**Neuren (NEU) – ASX Announcement** **7 November 2024**

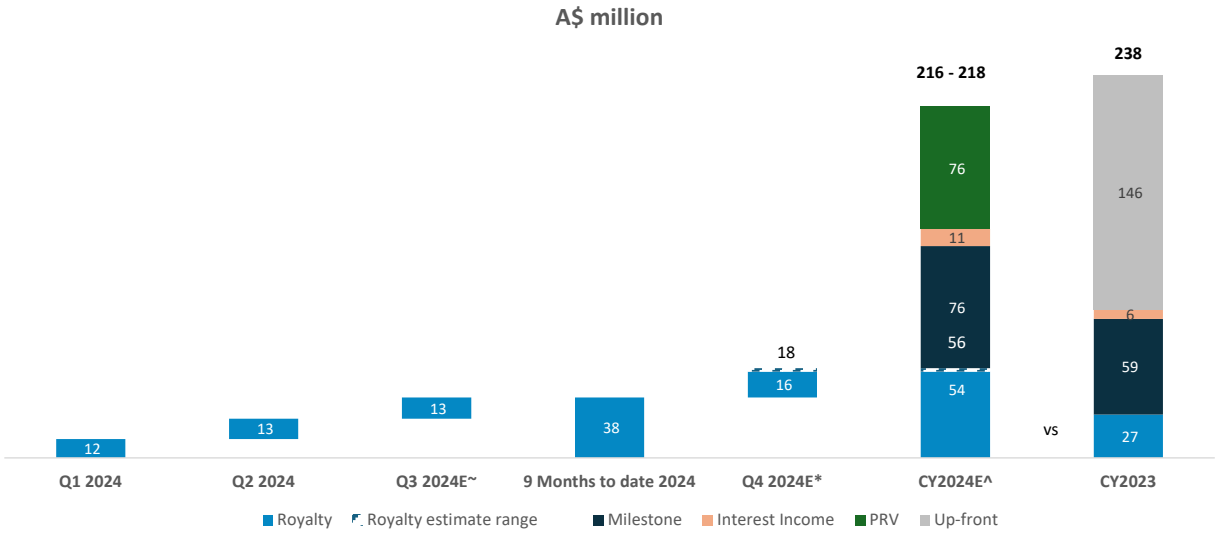
# Q3 2024 update

**Highlights:**

- **DAYBUE™ (trofinetide) net sales for 9 months exceeded the full-year threshold of US$250 million for Neuren's first sales milestone income of US$50 million**
- **Priority Review Voucher sold by Acadia for US$150 million, Neuren to receive one third share**
- **Q3 royalty income A$13.2 million, 9 months to date total A$37.5million**
- **Neuren full year 2024 income expected to be A$216 - 218 million**
- **A$210 million cash and short-term investments at 30 September 2024**
- **NZ tax losses to be recognised in 2024, providing additional tax credit of approximately A$17 million**
- **Q3 results for DAYBUE™ (trofinetide) reported by partner Acadia Pharmaceuticals:**
    - **Net sales of US$91.2 million for Q3 2024 up 8% from Q2 2024 and up 36% from Q3 2023**
    - **Year to date net sales of US$251.7 million, guidance for net sales in 2024 narrowed to US$340-350 million**
    - **DAYBUE™ (trofinetide) approved in Canada for the treatment of Rett syndrome**
    - **Europe launch teams currently being built**
- **Positive End of Phase 2 Meeting with FDA for NNZ-2591 in Phelan-McDermid syndrome:**
    - **Alignment reached on key aspects of Phase 3 program**
    - **Neuren to submit further information to FDA to confirm endpoints for the primary efficacy assessment**
    - **Preparations advancing for Phase 3 trial**
- **Phase 2 trial of NNZ-2591 showed significant improvements in Angelman syndrome**

**Melbourne, Australia:** Neuren Pharmaceuticals (ASX: NEU) today provided an update for Q3 2024, following the Q3 results reported by its partner Acadia Pharmaceuticals (Nasdaq: ACAD). Neuren CEO Jon Pilcher commented: "This quarter has clearly emphasised the value to Neuren of DAYBUE™ and our partnership with Acadia. Nine months into the first full year of sales, the threshold has already been passed for our first sales milestone income of US$50 million. Growth in sales and therefore our royalty income has continued and our one third share of the announced sale of the PRV for US$150 million will deliver another large amount of income. Once again this demonstrates we are in the enviable position that our share of the large global market opportunity for DAYBUE™ provides such a strong financial foundation to optimise the potential upside of NNZ-2591 in multiple indications."

