Neuren (NEU) – ASX Announcement **18 April 2023**

DAYBUE™ (trofinetide) launched in US - Neuren earns US$40m

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) today reported that its North America partner Acadia Pharmaceuticals (NASDAQ: ACAD) has announced that DAYBUE™ (trofinetide) is now available for the treatment of Rett syndrome in adult and pediatric patients two years of age and older in the United States. DAYBUE was approved by the US Food and Drug Administration (FDA) on 10 March 2023 and is the first and only drug approved by the FDA for the treatment of Rett syndrome. The announcement by Acadia is attached.

Neuren and Acadia have an exclusive license agreement for Acadia to develop and commercialise trofinetide for the treatment of Rett syndrome and other indications in North America. US$40 million is payable to Neuren following the first commercial sale of trofinetide in the United States. Neuren is eligible to receive ongoing 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 upon approval of the NDA, with the one third share estimated by Neuren as US$33 million. No royalties or similar costs are payable by Neuren to third parties, which means that Neuren's revenue from Acadia will flow through to pre-tax profit.

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 licence to Acadia Pharmaceuticals Inc. for the development and commercialisation of trofinetide in North America, while retaining all rights outside North America.

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.

Acadia Pharmaceuticals Announces DAYBUE™ (trofinetide) is Now Available for the Treatment of Rett Syndrome

-- Commercial launch of DAYBUE offers Rett syndrome community the first and only approved therapy for Rett syndrome, a rare, neurodevelopmental disorder, which affects 6,000 to 9,000 patients in the U.S.[1]

SAN DIEGO--(BUSINESS WIRE)-- Acadia Pharmaceuticals Inc. (Nasdaq: ACAD) today announced that DAYBUE™ (trofinetide) is now available for the treatment of Rett syndrome in adult and pediatric patients two years of age and older in the United States. DAYBUE has demonstrated the potential to improve the signs and symptoms of Rett syndrome. DAYBUE was approved by the U.S. Food and Drug Administration (FDA) on March 10, 2023, and is the first and only drug approved by the FDA for the treatment of Rett syndrome.

“The Rett syndrome community has been waiting a long time for a drug to treat this debilitating disorder. We have worked hard to make DAYBUE available as quickly as possible following FDA approval,” said Steve Davis, Acadia’s Chief Executive Officer. “We are focused on providing robust patient support resources through Acadia Connect® to help caregivers and healthcare providers access this important new therapy.”

“Following my experience as an investigator in the Lavender Phase 3 study I have already initiated the process of prescribing DAYBUE for my patients. I am thrilled to now be able to offer DAYBUE to more people living with Rett syndrome, outside of a clinical trial,” said Alan Percy, M.D., Professor of Pediatrics, Neurology, Neurobiology, Genetics, and Psychology at University of Alabama, Birmingham. “Having a therapy that has been shown to address multiple symptoms of Rett syndrome provides a promising treatment option that may lead to meaningful impact for patients and their families.”

Acadia Connect® Patient Access and Support Services

As part of the company’s commitment to prioritizing patient access to treatments for those who need them most, Acadia expanded the Acadia Connect® program for those prescribed DAYBUE. The multi-faceted support program offers personal assistance, financial resources and prescription support to patients and caregivers starting and continuing appropriate DAYBUE therapy. Each dedicated support team includes a nurse care coordinator, a family access manager and 24/7 clinical pharmacist support. For more information, visit AcadiaConnect.com or call 1-844-737-2223, Monday to Friday, 8 a.m. to 8 p.m. Eastern Time.

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 U.S., with

approximately 4,500 patients currently diagnosed according to an analysis of healthcare claims data.[1-4] 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.[3] Rett syndrome is typically caused by a genetic mutation on the MECP2 gene.[5] 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.[5-7]

Symptoms of Rett syndrome may also include development of hand stereotypies, such as hand wringing and clapping, and gait abnormalities.[8] Most Rett patients typically live into adulthood and require round-the-clock care.[2,9]

About DAYBUE™ (trofinetide)

Trofinetide is a synthetic version of a naturally occurring molecule known as the tripeptide glycine-proline-glutamate (GPE). The mechanism by which trofinetide exerts therapeutic effects in patients with Rett syndrome is unknown. In animal studies, trofinetide has been shown to increase branching of dendrites and synaptic plasticity signals.[10,11] More information can be found at DAYBUE.com.

