Neuren (NEU) – ASX Announcement **31 January 2024**

Q4 2023 Activity Report

Highlights:

- **Continued momentum of successful launch in the United States of DAYBUE™ (trofinetide) for Rett syndrome by partner Acadia:**
  - **Net sales of US$66.9 million in Q3 2023 and Acadia guidance for net sales of US$80-87.5 million in Q4 2023**
  - **Royalty to Neuren is currently 10% of net sales: A$10.4 million earned for Q3 2023 and approx. A$12.1-13.2 million anticipated for Q4 2023[1]**
- **Acadia advancing trofinetide outside the United States:**
  - **Canada: NDS filing in Q1 2024 and potential approval around year-end 2024**
  - **Europe: engaging with EMA in Q1 2024, MAA filing in H1 2025**
  - **Japan: engaging regulatory agency (PMDA) in 2024**
- **Highly encouraging top-line results in Phase 2 clinical trial of NNZ-2591 for Phelan-McDermid syndrome:**
  - **Significant improvement was assessed by both clinicians and caregivers across multiple efficacy measures**
  - **Improvements were consistently seen across clinically important aspects of Phelan-McDermid syndrome**
  - **Clinician and caregiver global efficacy measures showed a level of improvement typically considered clinically meaningful**
  - **NNZ-2591 was safe and well tolerated, with no clinically significant changes in laboratory values or other safety parameters during treatment**
- **Enrolment completed in Phase 2 trials of NNZ-2591 in Pitt Hopkins syndrome and Angelman syndrome - on track for top-line results for Pitt Hopkins in Q2 2024 and Angelman in Q3 2024**
- **Cash generated from operations: Q4 2023 A$4.8 million, full-year A$185 million**
- **Cash at 31 December 2023: A$229 million**

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today filed its quarterly activity and cash flow report for Q4 2023. Neuren CEO Jon Pilcher commented: "In Q4 NNZ-2591 successfully passed a key value inflection point with strongly positive Phase 2 trial results in Phelan-McDermid syndrome. In parallel, our revenues from DAYBUE™ continue to grow following the very successful US launch by Acadia. Neuren closed Q4 with cash of A$229 million, in a very strong position to capitalize on the opportunities ahead of us."

[1] Assuming Acadia guidance for Q4 is met and exchange rate of 0.66

neuren pharmaceuticals

AUSTRALIAN GROWTH COMPANY AWARDS 2023 WINNER Health & Life Sciences Growth Company of the Year Award

Commentary on events since 1 October and outlook

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

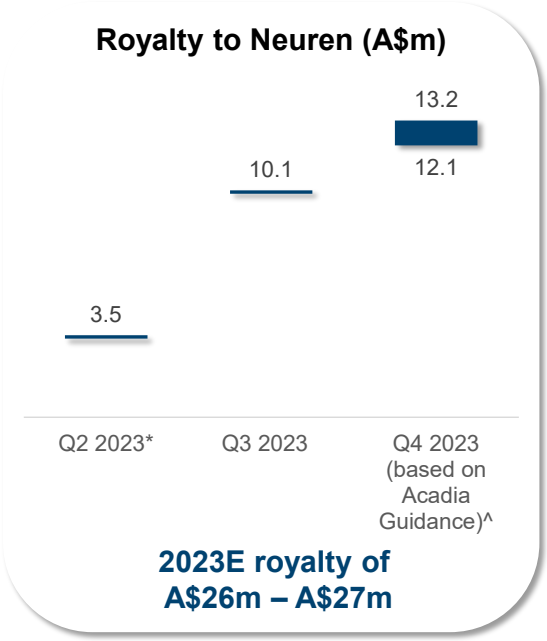
1 Realise Neuren's share of **trofinetide value in the US** through Acadia's successful commercialization of Daybue™ (trofinetide)

2 Realise Neuren's share of **trofinetide ex-US** value through expanded global partnership with Acadia

3 Confirm efficacy of **NNZ-2591** in Phase 2 trials for four valuable indications, with global rights retained by Neuren

1. DAYBUE in North America

On 17 April 2023, Neuren's partner Acadia Pharmaceuticals (NASDAQ: ACAD) launched DAYBUE™ (trofinetide) in the United States as the first approved treatment for Rett syndrome. Net sales grew to US$66.9 million in Q3 2023 and Acadia has provided guidance for net sales of US$80-87.5 million in Q4 2023. Neuren receives royalties as a percentage of net sales, currently 10%. For Q3 Neuren earned royalties of A$10.4 million, received in Q4. If Acadia achieves its guidance, royalties of approximately A$12.1-13.2 million are anticipated for Q4, receivable in Q1 2024.



