Neuren (NEU) - ASX Announcement **29 July 2022**

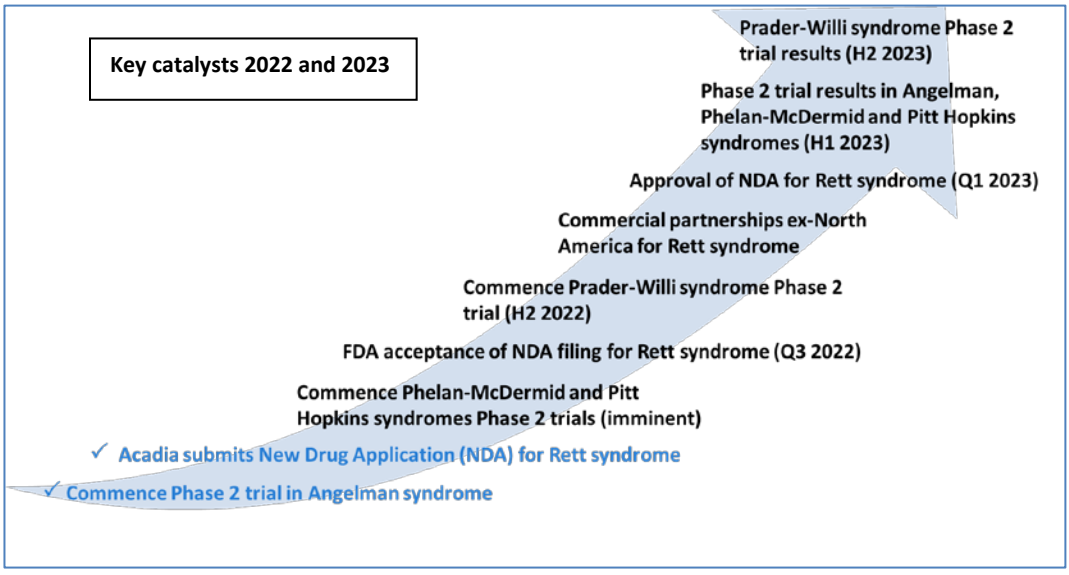
Q2 2022 Activity Report

Highlights:

- **Acadia submitted a New Drug Application (NDA) to the US Food and Drug Administration (FDA) for trofinetide for the treatment of Rett syndrome in adults and pediatric patients two years of age and older**
- **Subject to approval of the NDA, Neuren expects to receive revenue over 2022 and 2023 for Rett syndrome in the US alone of A$118 million plus double-digit percentage royalties on net sales**
- **Discussions with potential partners for trofinetide ex-North America are continuing**
- **Phase 2 clinical trial of NNZ-2591 in Angelman syndrome commenced**
- **$31.1 million cash at 30 June 2022 – well funded to execute NNZ-2591 Phase 2 trials and foundational work for Phase 3 across all indications, notwithstanding the anticipated material cash flows from trofinetide**

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today filed its quarterly activity and cash flow report for Q2 2022.

Neuren CEO Jon Pilcher commented: "Submission of the NDA for trofinetide in Rett syndrome is another major step forward. It marks the start of a series of catalysts over 2022 and 2023 that have the potential to transform the underlying value of Neuren's business."



Commentary on events since 31 March and outlook

Trofinetide for Rett syndrome

In July 2022, Neuren's US partner Acadia Pharmaceuticals (Nasdaq: ACAD) submitted a New Drug Application (NDA) to the US Food and Drug Administration (FDA) for trofinetide for the treatment of Rett syndrome in adults and pediatric patients two years of age and older.

The trofinetide program has Orphan Drug, Fast Track and Rare Pediatric Disease designations from the FDA. A NDA with Orphan Drug Designation is eligible for Priority Review in 6 months, compared with the standard review period of 10 months. The Review period commences when FDA formally accepts the NDA for review, which is due 60 days after its submission. Neuren therefore anticipates a decision on approval in March 2023, provided the NDA is accepted and receives Priority Review.

Acadia has exclusive rights to develop and commercialize trofinetide in North America. Under the terms of Neuren's agreement with Acadia, the development and commercialisation of trofinetide in North America is fully funded by Acadia and Neuren may receive potential milestone payments of up to US$455 million, plus 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.

If the NDA is approved by the FDA, Neuren expects to earn revenue over 2022 and 2023 for Rett syndrome in the US alone of A$118 million plus double-digit percentage royalties on net sales. The expected revenue in addition to the royalties comprises:

- A milestone payment in 2022 of US$10 million (A$14 million at assumed exchange rate of 0.70) following acceptance of the NDA for review by the FDA
- A milestone payment in 2023 of US$40 million (A$57 million), following the first commercial sale of trofinetide in the United States
- US$33 million (A$47 million) in 2023 as Neuren's one third share of the market value of a Priority Review Voucher, estimated as US$100 million.

Neuren's additional ongoing revenue from potential sales has two components:

- Double digit percentage royalties on net sales of trofinetide in all indications. The annual net sales are recorded in tiers and an escalating percentage is applied to each successive tier.
- Payments of up to US$350 million (approximately A$500 million) on achievement of a series of 4 thresholds of total annual net sales for all indications.

No royalties or similar costs are payable by Neuren to third parties, which means that Neuren's revenue from Acadia will flow through to pre-tax profit.

