phase 2 trials

Highlights:

- **Neuren and Acadia (Neuren's US partner for trofinetide) advancing to results from Rett syndrome LAVENDER Phase 3 trial in Q4 2021:**
  - **Enrolment on track for results in Q4 – 19 sites now open**
  - **Head of Rare Disease appointed to Acadia's executive team**
  - **Acadia's expenditure on external service providers for trofinetide approximately A$100 million from commencement of partnership to 31 Dec 2020**
- **Neuren on track to commence Phase 2 trials of NNZ-2591 in Phelan-McDermid, Angelman and Pitt Hopkins syndromes:**
  - **Successful Phase 1 trial – dosing for seven days safe and well tolerated at all doses**
  - **Completed drug substance manufacturing to supply trials**
  - **Preparing for FDA meetings and IND applications in Q2 2021**
- **Commercial value of NNZ-2591 increased:**
  - **Three orphan designations granted in the European Union**
  - **Proprietary process developed for large scale manufacturing with exceptional purity and high yield**
  - **Prader-Willi syndrome added to pipeline with compelling pre-clinical model results**
- **Discussions ongoing with potential partners for markets in Asia**
- **$22.6 million cash at 31 March 2021:**
  - **Acadia fully funding the trofinetide Phase 3 program**
  - **Neuren is funded to achieve Phase 2 data for NNZ-2591 in three indications**

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today filed its quarterly activity and cash flow Report for Q1 2021.

Neuren CEO Jon Pilcher commented: "In Q1 we significantly added to Neuren's value by achieving the first four of the milestones for 2021. We are now focused on obtaining FDA clearance for the NNZ-2591 Phase 2 trials and look forward to the results of the trofinetide Phase 3 trial in Rett syndrome in Q4."



Commentary on Q1 events and outlook

Rett syndrome Phase 3 trial

Neuren's US partner for trofinetide, Acadia Pharmaceuticals, is advancing towards top-line results of the Rett syndrome LAVENDER Phase 3 trial in Q4 2021. Enrolment in the trial remains on track with 19 trial sites now open in the United States. In February Acadia announced the appointment of Kathie Bishop PhD to its executive management team as Head of Rare Disease. Acadia's substantial commitment to trofinetide was illustrated by its 2020 10k Annual Report, which detailed expenditure from commencement of the partnership to 31 December 2020 of US$78 million (~A$100 million) on external service providers.

The development and commercialisation of trofinetide in North America is fully funded by Acadia and Neuren may receive milestone payments of up to US$455 million, double digit percentage royalties on all sales, plus one third of the sale value of a Priority Review Voucher. In addition, Neuren has free and full access to all data for use in countries outside North America. Acadia is a NASDAQ listed company (ACAD) that specialises in commercialising and developing breakthroughs in neuroscience.

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

Neuren's near-term milestones include the commencement of Phase 2 clinical trials for NNZ-2591 in patients with each of Phelan-McDermid syndrome, Angelman syndrome and Pitt Hopkins syndrome. Neuren is preparing to meet with the US Food and Drug Administration (FDA) and then submit Investigational New Drug (IND) applications in Q2 2021. The INDs will include data from manufacturing, non-clinical studies and the Phase 1 clinical trial, as well as the Phase 2 trial protocols.

The Phase 1 trial was successfully completed, with dosing for seven days safe and well tolerated at all dose levels tested in healthy volunteers. There were no serious adverse events or clinically significant findings from safety laboratory tests, vital signs or cardiac tests. In parallel with completing the Phase 1 trial, the program of non-clinical safety studies was completed, the drug substance manufacturing campaign to supply the Phase 2 trials was successfully completed and Neuren has continued to engage with the patient communities and key physicians across all three disorders in preparation for the Phase 2 trials.

NNZ-2591 commercial value

The underlying commercial value of NNZ-2591 was significantly increased by three important milestones achieved in Q1.

First, orphan designation was received for NNZ-2591 in each of Phelan-McDermid, Angelman and Pitt Hopkins syndromes in the European Union, which means that Neuren now has orphan designation for all three in both the US and the EU. 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.

Second, the successful completion of manufacturing for Phase 2 confirmed the development of a proprietary process for large scale manufacturing with exceptional purity and high yield, which is a key part of the NNZ-2591 asset. As well as supplying the upcoming trials, the campaign produced enough drug substance at no extra cost to supply a Phase 2 trial in Prader-Willi syndrome.

Third, following highly encouraging results in a pre-clinical model, Prader-Willi syndrome was added to the development pipeline for NNZ-2591. Neuren plans to submit applications for orphan drug designation in the US and Europe. The foundational data for NNZ-2591 from manufacturing, non-clinical studies and the Phase 1 trial should also enable an Investigational New Drug application (IND) and Phase 2 development for Prader-Willi syndrome. Neuren intends to use that foundational data further by investigating additional indications.

Asia markets and financials

Neuren is continuing to explore commercialisation options with potential partners for markets in Asia including China. To date the potential for Neuren's products in Asia has not been factored into any analyst valuations.

Cash reserves at 31 March 2021 were $22.6 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 item 6 of the Appendix 4C cash flow report for the quarter, payments to Related Parties of approximately $77,000 comprised 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 drug compound, trofinetide, is currently in a Phase 3 clinical trial for Rett syndrome and has completed a Phase 2 clinical trial in Fragile X syndrome. Both programs have been granted Fast Track designation by the US Food and Drug Administration (FDA). Neuren has granted an exclusive licence to ACADIA Pharmaceuticals Inc. for the development and commercialisation of trofinetide in North America, while retaining all rights outside North America.

Neuren plans 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 2021. Neuren is also preparing for 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	31 March 2021

Consolidated statement of cash flows		**Current quarter $A'000**	**Year to date (3 months) $A'000**
1.	**Cash flows from operating activities**		
1.1	Receipts from customers	-	-
1.2	Payments for		
	(a) research and development	(1,167)	(1,167)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	-	-
	(d) leased assets	-	-
	(e) staff costs	(362)	(362)
	(f) administration and corporate costs	(238)	(238)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	21	21
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**	**(1,746)**	**(1,746)**

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

Consolidated statement of cash flows		Current quarter $A'000	Year to date (3 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)**	**(4)**

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	24,188	24,188
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(1,746)	(1,746)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	(4)	(4)

Consolidated statement of cash flows		Current quarter $A'000	Year to date (3 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	116	116
4.6	**Cash and cash equivalents at end of period**	**22,554**	**22,554**

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	759	229
5.2	Call deposits	21,795	23,959
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)**	**22,554**	**24,188**

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	77
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)	(1,746)
8.2	Cash and cash equivalents at quarter end (item 4.6)	22,554
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	22,554
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	12.9

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: 22 April 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.