Important Safety Information for DAYBUE™ (trofinetide)

Important Safety Information

- **Warnings and Precautions**
  - **Diarrhea**: In a 12-week study and in long-term studies, an aggregate of 85% of patients treated with DAYBUE experienced diarrhea. In those treated with DAYBUE, 49% either had persistent diarrhea or recurrence after resolution despite dose interruptions, reductions, or concomitant antidiarrheal therapy. Diarrhea severity was of mild or moderate severity in 96% of cases. In the 12-week study, antidiarrheal medication was used in 51% of patients treated with DAYBUE.

    Patients should stop taking laxatives before starting DAYBUE. If diarrhea occurs, patients should notify their healthcare provider, consider starting antidiarrheal treatment, and monitor hydration status and increase oral fluids, if needed. Interrupt, reduce dose, or discontinue DAYBUE if severe diarrhea occurs or if dehydration is suspected.

    - **Weight Loss**: In the 12-week study, 12% of patients treated with DAYBUE experienced weight loss of greater than 7% from baseline, compared to 4% of patients who received placebo. In long-term studies, 2.2% of patients discontinued treatment with DAYBUE due to weight loss. Monitor weight and interrupt, reduce dose, or discontinue DAYBUE if significant weight loss occurs.
- **Adverse Reactions:** The common adverse reactions (≥5% for DAYBUE-treated patients and at least 2% greater than in placebo) reported in the 12-week study were diarrhea (82% vs 20%), vomiting (29% vs 12%), fever (9% vs 4%), seizure (9% vs 6%), anxiety (8% vs 1%), decreased appetite (8% vs 2%), fatigue (8% vs 2%), and nasopharyngitis (5% vs 1%).
- **Drug Interactions: Effect of DAYBUE on other Drugs**
    - DAYBUE is a weak CYP3A4 inhibitor; therefore, plasma concentrations of CYP3A4 substrates may be increased if given concomitantly with DAYBUE. Closely monitor when DAYBUE is used in combination with orally administered CYP3A4 sensitive substrates for which a small change in substrate plasma concentration may lead to serious toxicities.
    - Plasma concentrations of OATP1B1 and OATP1B3 substrates may be increased if given concomitantly with DAYBUE. Avoid the concomitant use of DAYBUE with OATP1B1 and OATP1B3 substrates for which a small change in substrate plasma concentration may lead to serious toxicities.
- **Use in Specific Population: Renal Impairment**
    - DAYBUE is not recommended for patients with moderate or severe renal impairment.

DAYBUE is available as an oral solution (200mg/mL).

Please read the accompanying full Prescribing Information, also available at DAYBUE.com

About Acadia Pharmaceuticals

Acadia is advancing breakthroughs in neuroscience to elevate life. For almost 30 years we have been working at the forefront of healthcare to bring vital solutions to people who need them most. We developed and commercialized the first and only approved therapies for hallucinations and delusions associated with Parkinson's disease psychosis and for the treatment of Rett syndrome. Our clinical-stage development efforts are focused on treating the negative symptoms of schizophrenia, Alzheimer's disease psychosis and neuropsychiatric symptoms in central nervous system disorders. For more information, visit us at www.acadia.com and follow us on LinkedIn and Twitter.

Forward-Looking Statements

Statements in this press release that are not strictly historical in nature are forward-looking statements. These statements include but are not limited to statements

regarding the timing of future events. These statements are only predictions based on current information and expectations and involve a number of risks and uncertainties. Actual events or results may differ materially from those projected in any of such statements due to various factors, including the risks and uncertainties inherent in drug development, approval and commercialization. For a discussion of these and other factors, please refer to Acadia's annual report on Form 10-K for the year ended December 31, 2022, as well as Acadia's subsequent filings with the Securities and Exchange Commission. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All forward-looking statements are qualified in their entirety by this cautionary statement and Acadia undertakes no obligation to revise or update this press release to reflect events or circumstances after the date hereof, except as required by law.

References

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