Neuren (NEU) – ASX announcement **14 July 2023**

Neuren and Acadia expand global partnership for trofinetide (DAYBUE™)

Highlights:

- **Acadia's exclusive licence for trofinetide in North America expanded to worldwide licence**
- **Neuren to receive US$100 million up-front, plus additional potential milestone payments of up to US$427 million, plus royalties**
- **Existing milestone payments and royalties for trofinetide in North America unchanged**
- **Expanded partnership leverages Acadia's unique knowledge and expertise from the successful development and commercialisation of trofinetide (marketed in the US as DAYBUE™) in the United States**
- **Update on DAYBUE launch in the US - Acadia expects net sales of $21-23 million in Q2 2023 and $45-55 million in Q3 2023**
- **Exclusive worldwide licence granted to Acadia for NNZ-2591 solely in Rett and Fragile X - enables coordinated global development and removes existing restrictions on Neuren for NNZ-2591 in those two indications. Milestone payments and royalties to Neuren for NNZ-2591 in Rett and Fragile X identical to trofinetide milestone payments and royalties.**
- **Neuren retains worldwide rights to NNZ-2591 in all other indications and is currently advancing Phase 2 trials in each of Phelan-McDermid, Pitt Hopkins, Angelman and Prader-Willi syndromes, with first results expected in December 2023**
- **Neuren to host webconference today at 9.30 am AEST**

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today announced the expansion of its partnership with Acadia Pharmaceuticals (NASDAQ: ACAD) for trofinetide (marketed in the US as DAYBUE™). Acadia's exclusive licence for trofinetide in North America has been expanded to a worldwide exclusive licence. The existing milestone payments and royalties to Neuren for trofinetide in North America are unchanged, with additional payments related to development and commercialisation outside North America. Neuren will receive US$100 million up-front, plus additional potential milestone payments of up to US$427 million and royalties on net sales of trofinetide outside North America.

Acadia today provided very encouraging early insights into the US launch of DAYBUE, expecting net sales of $21-23 million in Q2 2023 and $45-55 million in Q3 2023.

Neuren has also granted to Acadia an exclusive worldwide licence to develop and commercialise NNZ-2591 for Rett syndrome and Fragile X syndrome only. This enables coordinated global development, replacing the restrictions in the existing agreement on 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 and is currently conducting Phase 2 clinical trials in each of Phelan-McDermid, Pitt Hopkins, Angelman and Prader-Willi syndromes, with first top-line results expected in December 2023.

Neuren CEO Jon Pilcher commented "We are very pleased to be able to expand our highly successful partnership with Acadia. The unique knowledge and expertise that the Acadia team has built from the successful development and commercialisation of DAYBUE™ in the United States, as well as the established supply chain, places them in the ideal position to achieve the optimum outcome globally for all stakeholders. We have also enhanced the position for NNZ-2591, adding the exciting potential to further increase its value through Acadia in Rett and Fragile X. We very much look forward to continuing to collaborate with Acadia as we all strive to make a difference in neurodevelopmental disorders, which have such urgent unmet need."

Key terms of the agreement

Future payments to Neuren relating to trofinetide in North America remain unchanged, at up to US$350 million milestone payments on achievement of escalating thresholds of annual net sales, plus tiered royalties ranging from 10% to 15% of net sales, plus one third of the value realized by Acadia from the Rare Pediatric Disease Priority Review Voucher that was awarded on FDA approval of DAYBUE. Furthermore, Neuren is eligible for potential milestone payments of up to US$55 million relating to the development of trofinetide for Fragile X syndrome in the United States.

Additional future payments to Neuren relating to trofinetide outside North America comprise:

Trofinetide	Payment
Upfront payment	**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**

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.

Potential future payments to Neuren related to NNZ-2591 in Rett syndrome and Fragile X syndrome are identical to the payments for trofinetide in each of North America and outside North America.

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.

Neuren has an obligation not to develop NNZ-2591 or any other product for North America in an indication for which Acadia develops trofinetide, except for Phelan-McDermid, Pitt Hopkins, Angelman and Prader-Willi syndromes.

Web conference call details

Investor Zoom Webinar 9:30 am AEST Friday 14 July

You are invited to register using this link:

https://us06web.zoom.us/webinar/register/WN_iMzwf2n7S-qJPVVCNwy5Rw

Participants may submit questions during registration or during the session

About Rett syndrome

Rett syndrome is a rare, complex, neurodevelopmental disorder that may occur over four stages and affects approximately 6,000 to 9,000 patients in the United States, with approximately 4,500 patients currently diagnosed according to an analysis of healthcare claims data. A child with Rett syndrome exhibits an early period of apparently normal development until six to 18 months, when their skills seem to slow down or stagnate. This is typically followed by a duration of regression when the child loses acquired communication skills and purposeful hand use. The child may then experience a plateau period in which they show mild recovery in cognitive interests, but body movements remain severely diminished. As they age, those living with Rett may continue to experience a stage of motor deterioration which can last the rest of the patient's life. Rett syndrome is typically caused by a genetic mutation on the MECP2 gene. In preclinical studies, deficiency in MeCP2 function has been shown to lead to impairment in synaptic communication, and the deficits in synaptic function may be associated with Rett manifestations. Symptoms of Rett syndrome may also include development of hand stereotypies, such as hand wringing and clapping, and gait abnormalities. Most Rett patients typically live into adulthood and require round-the-clock care.

About Fragile X Syndrome

Fragile X syndrome is the most common inherited cause of intellectual disability and the most common known cause of autism. Fragile X syndrome is caused by a single gene defect on the X chromosome that impacts the FMRP protein, which is responsible for regulating the synapses of nerve cells. One of every 5,000 males and one of every 4,000 to 8,000 females are estimated to have the full gene mutation. Generally, males are more severely affected than females. Clinically, Fragile X syndrome is characterized by intellectual disability, hyperactivity and attentional problems, autistic symptoms, anxiety, emotional lability and epilepsy. Currently, there are no medicines approved for the treatment of Fragile X syndrome.

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.

Contact:

Jon Pilcher, CEO: jpilcher@neurenpharma.com; +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.