Neuren (NEU) – ASX Announcement **24 April 2024**

Q1 2024 Activity Report

Financials:

- **Net cash from operating activities for Q1 2024: A$8.0 million, including receipt of $13.4 million royalties for Q4 2023**
- **Cash and short-term investments at 31 March 2024: A$243.1 million (31 December 2023: A$228.5 million)**

DAYBUE™ (trofinetide) for Rett syndrome:

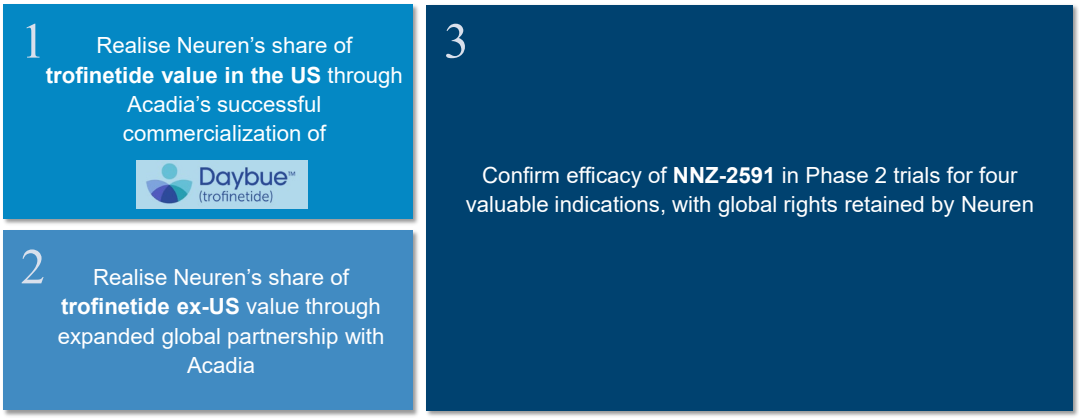
- **Highly successful United States launch by partner Acadia Pharmaceuticals:**
  - **Net sales of US$177.2 million for 2023 (earning Neuren royalties of A$27)**
  - **Guidance for net sales in 2024 of US$370-420 million (which would earn Neuren royalties of A$61-70 million plus sales milestone revenue of A$77 million)**
  - **Guidance for net sales in Q1 2024 of US$76-82 million (which would earn Neuren royalties of A$11.7-12.6 million)**
- **Additional longer-term efficacy and tolerability data from Daffodil study in Rett syndrome patients aged 2-4 years presented at American Academy of Neurology:**
  - **Mean CGI-I score improved to 2.2 at 78 weeks**
  - **80% of patients completed the study**
  - **100% of completers had CGI-I score ≤ 3, while 58% of completers had CGI-I score ≤ 2**
- **Acadia advancing outside the United States:**
  - **Canada: New Drug Submission accepted for Priority Review, potential approval around year-end 2024**
  - **Europe: currently engaging with EMA, MAA filing in H1 2025**
  - **Japan: engaging regulatory agency (PMDA) in 2024**

NNZ-2591:

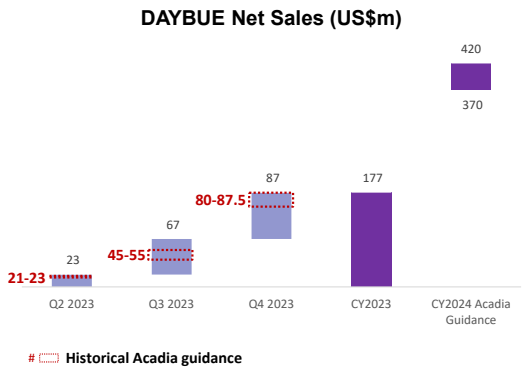
- **Extensive preparations in progress for End of Phase 2 Meeting with FDA for Phelan-McDermid syndrome in Q3 2024**
- **All subject visits completed on schedule in Pitt Hopkins syndrome Phase 2 trial – on track for top-line results in Q2 2024**
- **Last subjects progressing towards completion of Angelman syndrome Phase 2 trial - on track for top-line results in Q3 2024**

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today filed its Activity Report and cash flow statement for Q1 2024. Neuren CEO Jon Pilcher commented: "We remain on track for an exciting year of catalysts across all three value drivers in our business. DAYBUE™ in the US is delivering to Neuren substantial and growing cash flows, Acadia is making good progress towards expansion outside the US and Neuren is approaching results from two more indications for NNZ-2591 whilst preparing for an End of Phase 2 Meeting with FDA for Phelan-McDermid syndrome."

