Neuren (NEU) – ASX Announcement **31 July 2023**

Q2 2023 Activity Report

Highlights:

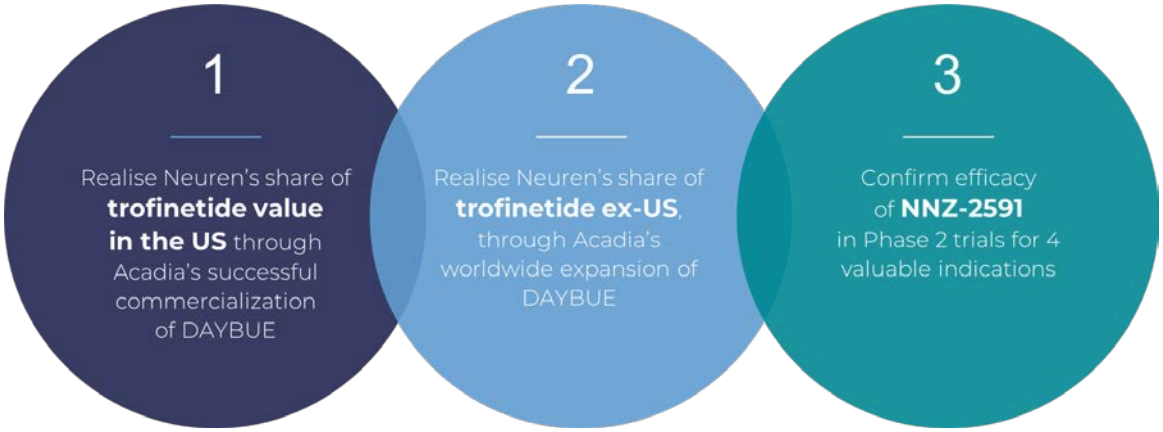
- **DAYBUE™ (trofinetide) launched by partner Acadia in the United States on 17 April 2023 as the first treatment ever approved for Rett syndrome:**
    - **US$40 million milestone payment received by Neuren on first commercial sale**
    - **Highly encouraging early progress, with expected net sales of US$21-23 million in Q2 2023 and US$45-55 million in Q3 2023**
    - **Neuren to receive quarterly royalties on net sales, plus milestone payments of up to US $350 million subject to achievement of annual net sales thresholds, plus one third of the market value of Rare Pediatric Disease Priority Review Voucher awarded to Acadia**
- **Transaction executed to expand trofinetide partnership with Acadia from North America to worldwide:**
    - **US$100 million up-front payment (received by Neuren on 27 July)**
    - **Neuren to receive additional potential milestone payments of up to US$427 million, plus royalties on net sales ex-North America**
    - **Expanded partnership leverages Acadia's unique knowledge and expertise from the successful development and commercialisation of DAYBUE in the United States**
- **Enrolment completed in Phase 2 clinical trial of NNZ-2591 in Phelan-McDermid syndrome, top-line results expected in December 2023**
- **Commenced Phase 2 trial of NNZ-2591 in Prader-Willi syndrome**
- **A$45 million net cash generated from operating activities in half-year to 30 June**
- **A$87 million cash at 30 June 2023 (A$226 million adjusted to include US$100 million up-front payment received in July)**

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today filed its quarterly activity and cash flow report for Q2 2023.

Neuren CEO Jon Pilcher commented: "This has been a hugely important period for Neuren. The early uptake and impact of DAYBUE in the US Rett syndrome community is highly encouraging, our partnering process to expand this to the world delivered US$100 million up-front plus attractive future economics and we remain on track for the first results in December from treatment of Phelan-McDermid syndrome with NNZ-2591. There is so much to look forward to as our revenues from DAYBUE grow and NNZ-2591 reaches a key value inflection point."

Commentary on events since 1 April and outlook

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



DAYBUE in the United States

On 10 March 2023, Neuren's partner Acadia Pharmaceuticals (NASDAQ: ACAD) received US Food and Drug Administration (FDA) approval of DAYBUE™ (trofinetide) for the treatment of Rett syndrome in adult and pediatric patients two years of age and older. DAYBUE is the first and only approved treatment for Rett syndrome. On 17 April, Acadia announced the commercial launch of DAYBUE in the United States. The first commercial sale earned Neuren a milestone payment of US$40 million.

