**Neuren (NEU) - ASX Announcement** **27 October 2022**

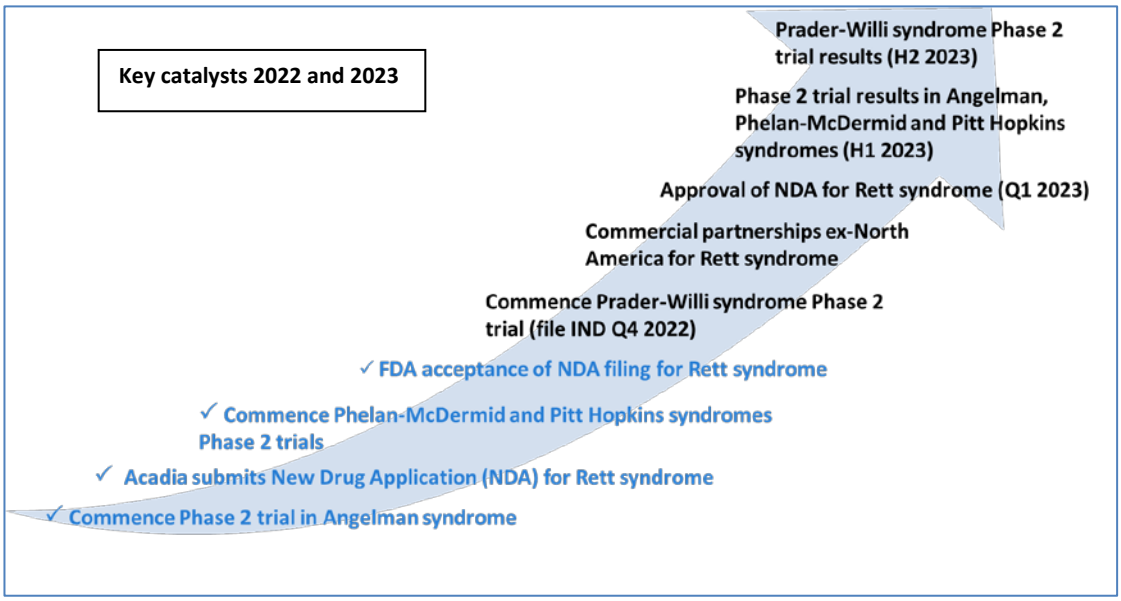
# Q3 2022 Activity Report

**Highlights:**

- **New Drug Application (NDA) for trofinetide to treat Rett syndrome accepted by the US Food and Drug Administration (FDA)**
    - **Priority Review granted**
    - **Prescription Drug User Fee Act (PDUFA) action date set for 12 March 2023**
    - **Milestone payment of US$10 million received from North America partner Acadia**
- **Subject to approval of the NDA, Neuren expects to receive revenue in 2023 for Rett syndrome in the US alone of A$112 million plus double-digit percentage royalties on net sales**
- **Discussions with potential partners for trofinetide ex-North America are continuing**
- **Commenced Phase 2 clinical trials of NNZ-2591 in Angelman, Phelan-McDermid and Pitt Hopkins syndromes**
- **Neuren promoted into the S&P/ASX 300 index**
- **Expertise in pediatric neurology and orphan drug development enhanced by appointment of Liza Squires M.D. as Chief Medical Officer**
- **A$27.3 million cash at 30 September 2022, with additional receipt of US$10 million in October – 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 Q3 2022.

Neuren CEO Jon Pilcher commented: “Neuren continued to achieve the planned milestones during the quarter, remaining on track for the transforming catalysts still to come, notably the FDA target action date for trofinetide in Rett syndrome on 12 March 2023, followed by Phase 2 results for NNZ-2591 in multiple indications.”




## Commentary on events since 30 June and outlook

### Trofinetide for Rett syndrome

In September 2022 the US Food and Drug Administration (FDA) accepted for review the New Drug Application (NDA) for trofinetide to treat Rett syndrome in adults and pediatric patients two years of age and older, that was submitted in July by Neuren's North America partner Acadia Pharmaceuticals (Nasdaq: ACAD). The FDA granted a Priority Review and assigned a Prescription Drug User Fee Act (PDUFA) action date of 12 March 2023. The FDA also informed Acadia that at that time they were not planning to hold an Advisory Committee meeting. The trofinetide program has Orphan Drug, Fast Track and Rare Pediatric Disease designations from the FDA. If approved, trofinetide will be the first drug for the treatment of Rett syndrome.

Acadia has exclusive rights to develop and commercialize trofinetide in North America, which is fully funded by Acadia.

Acceptance of the NDA earned a milestone payment of US$10 million from Acadia, which Neuren received in October. In 2023, if the NDA is approved by the FDA, Neuren expects to earn revenue for Rett syndrome in the US alone of A$112 million plus royalties. The next potential milestone payment to Neuren would be US$40 million (A$61 million at an assumed exchange rate of 0.65), payable following the first commercial sale of trofinetide in the United States. Subsequently, Neuren is eligible to receive double-digit percentage royalties on net sales of trofinetide in North America, plus milestone payments of up to US$350 million (A$538 million) on achievement of a series of four thresholds of total annual net sales, plus one third of

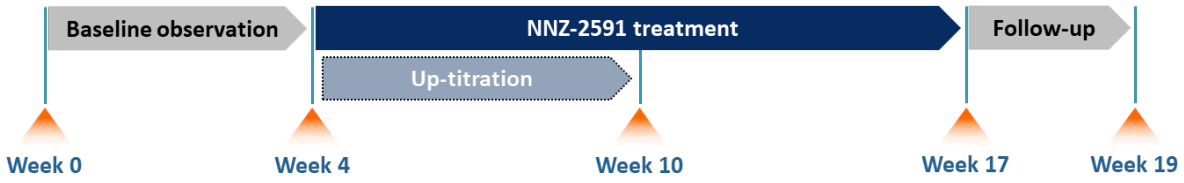
the market value of a Rare Pediatric Disease Priority Review Voucher if awarded by the FDA upon approval of the NDA, with the one third share estimated by Neuren as US$33 million (A$51 million). No royalties or similar costs are payable by Neuren to third parties, which means that Neuren's revenue from Acadia will flow through to pre-tax profit.