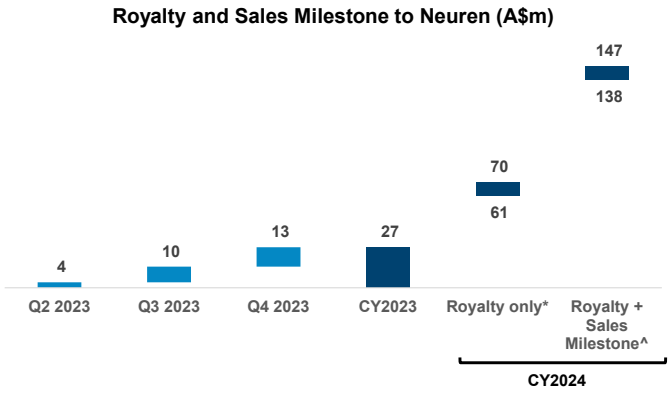
There are three key drivers adding value to Neuren's business:



1. DAYBUE in North America



2023 net sales of US$177m
2024E net sales of US$370 – 420m



2023E royalty of A$27m
2024E royalty of A$61 – 70m, plus A$77m sales milestone

* Based on 10% of DAYBUE net sales up to US$250m and 12% of DAYBUE net sales between US$250m and US$500m, and AUDUSD of 0.65
^ Neuren will be entitled to US$50m sales milestones (receivable in Q1 2025) if CY2024 DAYBUE net sales reaches US$250m; assumes AUDUSD of 0.65

Neuren's partner Acadia Pharmaceuticals (NASDAQ: ACAD) launched DAYBUE™ (trofinetide) in the United States in April 2023 as the first and only approved treatment for Rett syndrome. Net sales grew rapidly to reach US$177 million for 2023, delivering royalties of A$27 million to Neuren.

Acadia has provided guidance for net sales in 2024 of US$370-420 million. Assuming this is met and an exchange rate of 0.65, Neuren would earn royalties of A$61-70 million (US$39-45 million), plus A$77 million (US$50 million) from the first sales milestone payment due for the first calendar year in which net sales exceed US$250 million.

Seasonality between December and February is common for prescription drugs. Since the launch was in April, this was the first period of experience for DAYBUE and Acadia reported two seasonal impacts. Early re-fills in anticipation of the holiday season resulted in a shift in net sales of approximately US$3 million from January to December. Q1 2024 net sales was also negatively impacted by reduced or no clinic days in January at approximately half of the Rett syndrome Centers of Excellence which currently contribute approximately 40% of the new patient prescriptions. This recovered strongly in February, with prescription rates returning to trends observed prior to January. Acadia has provided guidance for net sales in Q1 2024 of US$76 to 82 million, which is included in the full-year guidance of US$370-420 million for 2024. Acadia is expected to report financial results for Q1 2024 next month.

At the recent meeting of the American Academy of Neurology, Acadia presented additional longer-term efficacy and tolerability data from the Daffodil study in Rett syndrome patients aged 2-4 years. Data was collected for up to 78 weeks of treatment with DAYBUE (the study was terminated early when DAYBUE was approved in March 2023, so 9 of the 12 completers had data at week 78, while all 12 had data at week 52). Efficacy data showed sustained improvements, which increased with time on therapy. The mean Clinical Global Impression of Improvement (CGI-I) score improved to 2.2 at 78 weeks. The proportion of patients with a "much improved" CGI-I score of 2 increased throughout the study, as did the proportion of those who saw some improvement (CGI-I score of 1-3). At week 52, 100% (N = 12) of patients had some improvement (up from 60% (N = 15) at week 12) and 58% (N = 12) were "much or very much improved" (up from 27% (N = 15) at week 12). At week 78, 100% (N=9) of patients had some improvement and 67% (N=9) were "much or very much improved"). The tolerability data was encouraging, with 80% (12/15) of subjects completing the trial, which was much higher than the proportion completing the Lilac trial in patients aged 5-20 years, notwithstanding that the incidence of mild to moderate diarrhea was similar to the incidence in Lilac.

Neuren is eligible to receive ongoing quarterly royalties on net sales of trofinetide in North America, plus milestone payments of up to US$350 million on achievement of a series of four thresholds of total annual net sales, plus one third of the market value of the Rare Pediatric Disease Priority Review Voucher that was awarded to Acadia by the FDA, to be paid when Acadia sells or uses the voucher. Neuren estimates the value of its one third share as US$33 million. The royalty rates and sales milestone payments are related to the total amount of annual net sales of trofinetide in North America, as set out in the following tables:

Tiered Royalty Rates (% of net sales)[1]	
Annual Net Sales	**Rates**
≤US$250m	10%
>US$250m, ≤US$500m	12%
>US$500m, ≤US$750m	14%
>US$750m	15%

Sales Milestones payments	
Net Sales in one calendar year	**US$m**
≥US$250m	50
≥US$500m	50
≥US$750m	100
≥US$1bn	150

[1] Royalty rates payable on the portion of annual net sales that fall within the applicable range. Each sales milestone payment is payable once only.

2. Trofinetide outside North America

Acadia is now advancing in key markets outside the United States. For Canada, which is included in the economics for North America detailed above, Acadia filed a New Drug Submission (NDS) in Q1 2024 as planned. The NDS has been accepted for Priority Review by Health Canada, which means there is the potential for approval around year-end 2024.

For Europe, Acadia is currently engaging with the European Medicines Agency (EMA), planning a potential Marketing Authorisation Application filing in H1 2025. For Japan, Acadia is engaging the regulatory agency (PMDA) in 2024.

Neuren is eligible to receive milestone payments and royalties related to development and commercialization of trofinetide outside North America, as detailed in the table below.