On 13 July, Acadia provided some valuable early launch insights, with launch execution going according to plan. Adoption of DAYBUE in the diagnosed Rett syndrome population has been faster than expected and caregivers and physicians have reported meaningful improvements in patients. Access to reimbursement through Medicaid and private health insurance to date was consistent with expectations, with formal written policies in place for 20% of covered lives. Acadia estimated preliminary net sales for the first partial quarter (Q2 2023) of US$21 to US$23 million and provided guidance for net sales in Q3 2023 of US$45 to US$55 million. Acadia will report Q2 2023 financial results on Wednesday 2 August, after the close of the US financial markets. Acadia's management team will also host a conference call and webcast on 2 August 2023, at 4:30 p.m. Eastern Time, which will be available on www.acadia.com under the investors section.

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, with the one third share estimated by Neuren as US$33 million. The royalty rates and sales milestone payments are related to the total amount of annual net sales of trofinetide in all indications, as set out in the following tables:

Tiered royalty rates (% of net sales)[1]		Sales Milestone payments	
Annual Net Sales	**Rates**	**Net Sales in one calendar year**	**US$m**
≤US$250m	10%	≥US$250m	50
>US$250m, ≤US$500m	12%	≥US$500m	50
>US$500m, ≤US$750m	14%	≥US$750m	100
>US$750m	15%	≥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.

Neuren is also eligible to receive development and first commercial sales milestone payments of up to US$55 million if Acadia develops trofinetide for Fragile X syndrome.

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.

Trofinetide outside North America

On 14 July, Neuren announced the expansion of its partnership with Acadia, with Acadia's exclusive licence for trofinetide in North America expanded to a worldwide exclusive licence. This leverages Acadia's unique knowledge and expertise from the successful development and commercialisation of DAYBUE in the United States.

The existing milestone payments and royalties to Neuren for trofinetide in North America remain unchanged, with additional payments related to development and commercialisation outside North America comprising:

Trofinetide	Payment
Upfront payment (received on 27 July)	**US$100m**
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**

Under the new agreement, Neuren also granted to Acadia an exclusive worldwide licence to develop and commercialise NNZ-2591 for Rett syndrome and Fragile X syndrome only. This replaced the restrictions in the existing agreement on use by Neuren in those two indications. Potential milestone payments and royalties payable to Neuren for NNZ-2591 in Rett and Fragile X are identical to the trofinetide milestone payments and royalties in each of North America and other regions. Neuren retains worldwide rights to NNZ-2591 in all other indications.

If Acadia sub-licenses trofinetide for any region outside North America within the first two years, Neuren is entitled to a share of any upfront and development milestones received by Acadia. Any such payment to Neuren will be credited against any future milestone and royalty payments payable to Neuren in the relevant region.

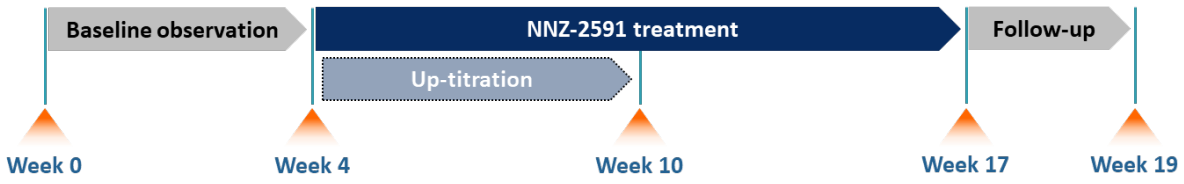
Acadia is responsible for all costs of development and commercialization globally for trofinetide in all indications and for NNZ-2591 in Rett and Fragile X only.

Neuren has an obligation not to develop NNZ-2591 or any other product for North America in an indication for which Acadia develops trofinetide, except for Phelan-McDermid, Pitt Hopkins, Angelman and Prader-Willi syndromes.

NNZ-2591 for multiple neurodevelopmental disorders

Neuren is developing NNZ-2591 for four serious neurological disorders that emerge in early childhood and have no or limited approved treatment options. Phase 2 clinical trials are currently ongoing in children with each of Phelan-McDermid, Pitt Hopkins, Angelman and Prader-Willi syndrome. All four programs have been granted Orphan Drug designation by the FDA and are being conducted under Investigational New Drug Applications (INDs). The estimated number of potential patients being targeted across these four disorders is more than five times larger than Rett syndrome.

The open label Phase 2 trials are each enrolling up to 20 children to examine safety, tolerability, pharmacokinetics and efficacy over 13 weeks of treatment with NNZ-2591. All subjects receive NNZ-2591 as an oral liquid dose twice daily, with escalation in two stages up to the target dose during the first 6 weeks of treatment, subject to independent review of safety and tolerability data.