* Since launch to 30 Jun 2023

^ Based on 10% of DAYBUE net sales and AUDUSD of 0.66 for Q4

Acadia has continued to provide early insights on the launch to date. Adoption of DAYBUE in the diagnosed Rett syndrome population has been faster than expected and caregivers and physicians have reported meaningful improvements in patients. Of the approximately 5,000 diagnosed Rett syndrome patients, more than 800 were on DAYBUE as at 30 September 2023. The high demand for DAYBUE has continued to be supported by access from Medicaid and private health insurance payors, with formal policies in place for over 80% of covered lives. After 6 months of treatment, 76% of patients persisted with treatment, based on confirmed discontinuations only.

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 all indications, 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.

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

2. Trofinetide outside North America

At the J.P. Morgan Healthcare Conference in January 2024, Acadia provided a further update on activities for trofinetide in key markets outside the United States. For Canada, which is included in the economics for North America detailed above, Acadia anticipates a New Drug Submission (NDS) filing in Q1 2024 and potential approval around year-end 2024.

For Europe, Acadia is engaging with the European Medicines Agency (EMA) in Q1 2024, with 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 comprising:

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. Positive top-line results were announced in Q4 from the Phase 2 clinical trial in Phelan-McDermid syndrome and Phase 2 clinical trials are currently ongoing in children with each of 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).

On 18 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 from treatment, across multiple efficacy measures. Improvements were consistently seen across many of the core PMS characteristics. 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.

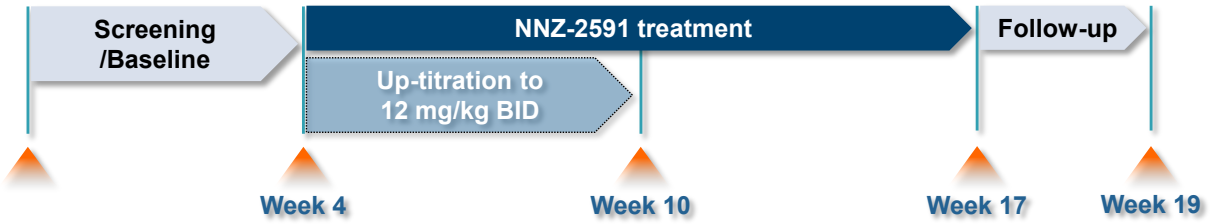
NNZ-2591 was well tolerated and demonstrated a good safety profile. Most Treatment Emergent Adverse Events (TEAEs) were mild to moderate. There was only one Serious TEAE (gastroenteritis), which was not related to study drug and occurred during the safety follow-up period after end of treatment. Three subjects discontinued due to TEAEs, two testing positive for COVID-19 and one due to seizures that were not related to study drug. No clinically significant changes in laboratory values, electrocardiogram (ECG) or other safety parameters were observed during treatment.

Improvement from baseline on overall/total scores was statistically significant (Wilcoxon signed rank test $p<0.05$) for 10 out of 14 efficacy endpoints. The results for the global efficacy measures rated by both clinicians and caregivers showed a level of improvement typically considered clinically meaningful. 16 out of 18 children showed improvement measured by the Clinical Global Impression of

Improvement (CGI-I), an assessment by the clinician of the child's overall status compared with baseline. The mean CGI-I score was 2.4. 10 children received a score of either 1 ("very much improved") or 2 ("much improved"). 15 out of 18 children showed improvement measured by the Caregiver Overall Impression of Change (CIC), an assessment by the caregiver of the child's overall status compared with baseline. The mean CIC score was 2.7. Seven children received a score of either 1 ("very much improved") or 2 ("much improved").

In Q4 enrolment was completed in the Pitt Hopkins and Angelman trials. Top-line results are on track for Pitt Hopkins in Q2 2024 and for Angelman in Q3 2024.

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 of 12 mg/kg during the first 6 weeks of treatment, subject to independent review of safety and tolerability data.



The overall aim of these first clinical trials in patients is to expedite the generation of data that will inform the design of subsequent 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.

Q4 Cash flows

Cash at 31 December 2023 was A$228.5 million, compared with A$230.4 million at 30 September 2023. Net cash generated from operating activities was A$4.8 million in Q4 2023 and A$185 million for the full-year.

Operating cash inflows for Q4 included receipt of A$10.1 million from Acadia for DAYBUE royalties, interest received of A$3.0 million and A$0.9 million received under the Australian R&D Tax Incentive. Total receipts from Acadia for the full-year were A$221 million, which included the up-front payment of US$100 million under the expanded global licence agreement for trofinetide in July 2023.

In operating cash outflows for Q4, R&D payments of A$7.5 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. Income taxes paid included A$0.5 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.

Net cash from Financing activities in Q4 was A$2.5million, comprising proceeds from the exercise of share options. The effect of movement in exchange rates in Q4 on the carrying value in AUD of cash held in USD was a loss of A$9.1m, due to the weakening of the USD against the AUD. This reversed previous gains, so that the overall effect of exchange rates was neutral for the full-year. Payments to related parties of approximately A$269,000 in Q4 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.

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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.