neuren pharmaceuticals

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

Neuren (NEU) – ASX Announcement **27 August 2024**

H1 2024 financial results

Highlights:

- **H1 2024 royalty income: A$24.3 million, up from A$3.5 million in H1 2023**
- **H1 2024 profit after tax: A$8.0 million**
- **Cash and short-term investments at 30 June 2024: A$213 million**
- **Guidance for Neuren's full-year 2024 North America DAYBUE™ (trofinetide) commercial income: A$132-138 million, up from A$86 million in 2023:**
  - **2024 comprises a milestone payment of A$77 million in H2 2024 and royalties of A$55-61 million**
  - **2023 comprised a milestone payment of A$59 million in H1 2023 and royalties of A$27 million**
- **US Net sales of DAYBUE™ (trofinetide) for Rett syndrome reported by partner Acadia Pharmaceuticals:**
  - **US$161 million for H1 2024, up from US$23 million in H1 2023**
  - **Guidance for full year 2024 of US$340-370 million, up from US$177 million in 2023**
- **Acadia advancing trofinetide outside the United States:**
  - **Canada: New Drug Submission (NDS) accepted for Priority Review, potential approval around year-end 2024**
  - **Europe: Pediatric investigation plan (PIP) filed with and accepted by EMA, potential Marketing Authorisation Application (MAA) filing in Q1 2025**
  - **Japan: productive discussions held with regulatory agency**
- **US Food and Drug Administration granted an End of Phase 2 Meeting for NNZ-2591 to treat Phelan-McDermid syndrome, scheduled for September 2024**
- **Manufacture of supplies for Phase 3 trials of NNZ-2591 progressing as planned**
- **Potential for NNZ-2591 to address core symptoms of diverse neurodevelopmental disorders, independent of the underlying genetics, now supported by positive Phase 2 trial results across three syndromes**

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today reported interim financial results for the first half of 2024. Neuren CEO Jon Pilcher commented: "We anticipate full-year revenue from DAYBUE™ of A$132-138 million and we now have highly encouraging results from Phase 2 trials of NNZ-2591 across three syndromes. With cash and short-term investments of A$213 million, Neuren is in the ideal position to optimise the potential of NNZ-2591 in multiple indications."

1. DAYBUE in North America

Acadia launched DAYBUE™ (trofinetide) in the United States in April 2023 as the first and only approved treatment for Rett syndrome. In H1 2024, Acadia reported US DAYBUE™ (trofinetide) net sales of US$161 million (up from US$23 million in H1 2023), earning Neuren royalties of A$24.3 million (up from A$3.5 million in H1 2023).

Acadia has issued guidance for US net sales in 2024 of US$340-370 million. Assuming updated guidance range is met and an exchange rate of 0.65, in the full-year 2024 Neuren will earn royalties of A$55-61 million, plus A$77 million from a sales milestone payment of US$50 million due for the first calendar year in which North America net sales exceed US$250 million. Total full-year 2024 DAYBUE North America commercial income to Neuren is expected to be A$132-138 million, up from A$86.2 million in 2023. Neuren earned milestone payment income of A$59.4 million in H1 2023 upon first commercial sale of DAYBUE™(trofinetide) in the US.

North America DAYBUE™ (trofinetide) Commercial Income to Neuren

A$m	**2023**			**2024**		
	H1	**H2**	**Full-year**	**H1**	**H2(E)[1]**	**Full-year (E)[1]**
Royalty income	3.5	23.3	26.8	24.3	31 - 36	55 - 61
Sales milestone payment income	-	-	-	-	77	77
First commercial sale milestone payment income	59.4	-	59.4	-	-	-
Total North America Commercial Income	**62.9**	**23.3**	**86.2**	**24.3**	**108 - 113**	**132 - 138**

[1] Estimate assuming Acadia's guidance for net sales is met and USD/AUD exchange rate of 0.65

In Q2 2024, 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 2024. 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.

Real-world experience on therapy is an important source of information, which can be more readily understood than clinical trial data. In June 2024 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 reported 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 US$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).

Since the end of H1, positive results have also been announced in a Phase 2 clinical trial of NNZ-2591 in Angelman syndrome (AS). After treatment for 13 weeks, significant improvement was observed by both clinicians and caregivers in clinically important aspects of Angelman syndrome, including communication, behavior, 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 3.0, with 11 out of 13 children showing improvement assessed by clinicians. The Caregiver Overall Impression of Change (CIC) mean score was 3.2, with 8 out of 12 children showing improvement assessed by caregivers. Every child in the younger age segment of 3-12 years showed improvement measured by both the CGI-I (mean score 2.8) and the CIC (mean score 2.6). NNZ-2591 was well tolerated and demonstrated a good safety profile.

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.

The potential of NNZ-2591 to address the core symptoms of diverse neurodevelopmental disorders, independent of the origin of the underlying genetics, is now supported by positive results across all three Phase 2 clinical trials for PMS, PTHS and AS, demonstrating a good safety profile and consistent areas of improvement assessed by both clinicians and caregivers.

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

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.

H1 financial highlights

A$ million	**H1 2024**	**H1 2023**
Royalty income	24.3	3.5
Sales milestone payment income	-	59.4
Interest income	5.8	0.7
Other income	1.9	0.8
Research & development expenses	(17.9)	(11.7)
Corporate & administration expenses	(2.4)	(3.0)
Profit before tax	11.8	49.6
Income taxes	(3.8)	(1.8)
Profit after tax	**8.0**	**47.8**
Cash flows from operating activities before income tax payments	*14.9*	*44.9*
Income taxes paid	*(35.4)*	-
	30 June 2024	**31 December 2023**
Cash and short-term investments	213.2	228.5

Cash and short-term investments at 30 June 2024 was A$213.2 million, compared with A$228.5 million at 31 December 2023. Income taxes paid included Neuren's first payment of Australian income tax of A$34 million for 2023 and A$1.2 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, Pitt Hopkins syndrome and Angelman 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.