**Neuren income analysis**




~ Based on 10% of DAYBUE net sales of US$89.5, 12% of DAYBUE net sales of US$1.7 and AUDUSD of 0.692842
* Based on 12% of DAYBUE net sales and assumed AUDUSD of 0.66
^ PRV based on US$50m, which is 1/3 share of the US$150m total sale price, before applicable cost, and assumed AUDUSD of 0.66; milestone payment based on US$50m and assumed AUDUSD of 0.66

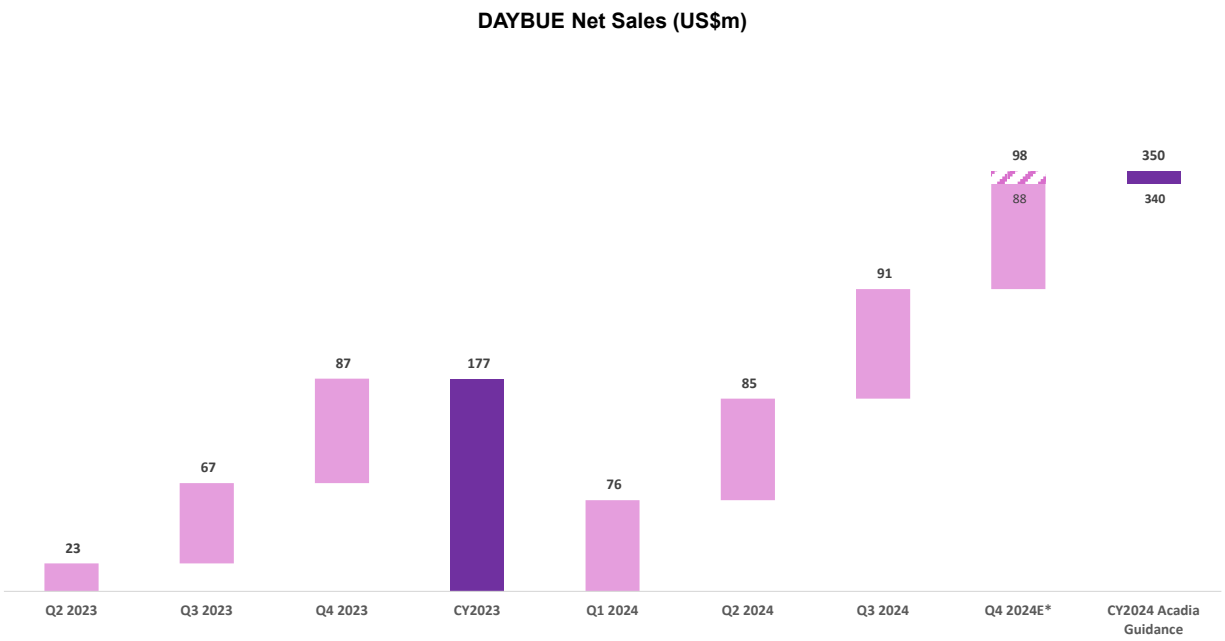
Royalties earned in Q3 2024 were A$13.2 million, compared with A$12.7 million in Q2, bringing the cumulative royalties for the year to date to A$37.5 million. Based on Acadia's full year guidance for DAYBUE net sales and actual cumulative net sales achieved year to date, Neuren estimates Q4 2024 royalties to be between A$16 million and A$18 million.

In addition, DAYBUE's actual cumulative net sales achieved year to date has already exceeded the full-year net sales threshold of US$250 million for Neuren to earn the first sales milestone income of US$50 million, which will be received in Q1 2025 after finalizing the total net sales for the full year 2024.

Yesterday, Acadia announced that it had entered into a definitive asset purchase agreement to sell the Rare Pediatric Disease Priority Review Voucher (PRV) for US$150m, subject to customary closing conditions, including expiration of applicable waiting period under the Hart-Scott Rodino (HSR) Antitrust Improvements Act. Neuren will be paid one-third share of the net proceeds after the closing of the transaction, expected in Q4 2024, with receipt expected in Q1 2025.

Neuren expects its total income for 2024, including royalties, sales milestone payment, share of the PRV net proceeds, and approximately A$11m in interest income, to range between A$216 million and A$218 million.

## DAYBUE in North America




* Implied by the difference between Acadia's full year CY2024 net sales guidance and actual net sales for 9 months to date

Acadia 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 reported net sales of US$91.2 million for Q3 2024, up 8% from Q2 2024 and up 36% from Q3 2023, continuing the momentum of the successful launch.

