neuren pharmaceuticals

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

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

Q2 2024 update

DAYBUE™ (trofinetide) for Rett syndrome:

- **Net sales update reported by partner Acadia Pharmaceuticals:**
  - **Net sales of US$84.6 million for Q2 2024 (earning Neuren royalties of A$13 million), up from US$75.9 million in Q1 2024**
  - **Updated guidance for net sales in 2024 of US$340-370 million (which would earn Neuren royalties of A$55-61 million plus sales milestone revenue of A$77 million)**
- **Real-world evidence from LOTUS™ study presented at the 2024 International Rett Syndrome Foundation (IRSF) Annual Scientific Meeting:**
  - **During months 1 to 6 of treatment with DAYBUE caregivers for 67.7% to 82.2% of enrolled participants reported improvements in Rett syndrome symptoms**
  - **The most consistently reported improvements over six months were non-verbal communication (58.5%), alertness (51.2%) and social interaction/connectedness (40.2%)**
- **Acadia advancing outside the United States:**
  - **Canada: NDS accepted for Priority Review, potential approval around year-end 2024**
  - **Europe: Pediatric investigation plan (PIP) filed with and accepted by EMA, Marketing Authorisation Application (MAA) filing in Q1 2025**
  - **Japan: productive discussions held with regulatory agency**

NNZ-2591 for multiple neurodevelopmental disorders:

- **Phase 2 trial showed significant improvements in Pitt Hopkins syndrome:**
  - **Clinical Global Impression of Improvement (CGI-I) mean score of 2.6, with 9 out of 11 children showing improvement assessed by clinicians**
  - **Improvements were seen in clinically important aspects of Pitt Hopkins syndrome, including communication, social interaction, cognition and motor abilities**
- **End of Phase 2 Meeting with FDA for Phelan-McDermid syndrome scheduled in September 2024**
- **Manufacture of supplies for Phase 3 trials in progress**

Financials:

- **Cash and short-term investments at 30 June 2024: A$213 million (31 March 2024: A$243 million)**
- **Royalties of A$13 million earned in Q2 2024, to be received in Q3 2024**
- **Royalties of A$11.6 million received in Q2 2024**
- **First Australian income tax of A$34 million paid in Q2 2024, for 2023**

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today provided an update for Q2 2024, following the Q2 results reported by its partner Acadia Pharmaceuticals (Nasdaq: ACAD). Neuren CEO Jon Pilcher commented: "In Q2 DAYBUE™ sales returned to growth and our Phase 2 trial of NNZ-2591 in Pitt Hopkins syndrome again achieved highly encouraging results. We are optimistic about the large

global market opportunity for DAYBUE™ and our share of those revenues provides a strong financial foundation to optimise the potential of NNZ-2591 in multiple indications."

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

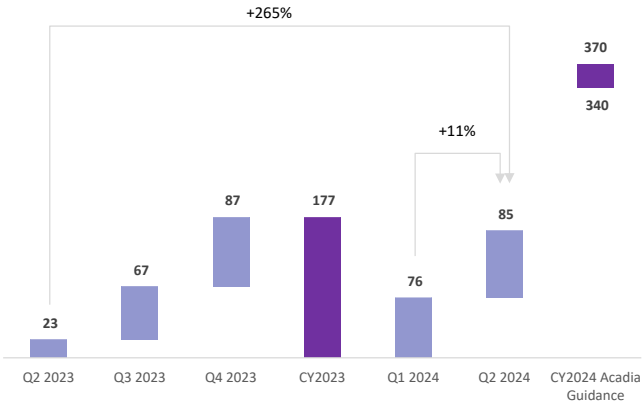
1 Realise Neuren's share of **trofinetide value in the US** through Acadia's successful commercialization of Daybue™ (trofinetide)

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 multiple indications, with global rights retained by Neuren

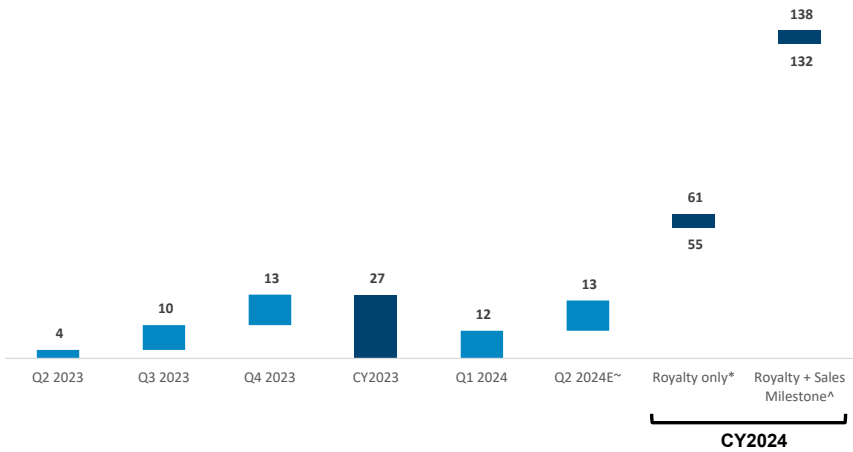
1. DAYBUE in North America

DAYBUE Net Sales (US$m)



