Neuren (NEU) – ASX Announcement **28 August 2023**

Neuren reports 2023 half-year profit after tax of A$48 million

Highlights:

- **Key financials for half-year to 30 June 2023:**
  - **Total income A$64.4 million, including A$62.9 million revenue from DAYBUE**
  - **Profit after tax A$47.8 million**
  - **Cash generated by operations A$44.9 million**
  - **Total cash and short term investments at 30 June 2023 A$85.7 million (A$224 million adjusted to include ex-North America up-front payment received in July)**
- **DAYBUE™ (trofinetide) launched by Acadia in the United States on 17 April 2023 as the first treatment ever approved for Rett syndrome:**
  - **Highly encouraging early progress, with net sales of US$23.2 million in Q2 2023 and guidance of US$45-55 million for Q3 2023**
  - **US$40 (A$59.4) million milestone payment received by Neuren on first commercial sale**
  - **Royalty of US$2.3 (A$3.5) million earned by Neuren for Q2 2023**
  - **In North America Neuren receives quarterly royalties, plus milestone payments of up to US$350 million subject to achievement of annual net sales thresholds, plus one third of the market value of Rare Pediatric Disease Priority Review Voucher when sold or used by Acadia**
- **Transaction executed in July 2023 to expand trofinetide partnership with Acadia from North America to worldwide:**
  - **US$100 (A$146) million up-front payment, received by Neuren in July**
  - **Neuren to receive additional potential milestone payments of up to US$427 million, plus royalties on net sales ex-North America**
  - **Expanded partnership leverages Acadia's unique knowledge and expertise from the successful development and commercialisation of DAYBUE in the United States**
- **Phase 2 clinical trials of NNZ-2591 in 4 indications advancing towards first results:**
  - **Enrolment completed for Phelan-McDermid syndrome, top-line results expected in Dec 2023**
  - **Prader-Willi syndrome trial commenced in June 2023**

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today reported profit after tax of A$47.8 million in its financial results for the half year ended 30 June 2023.

Neuren CEO Jon Pilcher commented: "Progress across the three elements of Neuren's business has been transformational. The approval and exceptional launch of DAYBUE by Acadia in the US has driven H1 2023 profit after tax for Neuren of A$48 million, including the first ongoing royalties. Subsequently in July our new agreement with Acadia to expand this to the world delivered A$146 million plus attractive future economics. As our revenues from DAYBUE grow, we are on track to reach a key value inflection point in December with the first results from treatment of Phelan-McDermid syndrome with NNZ-2591."

Summary financial results:

	H1 2023 A$ m	H1 2022 A$ m
Royalties	3.5	-
Milestone payments	59.4	-
Revenue from DAYBUE	**62.9**	**-**
Other income	1.5	0.3
Total income	**64.4**	**0.3**
R&D	(11.1)	(4.6)
Corporate & administration	(2.7)	(1.6)
Non-cash share based payments	(1.0)	(1.2)
Total expenses	**(14.8)**	**(7.4)**
Profit before tax	**49.6**	**(7.1)**
Income tax	(1.8)	-
Profit after tax	**47.8**	**(7.1)**
Cash flow from operations	44.9	(5.8)
	30 Jun 2023	31 Dec 2022
Total cash and short term investments	**85.7**	**40.2**

Commentary on events and outlook

There are three key drivers growing the value of 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

   First top-line results in **Dec 2023** for **Phelan-McDermid syndrome**

1. DAYBUE in North America

On 10 March 2023, Neuren's partner Acadia Pharmaceuticals (NASDAQ: ACAD) received US Food and Drug Administration (FDA) approval of DAYBUE™ (trofinetide) for the treatment of Rett syndrome in adult and pediatric patients two years of age and older. DAYBUE is the first and only approved treatment for Rett syndrome. On 17 April, Acadia announced the commercial launch of DAYBUE in the United States. The first commercial sale earned Neuren a milestone payment of US$40 (A$59.4) million.

On 2 August, Acadia released Q2 2023 financial results, reporting DAYBUE net sales of US$23.2 million in Q2 2023, the first partial quarter of sales, and reiterating net sales guidance for Q3 2023 of US$45 to US$55 million.