923 patients were active on DAYBUE at the end of Q3 (vs 900 as at 1 August), with persistency after 10 months of treatment at 60% (vs 58% after 9 months of treatment reported in Q2). Penetration continues to increase, with more than 30% of the 5,000 diagnosed patients having initiated therapy.

Acadia narrowed its guidance for net sales in 2024 to US$340-350 million (within the previous range of US$340-370 million).

In October 2024 Health Canada approved Acadia's New Drug Submission for DAYBUE™ (trofinetide) to treat Rett syndrome in patients 2 years of age and older and weighing at least 9kg. Canada net sales will be added to US net sales to give total net sales for calculation of Neuren's North America royalties and sales milestone payments. In Canada, the prevalence of Rett syndrome is estimated to be 600 to 900 patients.

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.

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.

**Trofinetide outside North America**

Acadia is also advancing in key markets outside North America. For Europe, Acadia is planning a potential Marketing Authorisation Application filing in Q1 2025 and is currently building out Europe launch teams. For Japan, Acadia has had productive discussions with the regulatory agency (PMDA), including potential clinical development plans.

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** |

**NNZ-2591 for multiple neurodevelopmental disorders**

Neuren is developing NNZ-2591 for multiple serious neurodevelopmental disorders that emerge in early childhood and have no or limited approved treatment options.

In August 2024, Neuren announced positive top-line results from the Phase 2 clinical trial of NNZ-2591 in children with Angelman syndrome (AS). NNZ-2591 was well tolerated and demonstrated a good safety profile. After treatment for 13 weeks, significant improvement was observed by both clinicians and caregivers in clinically important aspects of AS, including communication, behavior, cognition and motor abilities. Clinician and caregiver global efficacy measures showed a level of improvement considered clinically meaningful.

This result followed earlier positive results in Phase 2 clinical trials of NNZ-2591 in each of Phelan-McDermid syndrome (PMS) and Pitt Hopkins syndrome. There are no approved treatments for PMS, PTHS, or AS despite the severe quality of life impacts for those living with each syndrome, as well as parents and siblings.

In September 2024, Neuren conducted an End of Phase 2 Meeting with the US Food and Drug Administration (FDA) for NNZ-2591 in PMS, at which Neuren sought guidance from FDA on the remaining development program. Alignment was reached on key aspects of program. The single pivotal Phase 3 trial will be a randomised, double-blind, placebo-controlled trial of treatment for 13 weeks in children aged 3 to 12 years with PMS, with Participants able to continue into an open-label extension study. There will be one active treatment group versus placebo, with a target dose equivalent to the dose tested in the Phase 2 trial. Based on the safety data from the Phase 2 clinical trial, Neuren proposed a less burdensome safety monitoring plan for the Phase 3 and open label extension trials, which was considered reasonable by the FDA, subject to review of the final protocol. This study is the first ever pivotal clinical trial in PMS, which means there is no precedent for efficacy assessment. Primary efficacy endpoints for the Phase 3 trial were considered in depth at the meeting, with a range of potential options discussed. The FDA requested that Neuren submit further information before agreeing the final selection of the endpoints.

In parallel with the process to confirm the primary efficacy endpoints, Neuren is continuing to advance preparations for the Phase 3 program, including the selection of service providers, the identification of potential trial sites and the campaign to manufacture the required supplies of NNZ-2591.

Neuren has an open IND with the FDA for NNZ-2591 in Prader-Willi syndrome and is also conducting pre-clinical studies for NNZ-2591 in other undisclosed indications.

**Cash and income tax**

At 30 September 2024 total cash and term deposits classified as short-term investments was A$210.2 million, compared with A$213.2 million at 30 June 2024. Year to date interest income has more than covered Neuren's corporate expenses.

At 31 December 2023, Neuren had A$62.5 million of New Zealand tax losses for which no deferred tax asset was recognized. Those losses are now expected to be utilized in relation to a portion of taxable income from Trofinetide milestone and royalty payments. A deferred tax asset is therefore expected to

be recognized in 2024 for the New Zealand tax losses, resulting in a tax credit of approximately A$17 million. This will partially offset the tax charge on Neuren's profit for 2024. Neuren has filed a New Zealand tax return for the year ended 31 December 2023, which resulted in utilization of A$12.5 million of the losses.

**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 multiple neurodevelopmental disorders, with positive results achieved in Phase 2 clinical trials in Phelan-McDermid syndrome and Pitt Hopkins syndrome.

Neuren received the Australian Growth Company of the Year award for Health and Life Sciences in 2023 and 2024.

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**ASX Listing Rules information**

This announcement was authorized to be given to the ASX by the CEO & Managing Director 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.*