In June, Neuren announced commencement of the Prader-Willi trial in the United States and the completion of enrolment in the Phelan-McDermid syndrome trial. Top-line results from the Phelan McDermid trial are expected in December 2023.

The overall aim of these first clinical trials in patients is to expedite the generation of data that will enable the subsequent trials to be designed as registration trials. In order to accelerate 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.

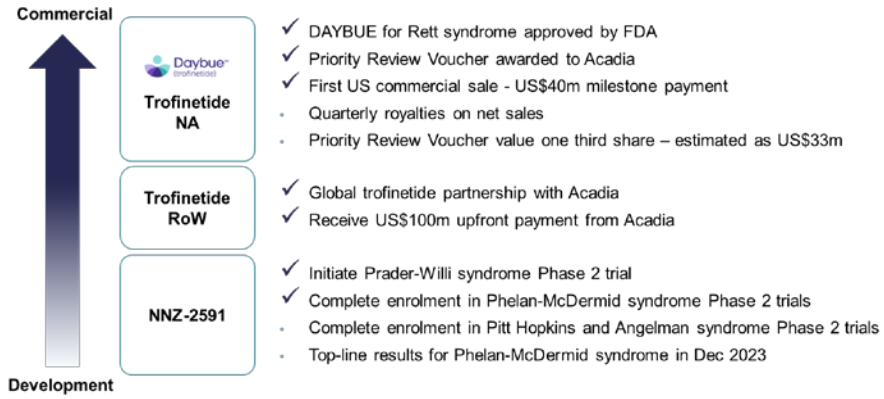
Q2 Cash flows

Cash reserves at 30 June 2023 were A$86.7 million, compared with A$37.3 million at 31 March 2023. Net cash generated from operating activities was A$48.1 million in Q2 and A$44.9 million in the half year to 30 June, including the receipt of the milestone payment of A$59.8 million (US$40 million) earned following the first commercial sale of DAYBUE by Acadia in April. 5% withholding tax (A$2.9 million or US$2 million) was paid to the US Internal Revenue Service. Generally, a company will be entitled to claim withholding tax paid as a foreign income tax offset in the year the foreign income is included in assessable income for Australian tax purposes. Neuren expects to claim this offset against Australian tax payable for the year ended 31 December 2023.

In operating cash outflows, R&D payments of A$6.6 million mainly related to the NNZ-2591 Phase 2 clinical trials and the foundational work to prepare for Phase 3 development of NNZ-2591 across multiple indications. Staff costs were higher in Q2 due to one-time bonus payments following the receipt of the first commercial sale milestone payment of A$59.8 million from Acadia.

The effect of movement in exchange rates on the carrying value in AUD of cash held in USD was a gain of A$0.4m, due to the strengthening of the USD against the AUD. Payments to related parties of approximately A$751,000 comprised non-executive directors' fees and the Managing Director's executive salary and bonus following the receipt of the first commercial sale milestone payment of A$59.8 million from Acadia.

Progress towards achieving transforming catalysts in 2023



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.

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 is conducting 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 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 2023

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	59,810	59,810
1.2	Payments for		
	(a) research and development	(6,630)	(8,724)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	-	-
	(d) leased assets	-	-
	(e) staff costs	(2,264)	(2,993)
	(f) administration and corporate costs	(407)	(1,093)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	470	766
1.5	Interest and other costs of finance paid	-	-
1.6	Income taxes paid	(2,910)	(2,910)
1.7	Government grants and tax incentives	-	-
1.8	Other (provide details if material)	-	-
1.9	**Net cash from / (used in) operating activities**	**48,069**	**44,856**

2.	**Cash flows from investing activities**		
2.1	Payments to acquire or for:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	(18)	(18)
	(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**	**(18)**	**(18)**

3.	**Cash flows from financing activities**		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	-	1,104
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	-	(7)
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**	**-**	**1,097**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	37,263	40,180
4.2	Net cash from / (used in) operating activities (item 1.9 above)	48,069	44,856
4.3	Net cash from / (used in) investing activities (item 2.6 above)	(18)	(18)

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)	-	1,097
4.5	Effect of movement in exchange rates on cash held	361	(440)
4.6	**Cash and cash equivalents at end of period**	**85,675**	**85,675**

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	38,389	1,683
5.2	Call deposits	47,286	35,580
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)**	**85,675**	**37,263**

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	751
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)	48,069
8.2	Cash and cash equivalents at quarter end (item 4.6)	85,675
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	85,675
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: 31 July 2023

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.