Trofinetide	Payment
Upon 1st commercial sale for Rett in Europe	US$35m
Upon 1st commercial sale for Rett in Japan	US$15m
Upon 1st commercial sale for second indication in Europe	US$10m
Upon 1st commercial sale for second indication in Japan	US$4m
Total development milestones	**US$64m**
Europe	Up to US$170m
Japan	Up to $110m
Rest of World	Up to US$83m
Total sales milestones on achievement of escalating annual net sales thresholds	**Up to US$363m**
Tiered royalties on net sales	**Mid-teen to low twenties per cent**

3. NNZ-2591 for multiple neurodevelopmental disorders

Neuren is developing NNZ-2591 for four serious neurodevelopmental disorders that emerge in early childhood and have no or limited approved treatment options. All subject visits were completed on schedule in the Pitt Hopkins syndrome Phase 2 trial and top-line results are expected in Q2 2024. The last subjects are progressing towards completion of the Angelman syndrome Phase 2 trial, with top-line results anticipated in Q3 2024.

In December 2023, Neuren announced positive top-line results from the Phase 2 clinical trial of NNZ-2591 in children with Phelan-McDermid syndrome (PMS). Significant improvement was observed by both clinicians and caregivers across multiple efficacy measures after treatment for 13 weeks. Improvements were consistently seen across many of the core PMS characteristics. NNZ-2591 was well tolerated and demonstrated a good safety profile. PMS has severe quality of life impacts for those living with the syndrome, as well as parents and siblings. There are no approved treatments for PMS despite its severely debilitating impact. Extensive preparations are in progress for an End of Phase 2 Meeting with the US Food and Drug Administration (FDA) for Phelan-McDermid syndrome in Q3 2024, at

which Neuren will seek guidance on the remaining development program. In parallel, manufacturing of drug supplies for Phase 3 trials has recently commenced. Neuren has also completed non-clinical toxicity studies to support longer clinical trials and commercial use of the product.

Q1 cash flows

Cash at 31 March 2024 was A$243.1 million, compared with A$228.5 million at 31 December 2023. Net cash generated from operating activities was A$8.0 million in Q1, including receipt of A$13.4 million from Acadia for the Q4 2023 DAYBUE royalty. Interest received was A$2.8 million and Income taxes paid included A$0.6 million of withholding tax paid to the US Internal Revenue Service by Acadia on Neuren's behalf. This will be offset against Neuren's Australian tax liability.

In operating cash outflows, R&D payments of A$5.5 million mainly related to the NNZ-2591 Phase 2 clinical trials and preparation for Phase 3 development of NNZ-2591. Administration and corporate payments were increased in Q1 due to the timing of annual insurance premiums.

The effect of movement in exchange rates on the carrying value in AUD of cash held in USD was a gain of A$6.0m, due to the strengthening of the USD against the AUD. Payments to related parties of approximately A$269,000 comprised the Managing Director's executive salary and non-executive directors' fees.

About Neuren

Neuren is developing new drug therapies to treat multiple serious neurological disorders that emerge in early childhood and have no or limited approved treatment options. Recognising the urgent unmet need, all 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.

DAYBUE™ (trofinetide) is approved by the US Food and Drug Administration (FDA) for the treatment of Rett syndrome in adult and pediatric patients two years of age and older. Neuren has granted an exclusive worldwide licence to Acadia Pharmaceuticals Inc. for the development and commercialisation of trofinetide.

Neuren's second drug candidate, NNZ-2591, is in Phase 2 development for each of Phelan-McDermid syndrome, Angelman syndrome, Pitt Hopkins syndrome and Prader-Willi syndrome.

Contact:

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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 2024

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	13,368	13,368
1.2	Payments for		
	(a) research and development	(5,454)	(5,454)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	-	-
	(d) leased assets	-	-
	(e) staff costs	(1,018)	(1,018)
	(f) administration and corporate costs	(1,032)	(1,032)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	2,783	2,783
1.5	Interest and other costs of finance paid	-	-
1.6	Income taxes paid	(640)	(640)
1.7	Government grants and tax incentives	-	-
1.8	Other (provide details if material)	-	-
1.9	**Net cash from / (used in) operating activities**	**8,007**	**8,007**

2.	**Cash flows from investing activities**		
2.1	Payments to acquire or for:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	(3)	(3)
	(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**	**(3)**	**(3)**

3.	**Cash flows from financing activities**		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	553	553
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	(5)	(5)
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**	**548**	**548**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	228,539	228,539
4.2	Net cash from / (used in) operating activities (item 1.9 above)	8,007	8,007
4.3	Net cash from / (used in) investing activities (item 2.6 above)	(3)	(3)

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)	548	548
4.5	Effect of movement in exchange rates on cash held	6,042	6,042
4.6	**Cash and cash equivalents at end of period**	**243,133**	**243,133**

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	58,898	58,898
5.2	Call deposits	184,235	184,235
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)**	**243,133**	**243,133**

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	269
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)	8,007
8.2	Cash and cash equivalents at quarter end (item 4.6)	243,133
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	243,133
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	N/A

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: 24 April 2024

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.