Q2 2024 net sales US$85m
2024E net sales of US$340 – 370m

Royalty and Sales Milestone Payments to Neuren (A$m)



Q2 2024E royalty of A$13m
2024E royalty of A$55 – 61m, plus A$77m sales milestone

~ Based on 10% of DAYBUE net sales and AUDUSD of 0.666671
* 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

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$84.6 million for Q2 2024, (increased from US$75.9 million in Q1), earning Neuren royalties of A$13 million. The rate of new patient starts was 12% higher than the previous quarter and the rate of discontinuations was 46% lower than in the previous quarter. The number of patients on active therapy increased to 900 at 1 August. The rate of persistence on therapy continues to trend more than 10% higher than the experience in clinical trials, with the current rate after 9 months of treatment at 58%. Penetration continues to increase, with approximately 30% of the 5,000 diagnosed patients having initiated therapy. In market research, physicians surveyed stated that over the next 24 months they expect to expand prescribing to more than 70% of their eligible patients.

The momentum in Q2 was encouraging, however the net rate of patient additions in Q2 was slower than expected, which has caused Acadia to update its guidance for net sales in 2024 to US$340-370 million (lower and narrower than the previous range of US$370-420 million). Assuming the updated guidance range is met and an exchange rate of 0.65, Neuren would earn royalties of A$55-61 million (was A$61-70 million), plus A$77 million from the first sales milestone payment of US$50 million due for the first calendar year in which net sales exceed US$250 million.

Real-world experience on therapy is an important source of information, which can be more readily understood than clinical trial data. In June Acadia presented interim data from the open-label real-world LOTUS™ study at the 2024 International Rett Syndrome Foundation (IRSF) Annual Scientific Meeting. LOTUS is an ongoing, caregiver-reported study evaluating the efficacy and tolerability outcomes in patients with Rett syndrome treated with DAYBUE. Six-month interim findings evaluating DAYBUE in 101 Rett syndrome patients with an age range of two to 60 years old from the Phase 4, observational, prospective study showed caregivers for 67.7% to 82.2% of enrolled participants reported improvements at Months 1 to 6 in at least one Rett syndrome symptoms category. This was measured using the Behavioral Improvement Questionnaire (BIQ) developed by Acadia in consultation with Rett experts and caregivers. The most consistently reported improvements over six months were nonverbal communication (58.5%), alertness (51.2%) and social interaction/connectedness (40.2%). Caregivers also completed the Gastrointestinal (GI) Health Questionnaire, developed by Acadia for this study. At month 6 diarrhea was reported by 31.7% of caregivers. Some participants reported initiating therapy on doses less than half of the FDA approved dose and increasing over several weeks; the majority of patients were on >90% of labeled dose by week 10.

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.

For Canada, which is included in the economics for North America, Acadia's New Drug Submission (NDS) was accepted for Priority Review by Health Canada, which means there is the potential for approval around year-end 2024.

2. Trofinetide outside North America

Acadia is also advancing in key markets outside North America. For Europe, Acadia's Pediatric investigation plan (PIP) was filed with and accepted by the European Medicines Agency (EMA). Acadia is planning a potential Marketing Authorisation Application filing in Q1 2025. 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**

3. 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 May 2024, Neuren announced positive top-line results from the Phase 2 clinical trial of NNZ-2591 in children with Pitt Hopkins syndrome (PTHS). After treatment for 13 weeks, significant improvement was observed by both clinicians and caregivers in clinically important aspects of Pitt Hopkins syndrome, including communication, social interaction, cognition and motor abilities. Clinician and caregiver global efficacy measures showed a level of improvement considered clinically meaningful. The Clinical Global Impression of Improvement (CGI-I) mean score was 2.6, with 9 out of 11 children showing improvement assessed by clinicians. The Caregiver Overall Impression of Change (CIC) mean score was 3.0, with 8 out of 11 children showing improvement assessed by caregivers. NNZ-2591 was well tolerated and demonstrated a good safety profile.

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

An End of Phase 2 Meeting with the US Food and Drug Administration (FDA) for NNZ-2591 in PMS is scheduled for September 2024, at which Neuren will seek guidance on the remaining development program. In parallel, manufacture of supplies for Phase 3 clinical trials is in progress.

Q2 financial highlights

A$ million	**Q2 2024**	**Q1 2024**
Current quarter royalties earned	13.0	11.6
Prior quarter royalties received	11.6	12.8
Interest received	3.1	2.8
R&D and corporate payments	(8.0)	(7.5)
Income taxes paid	(34.7)	(0.6)
Cash and short-term investments at quarter end	213.2	243.1

Royalties earned in Q2 2024 were A$13.0 million, compared with A$11.6 million in Q1.

Cash at 30 June 2024 was A$213.2 million, compared with A$243.1 million at 31 March 2024. Royalties of A$11.6 million were received in Q2 from Acadia for the Q1 2024 DAYBUE royalty and interest received was A$3.1 million. Income taxes paid included Neuren's first payment of Australian income tax of A$34 million for 2023 and A$0.6 million of withholding tax paid to the US Internal Revenue Service by Acadia on Neuren's behalf.

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.

Contact:

investorrelations@neurenpharma.com
Jon Pilcher, CEO: +61 438 422 271

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.