Neuren (NEU) – ASX Announcement **29 February 2024**

Neuren reports profit of $157 million for 2023

Financials:

- **Profit after tax: A$157 million**
- **Licensing revenue: A$232 million**
    - **Royalties: A$27 million**
    - **Milestone and up-front payments: A$205 million**
- **Net cash from operating activities: A$185 million**
- **Cash and short-term investments at 31 December 2023: A$228.5 million**

DAYBUE™ (trofinetide) for Rett syndrome:

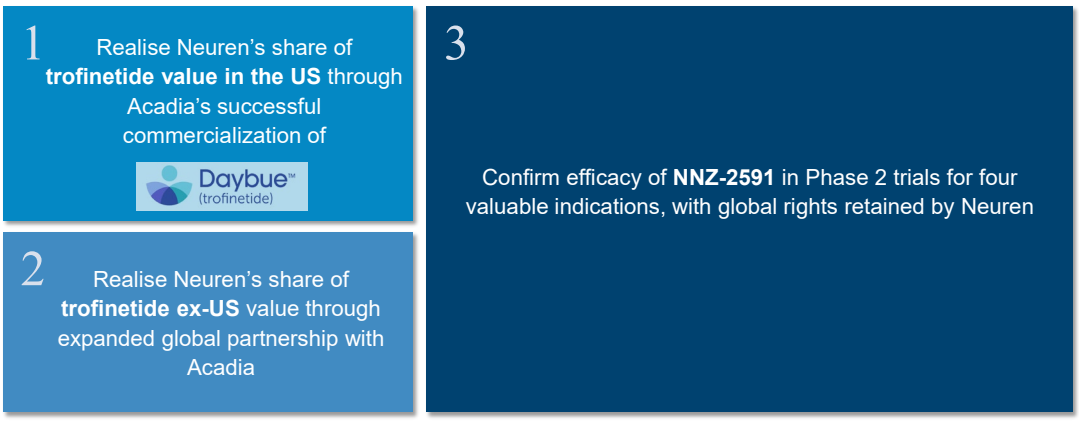
- **Successful United States launch by partner Acadia Pharmaceuticals:**
    - **Net sales of US$177.2 million for 2023 since launch in April**
    - **Guidance for net sales in 2024 of US$370-420 million (first sales milestone payment of US$50 million to Neuren expected to be earned for 2024)**
- **Acadia advancing outside the United States:**
    - **Expanded worldwide partnership in July 2023 delivered to Neuren US$100 million up-front payment, plus milestone payments and royalties**
    - **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**

NNZ-2591:

- **Highly encouraging top-line results in Phase 2 trial for Phelan-McDermid syndrome:**
    - **Significant improvement assessed by both clinicians and caregivers across multiple efficacy measures**
    - **Improvements were consistently seen across clinically important aspects**
    - **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 in Pitt Hopkins syndrome and Angelman syndrome - on track for top-line results for Pitt Hopkins in Q2 2024 and Angelman in Q3 2024**

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today reported its full-year results for 2023. Neuren CEO Jon Pilcher commented: "2023 delivered a profit of A$157 million, an exceptional US launch of DAYBUE™ by Acadia, US$100 million up-front from an expanded partnership with Acadia for trofinetide worldwide and outstanding results from the first clinical trial of NNZ-2591 in patients. Neuren has never been in a stronger position, with substantial ongoing cash flows and a series of value-creating catalysts approaching in 2024."

