



Acadia Pharmaceuticals Announces Trofinetide New Drug Application for the Treatment of Rett Syndrome has been Accepted for Filing and Review by U.S. FDA

September 12, 2022

-- NDA granted priority review

-- Prescription Drug User Fee Act action date set for March 12, 2023

SAN DIEGO--(BUSINESS WIRE)--Sep. 12, 2022-- Acadia Pharmaceuticals Inc. (Nasdaq: ACAD) today announced that the U.S. