



Neuren (NEU) – ASX Announcement

19 July 2022

Acadia submits Rett Syndrome New Drug Application to the FDA

Melbourne, Australia: Neuren Pharmaceuticals (ASX: NEU) is pleased to report that its US partner Acadia Pharmaceuticals (Nasdaq: ACAD) has submitted a New Drug Application (NDA) to the US Food and Drug Administration (FDA) for trofinetide for the treatment of Rett syndrome in adults and pediatric patients two years of age and older. Acadia's news release is attached to this ASX announcement.

Acadia has exclusive rights to develop and commercialize trofinetide in North America. Under the terms of Neuren's agreement with Acadia, the development and commercialisation of trofinetide in North America is fully funded by Acadia and Neuren may receive potential milestone payments of up to US\$455 million, plus double-digit percentage royalties on net sales of trofinetide in North America, plus one third of the market value of a Rare Pediatric Disease Priority Review Voucher if awarded by the FDA upon approval of a NDA for trofinetide.

If the NDA is approved by the FDA, Neuren expects to earn revenue over 2022 and 2023 for Rett syndrome in the US alone of A\$118 million plus double-digit percentage royalties on net sales. The expected revenue in addition to the royalties comprises:

- A milestone payment in 2022 of US\$10 million (A\$14 million at assumed exchange rate of 0.70) following acceptance of the NDA for review by the FDA
- A milestone payment in 2023 of US\$40 million (A\$57 million), following the first commercial sale of trofinetide in the United States
- US\$33 million (A\$47 million) in 2023 as Neuren's one third share of the market value of a Priority Review Voucher, estimated as US\$100 million.

Neuren's additional ongoing revenue from potential sales has two components:

- Double digit percentage royalties on net sales of trofinetide in all indications. The annual net sales are recorded in tiers and an escalating percentage is applied to each successive tier.
- Payments of up to US\$350 million (approximately A\$500 million) on achievement of a series of 4 thresholds of total annual net sales for all indications.

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.

Neuren retained all rights to trofinetide for all countries outside North America and has a fully paid-up, irrevocable licence for use in those countries to all data generated by Acadia. Rett syndrome is a devastating condition with no approved therapies and there is urgent unmet



need around the world for a treatment. Neuren has received strong interest for potential commercial partnerships and discussions are continuing under a process to secure the optimum outcome for shareholders and for patients.

About Neuren

Neuren is developing two new drug therapies to treat multiple serious neurological disorders that emerge in early childhood, none of which have any approved medicines.

The lead compound, trofinetide, achieved positive results in a Phase 3 clinical trial for Rett syndrome and has also completed a Phase 2 clinical trial in Fragile X syndrome. Both programs have Fast Track designation from the US Food and Drug Administration (FDA). 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 initiating 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 six 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 Submits New Drug Application to the U.S. FDA for Trofinetide for the Treatment of Rett Syndrome

SAN DIEGO--(BUSINESS WIRE)--July 18, 2022-- Acadia Pharmaceuticals Inc. (Nasdaq: ACAD) today announced that the company has submitted a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for trofinetide for the treatment of Rett syndrome in adults and pediatric patients two years of age and older.

“This is an important step forward for members of the Rett community who face a devastating disease with no approved therapies,” said Steve Davis, Chief Executive Officer. “We are grateful to the patients, their families and the physicians who have participated in the trofinetide clinical studies, including our pivotal Phase 3 Lavender study. We look forward to working with the FDA as it evaluates the NDA.”

The NDA submission is supported by results from the pivotal Phase 3 Lavender™ study evaluating the efficacy and safety of trofinetide versus placebo in 187 girls and young women aged 5-20 years with Rett syndrome. The study demonstrated a statistically significant improvement over placebo on the co-primary endpoints, the Rett Syndrome Behaviour Questionnaire (RSBQ) change from baseline to 12 weeks ($p=0.0175$; effect size=0.37) and the Clinical Global Impression-Improvement (CGI-I) scale score ($p=0.0030$; effect size=0.47) at 12 weeks. The RSBQ is a caregiver assessment of the core symptoms of Rett syndrome and the CGI-I is a global physician assessment of worsening or improving of Rett syndrome. In addition, the study also met its key secondary endpoint, the Communication and Symbolic Behavior Scales Developmental Profile™ Infant-Toddler Checklist–Social composite score (CSBS-DP-IT–Social) change from baseline to week 12 ($p=0.0064$; effect size=0.43), a caregiver scale of the ability to communicate.

In 2018, Acadia entered into an exclusive license agreement with Neuren Pharmaceuticals (ASX: NEU) for the development and commercialization of trofinetide for the treatment of Rett syndrome and other indications in North America. Trofinetide has been granted Fast Track Status and Orphan Drug Designation for the treatment of Rett syndrome in the United States. An NDA with Orphan Drug Designation is eligible for priority review. Trofinetide has also been granted Rare Pediatric Disease (RPD) designation by the FDA. With such designation, Acadia expects to be awarded a Priority Review Voucher if the NDA is approved.

About Lavender™

The Lavender study was a Phase 3, 12-week, double-blind, randomized, placebo-controlled study of trofinetide in 187 girls and young women aged 5-20 years with Rett syndrome, designed to evaluate its efficacy and safety. The co-primary endpoints of Lavender included both a caregiver (Rett Syndrome Behaviour Questionnaire [RSBQ]) and physician (Clinical Global Impression–Improvement [CGI-I]) assessment. The key secondary endpoint was also a caregiver assessment designed to evaluate communication skills, the Communication and Symbolic Behavior Scales Developmental Profile™ Infant-Toddler Checklist – Social Composite Score (CSBS-DP- IT–Social).

About Rett Syndrome

Rett syndrome is a rare genetic neurodevelopmental disorder that occurs primarily in females following a near normal development in the first two years of life.^{1,2} It is caused by mutations on the X chromosome on a gene called *MECP2*.³ Occurring worldwide in approximately one of every 10,000 to 15,000 female births and in the United States impacts 6,000 to 9,000 patients.⁴ Children

with Rett syndrome experience a period of developmental regression between 18-30 months of age, which is typically followed by a plateau period lasting years to decades.^{1,2,5} Rett syndrome is diagnosed based on clinical evaluation, typically by about three years of age.^{2,6}

A complex and multisystem disorder, Rett syndrome causes profound impairment to central nervous system (CNS) function, including loss of communication skills, purposeful hand use, gait abnormalities, and stereotypic hand movements such as hand wringing/squeezing, clapping/tapping, mouthing and washing/rubbing automatisms.² People living with Rett syndrome may also experience a range of additional symptoms, such as gastrointestinal complications, skeletal abnormalities, neuroendocrine abnormalities, disruptive and anxiety-like behaviors, as well as mood dysregulation and sleep disturbances.¹ Currently, there are no FDA-approved medicines for the treatment of Rett syndrome.

About Trofinetide

Trofinetide is an investigational drug. It is a novel synthetic analog of the amino-terminal tripeptide of IGF-1 designed to treat the core symptoms of Rett syndrome by potentially reducing neuroinflammation and supporting synaptic function. Trofinetide is thought to stimulate synaptic maturation and overcome the synaptic and neuronal immaturities that are characteristic of Rett syndrome pathophysiology. In the central nervous system, IGF-1 is produced by both of the major types of brain cells – neurons and glia. IGF-1 in the brain is critical for both normal development and for response to injury and disease. Trofinetide has been granted Fast Track Status and Orphan Drug Designation for Rett syndrome and has also been granted Rare Pediatric Disease (RPD) designation by the FDA.

About Acadia Pharmaceuticals

Acadia is advancing breakthroughs in neuroscience to elevate life. For more than 25 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 therapy for hallucinations and delusions associated with Parkinson's disease psychosis. Our late-stage development efforts are focused on treating psychosis in patients with dementia, the negative symptoms of schizophrenia and Rett syndrome. Our early-stage development efforts are focused on novel approaches to pain management, cognition 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, 2021 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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- ⁵ NINDS. Rett Syndrome Fact Sheet. Retrieved from <https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Rett-Syndrome-Fact-Sheet>. Accessed February 2022.
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