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

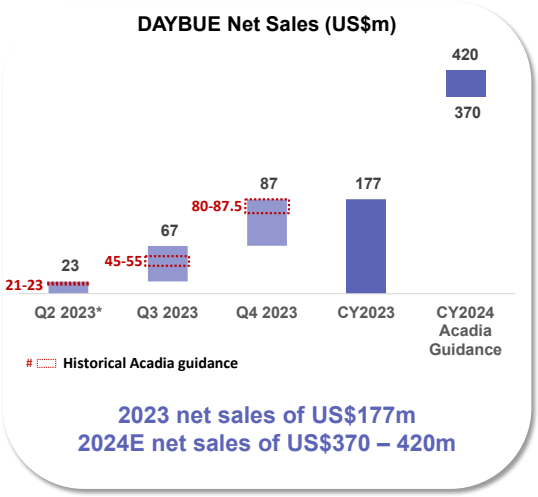


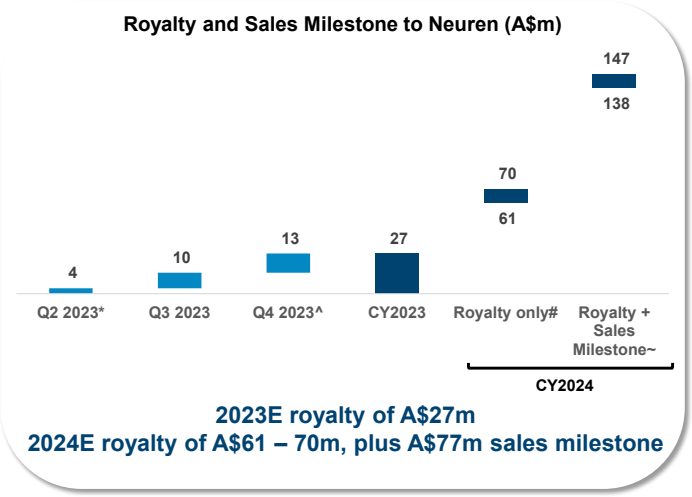
1. DAYBUE in North America

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 rapidly to US$87.1 million in Q4 2023, which was the second full quarter of sales, compared with Acadia's guidance of US$80-87.5 million. Net sales for 2023 since launch in April were US$177 million, 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 anticipates 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. Net sales for Q4 2023 was positively impacted and net sales guidance for Q1 2024 is negatively impacted by approximately US$3 million due to a seasonal shift in sales from January to December. Q1 2024 net sales guidance is 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. Q1 2024 net sales are therefore expected to be US$76 to 82 million, which is included in the full-year guidance of US$370-420 million for 2024.





* Since launch to 30 Jun 2023
^ Based on 10% of DAYBUE net sales and AUDUSD of 0.6805 for Q4 2023
# 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

Adoption of DAYBUE in the diagnosed Rett syndrome population has been faster than expected and caregivers and physicians have continued to report meaningful improvements in patients. There are approximately 860 patients currently on DAYBUE, with the high demand well supported by access from Medicaid and private health insurance payors. In the United States there are approximately 5,000 diagnosed Rett syndrome patients and prevalence studies suggest the total number of patients may be 6,000 to 9,000.

A characteristic of all long-term medicines is that not all patients who commence treatment will persist with treatment. Furthermore, for patients and caregivers, adjusting to a novel treatment regimen can take time, especially when it is the first treatment ever to become available. The number of patients commencing treatment and the proportion that persist with treatment long-term are key factors in the sales outcome. Acadia has provided detailed metrics for real world persistency since launch, which continues to outperform the clinical trial experience and has improved as new patient cohorts are added. The table below shows the data reported in Acadia's Q4 earnings call presentation. The full presentation and a recording of the call are available in the Investors/Events and Presentations section of Acadia's website www.acadia.com).

	Previously Presented Real World Persistency*	Current Real World Persistency*	Lilac-1 Clinical Experience
Month 4	75% (Nov '23)	80%	66%
Month 5	-	76%	64%
Month 6	68% (Jan '24)	70%	58%
Month 7	-	63%	51%

Real world persistency consistently 10+ percentage points above clinical experience

Monthly cohort persistency rates are trending up

*Based on confirmed discontinuations and patients who were 60 days past their scheduled refill

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

In July 2023 Neuren and Acadia expanded their partnership for trofinetide from North America to worldwide. Neuren received US$100 million up-front and is eligible to receive milestone payments and royalties related to development and commercialization of trofinetide outside North America, as detailed in the table below.

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 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.

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. Phase 2 clinical trials are currently ongoing in children with each of Pitt Hopkins, Angelman and Prader-Willi syndromes. In Q4 2023 enrolment was completed in the Pitt Hopkins and Angelman syndrome trials. Top-line results are on track for Pitt Hopkins in Q2 2024 and for Angelman in Q3 2024.

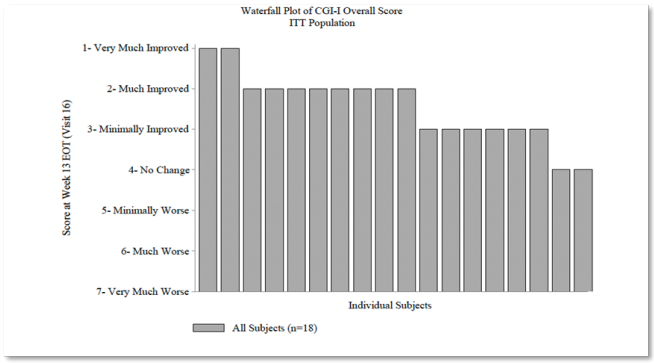
In December 2023, Neuren announced positive top-line results from the Phase 2 clinical trial of NNZ-2591 in children with Phelan-McDermid syndrome (PMS). Significant improvement was observed by both clinicians and caregivers from treatment, across multiple efficacy measures. Improvements were consistently 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.

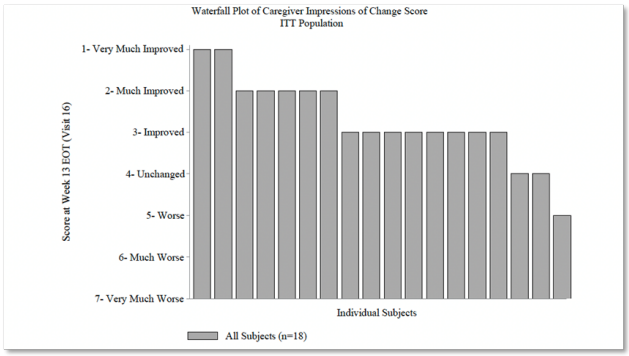
The results for the global efficacy measures rated by both clinicians and caregivers showed a level of improvement typically considered clinically meaningful. 16 out of 18 children showed improvement measured by the Clinical Global Impression of Improvement (CGI-I), an assessment by the clinician of 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”).