Acadia also provided further early insights on the launch to date. Adoption of DAYBUE in the diagnosed Rett syndrome population had been faster than expected and caregivers and physicians have reported meaningful improvements in patients. More than 400 prescribers from all regions and sectors had written prescriptions and as at 2 August, 7 out of 10 written prescriptions from Q2 had converted to paid. The patient mix was consistent with the broad approved label for treatment of all people with Rett syndrome 2 years of age and older. Access to reimbursement through Medicaid and private health insurance was accelerating, with formal written policies in place for one third of covered lives and those not yet covered by formal policies able to seek coverage through medical exception or letter of medical necessity processes. The payer mix was consistent with expectations (60% Medicaid, 25% commercial plans, remainder Medicare & other federal programs).

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, with the one third share estimated by Neuren 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]		Sales Milestone payments	
Annual Net Sales	**Rates**	**Net Sales in one calendar year**	**US$m**
≤US$250m	10%	≥US$250m	50
>US$250m, ≤US$500m	12%	≥US$500m	50
>US$500m, ≤US$750m	14%	≥US$750m	100
>US$750m	15%	≥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 sales milestone payments of up to US$55 million if Acadia develops trofinetide for Fragile X syndrome.

2. Trofinetide outside North America

On 14 July 2023, Neuren announced the expansion of its partnership with Acadia, with Acadia's exclusive licence for trofinetide in North America expanded to a worldwide exclusive licence. This leverages Acadia's unique knowledge and expertise from the successful development and commercialisation of DAYBUE in the United States.

The existing milestone payments and royalties to Neuren for trofinetide in North America remain unchanged, with additional payments related to development and commercialisation outside North America comprising:

Trofinetide	Payment
Upfront payment (received on 27 July)	**US$100m**
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**

Under the new agreement, Neuren also granted to Acadia an exclusive worldwide licence to develop and commercialise NNZ-2591 for Rett syndrome and Fragile X syndrome only. This replaced the restrictions in the existing agreement on its use by Neuren in those two indications. Potential milestone payments and royalties payable to Neuren for NNZ-2591 in Rett and Fragile X are identical to the trofinetide milestone payments and royalties in each of North America and other regions. Neuren retains worldwide rights to NNZ-2591 in all other indications.

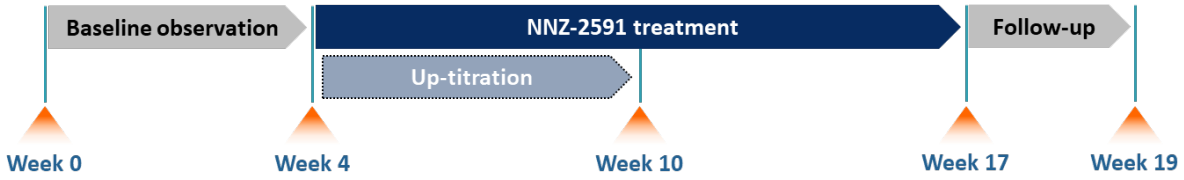
If Acadia sub-licenses trofinetide for any region outside North America within the first two years, Neuren is entitled to a share of any upfront and development milestones received by Acadia. Any such payment to Neuren will be credited against any future milestone and royalty payments payable to Neuren in the relevant region.

Acadia is responsible for all costs of development and commercialization globally for trofinetide in all indications and for NNZ-2591 in Rett and Fragile X only.

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 Phelan-McDermid, 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). The estimated number of potential patients being targeted across these four disorders is more than five times larger than Rett syndrome.

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



In June, Neuren announced commencement of the Prader-Willi syndrome trial in the United States and the completion of enrolment in the Phelan-McDermid syndrome trial. Top-line results from the Phelan-McDermid trial are expected in December 2023.

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.

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.

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 is conducting Phase 2 trials of its second drug candidate, NNZ-2591, for each of Phelan-McDermid syndrome, Angelman syndrome, Pitt Hopkins syndrome and Prader-Willi syndrome.

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.

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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.