Neuren retained all rights to trofinetide for all countries outside North America and has a fully paid-up, irrevocable licence for use in those countries to all data generated by Acadia. Rett syndrome is a devastating condition with no approved therapies and there is urgent unmet need around the world for a treatment. Neuren has received strong interest for potential commercial partnerships and discussions are continuing under a process to secure the optimum outcome for shareholders and for patients.

NNZ-2591 for multiple neurodevelopmental disorders

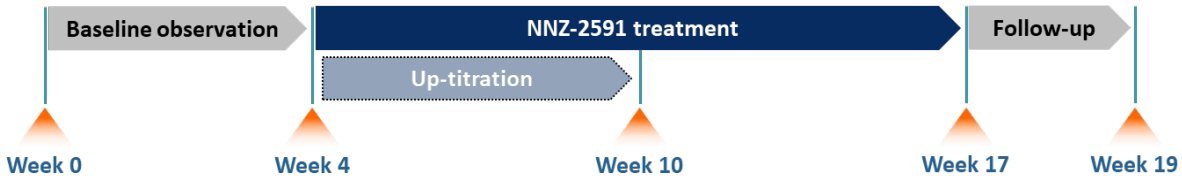
In July 2022, Neuren announced the commencement of its Phase 2 clinical trial of NNZ-2591 in Angelman syndrome. The open label Phase 2 trial will enrol a single group of up to 20 children aged 3 to 17 years with AS to examine safety, tolerability, pharmacokinetics and efficacy over 13 weeks of treatment with NNZ-2591. All subjects will receive NNZ-2591 as an oral liquid dose twice daily, with titration up to the target mg/kg dose during the first 6 weeks of treatment, subject to safety and tolerability. The treatment period is preceded by 4 weeks of observation to thoroughly examine the baseline characteristics prior to treatment, against which safety and efficacy will be assessed for each child. A follow-up assessment will be made 2 weeks after end of treatment.

Neuren also expects imminently to commence Phase 2 clinical trials of NNZ-2591 for each of Phelan-McDermid syndrome (PMS) and Pitt Hopkins syndrome (PTHS). Top-line results from all three trials are anticipated in H1 2023. Neuren is also planning a Phase 2 trial in a fourth disorder, Prader-Willi syndrome, with results targeted for H2 2023.

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 estimated number of potential patients being targeted across these four disorders is more than five times larger than Rett syndrome. Neuren retains all global rights to NNZ-2591.

The overall aim of these first trials in patients is to expedite the generation of data that will enable the subsequent trials to be designed as registration trials. Prioritising fast enrolment of subjects, the AS trial is being conducted in Australia, whilst the PMS and PTHS trials are being conducted in the US.

	PMS	PTHS	AS
Subjects	Up to 20, aged 3 to 12	Up to 20, aged 3 to 17	Up to 20, aged 3 to 17
Number of sites	4 (US)	5 (US)	3 (Australia)
www.clinicaltrials.gov	NCT05025241	NCT05025332	NCT05011851



In order to expedite the overall development plan, in parallel with conducting the Phase 2 trials Neuren is executing the additional development work required to be ready for Phase 3 development. This includes non-clinical toxicity studies to support longer clinical trials and commercial use of the product, as well as optimisation of the drug product and drug substance manufacturing arrangements.

Neuren is well funded from current cash reserves to execute the Phase 2 trials and Phase 3 preparation, notwithstanding the anticipated material cash flows from trofinetide.

Investor relations

Since 31 March, Neuren has presented at the healthcare conferences of Jefferies, Goldman Sachs, PAC Partners, Euroz Hartleys and Bioshares. Presentations are scheduled at the Evans & Partners and Wilsons healthcare conferences, as well as the ASX Small and Mid-Cap conference.

Neuren is now covered by six analysts, with coverage initiated during Q2 by Petra Capital, Jefferies and PAC Partners.

Financials

Cash reserves at 30 June 2022 were $31.1 million, compared with $34.1 million at 31 March 2022. In Q2 net cash of $3.3 million was used in operating activities, with R&D payments of $2.5 million mainly relating to the NNZ-2591 Phase 2 clinical trials and the foundational work to prepare for Phase 3 development of NNZ-2591 across multiple indications. The carrying value in AUD of USD cash held to mitigate exchange rate risk for USD expenditure increased by $0.3m for the quarter, due to the strengthening of the USD against the AUD. Payments to related parties of approximately $202,000 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 initiating 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 June 2022

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	(2,470)	(3,740)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	-	-
	(d) leased assets	-	-
	(e) staff costs	(685)	(1,275)
	(f) administration and corporate costs	(227)	(834)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	20	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**	**(3,362)**	**(5,816)**

2.	**Cash flows from investing activities**		
2.1	Payments to acquire or for:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	(5)	(10)
	(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**	**(5)**	**(10)**

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	-	(2)
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**	**-**	**(2)**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	34,126	36,783
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(3,362)	(5,816)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	(5)	(10)

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)	-	(2)
4.5	Effect of movement in exchange rates on cash held	329	133
4.6	**Cash and cash equivalents at end of period**	**31,088**	**31,088**

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	3,888	5,731
5.2	Call deposits	27,200	28,395
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)**	**31,088**	**34,126**

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	202
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)	(3,362)
8.2	Cash and cash equivalents at quarter end (item 4.6)	31,088
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	31,088
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	9.2

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 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.