Mean CGI-I score of 2.4 with 16 out of 18 children showing improvement

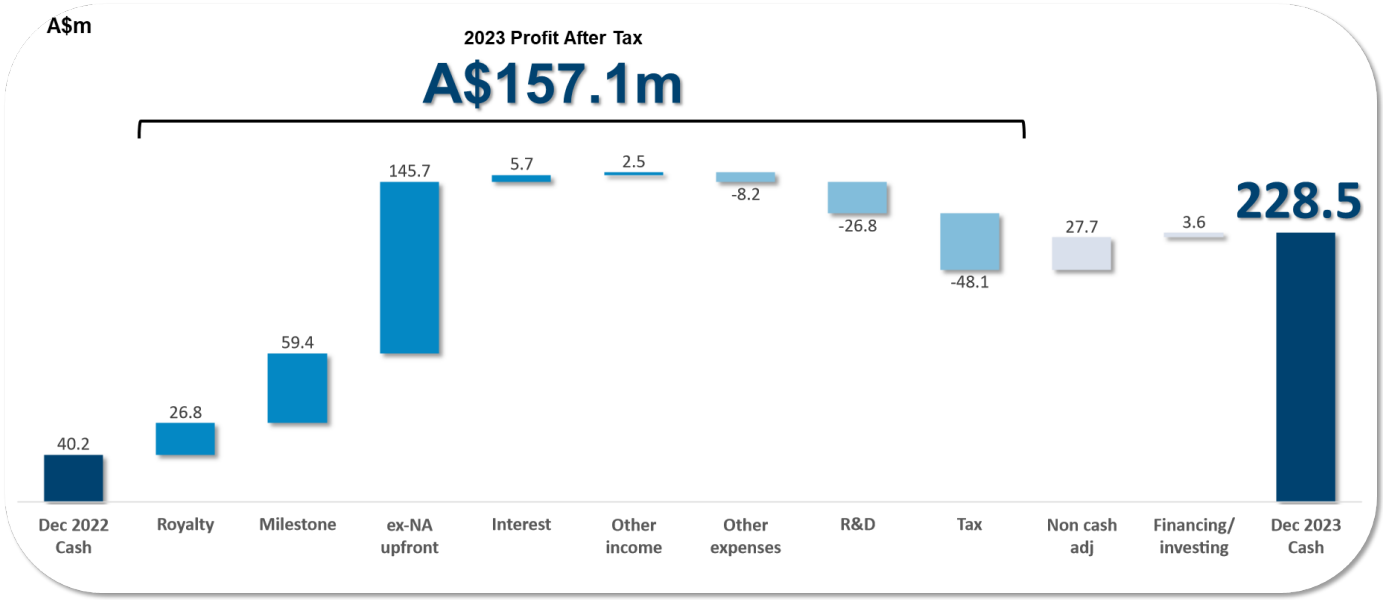


Mean CIC score of 2.7 with 15 out of 18 children showing improvement



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 has been 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.

2023 Financials



Profit after tax for 2023 was A$157.1 million (2022: A$0.2 million). Revenue of A$231.9 million was received under the licence agreement with Acadia (2022: A$14.6 million). This includes A$59.4 million for the first US commercial sale milestone, an upfront of A$145.7 million under the expanded global licence agreement with Acadia and A$26.8 million from quarterly royalty income. Other income included interest income of A$5.7 million (2022: A$0.4 million) and foreign exchange gains of A$2.4 million (2022: A$1.2 million).

There was an increase of A$14.0 million in research and development costs, due to higher expenditures in for the NNZ-2591 Phase 2 clinical trials and the foundational work to prepare for Phase 3 development of NNZ-2591 across multiple indications. There was also an increase in corporate and administrative costs of A$2.5 million, mainly due to higher employee benefits and share-based payments expense. In addition, a loss of A$2.2 million on the fair value of outstanding forward contracts to sell Australian dollars and buy US dollars was recognised at 31 December 2023 (2022: A$0.7 million).

The net income tax expense was A$48.1 million (2022: nil). After utilising Australian carried forward tax losses and the expectation of offsetting the 5% withholding tax paid to the US Internal Revenue Service in relation to the Acadia milestone payments, Neuren has recognised a current tax liability of A$37.1 million.

Total cash and short-term investments at 31 December 2023 were A$228.5 million (2022: A$40.2 million). Net cash received from operating activities was A$184.9 million (2022: A$3.6 million). The increase of $181.3 million was primarily due to the receipt of A$221.0 million (2022: A$15.9 million) from Acadia for the first commercial sale milestone payment, the up-front payment under the expanded global licence agreement for trofinetide and receipt of quarterly royalty payments. This was offset by higher payments to other suppliers of A$24.6 million (2022: A$11.3 million) due to higher R&D expenditures. Withholding tax of A$11.8 million was 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 for 31 December 2023 was A$3.6 million (2022: nil), comprising proceeds received on conversion of loan funded shares and exercise of share options.

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.