Neuren retains 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**

During Q3 Neuren commenced its Phase 2 clinical trials of NNZ-2591 in each of Angelman syndrome (AS), Phelan-McDermid syndrome (PMS) and Pitt Hopkins syndrome (PTHS). The open label Phase 2 trials will each enrol up to 20 children 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. For each trial there are three age cohorts. Safety and tolerability is assessed in the oldest cohort before proceeding with the middle cohort and then safety and tolerability is assessed in the middle cohort before proceeding with the youngest cohort.

| | 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 |



Neuren is also planning a Phase 2 trial in a fourth disorder, Prader-Willi syndrome, with an Investigational New Drug (IND) Application to be submitted to the FDA in Q4 2022.

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.

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**

In September, Neuren was added into the S&P/ASX 300 index. Since 30 June, Neuren has presented at the healthcare conferences of Evans & Partners, Euroz Hartleys and Goldman Sachs, as well as at the ASX Small and Mid-Cap conference. Presentations are scheduled at the Wilsons and Bell Potter healthcare conferences. Neuren will also present at the Jefferies London Healthcare Conference in November.

**Human resources**

In July, Neuren's skills and experience in pediatric neurology and orphan drug development were further enhanced by the appointment of Liza Squires M.D. to the new position of Chief Medical Officer, based in the United States. Dr Squires is a board-certified physician in General Pediatrics and Neurology with Special Competence in Child Neurology. Over the past 20 years, she has held positions of increasing responsibilities in both early and late-stage development at Johnson and Johnson, Shire Pharmaceuticals, Lumos Pharma, Aevi Genomic Medicine and Origin Biosciences. She has led and contributed to multiple New Drug Applications resulting in global regulatory approvals and has extensive experience in orphan drug development.

## Financials

Cash reserves at 30 September 2022 were $27.3 million, compared with $31.1 million at 30 June 2022. In Q3 net cash of $4.0 million was used in operating activities, with R&D payments of $2.8 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 $0.2m for the quarter, due to the strengthening of the USD against the AUD. Payments to related parties of approximately $194,000 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.

A New Drug Application for the lead compound, trofinetide, to treat Rett syndrome is under Priority Review by the US Food and Drug Administration (FDA), with a PDUFA action date of 12 March 2023. 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 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 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 September 2022 |

| **Consolidated statement of cash flows** | | **Current quarter $A'000** | **Year to date (9 months) $A'000** |
|---|---|---|---|
| **1.** | **Cash flows from operating activities** | | |
| 1.1 | Receipts from customers | - | - |
| 1.2 | Payments for | | |
| | (a) research and development | (2,934) | (6,674) |
| | (b) product manufacturing and operating costs | - | - |
| | (c) advertising and marketing | - | - |
| | (d) leased assets | - | - |
| | (e) staff costs | (794) | (2,069) |
| | (f) administration and corporate costs | (331) | (1,165) |
| 1.3 | Dividends received (see note 3) | - | - |
| 1.4 | Interest received | 41 | 74 |
| 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** | **(4,018)** | **(9,834)** |

| **2.** | **Cash flows from investing activities** | | |
|---|---|---|---|
| 2.1 | Payments to acquire or for: | | |
| | (a) entities | - | - |
| | (b) businesses | - | - |
| | (c) property, plant and equipment | (9) | (19) |
| | (d) investments | - | - |
| | (e) intellectual property | - | - |
| | (f) other non-current assets | - | - |

| Consolidated statement of cash flows | | Current quarter $A'000 | Year to date (9 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** | **(9)** | **(19)** |

| **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 | 31,088 | 36,783 |
| 4.2 | Net cash from / (used in) operating activities (item 1.9 above) | (4,018) | (9,834) |
| 4.3 | Net cash from / (used in) investing activities (item 2.6 above) | (9) | (19) |

| Consolidated statement of cash flows | | Current quarter $A'000 | Year to date (9 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 | 231 | 364 |
| **4.6** | **Cash and cash equivalents at end of period** | **27,292** | **27,292** |

| 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 | 1,912 | 3,888 |
| 5.2 | Call deposits | 25,380 | 27,200 |
| 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)** | **27,292** | **31,088** |

| 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 | 194 |
| 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**<br>*Note: the term "facility' includes all forms of financing arrangements available to the entity.*<br>*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) | (4,018) |
| 8.2 | Cash and cash equivalents at quarter end (item 4.6) | 27,292 |
| 8.3 | Unused finance facilities available at quarter end (item 7.5) | - |
| 8.4 | Total available funding (item 8.2 + item 8.3) | 27,292 |
| 8.5 | **Estimated quarters of funding available (item 8.4 divided by item 8.1)** | 6.8 |

*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: 27 October 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.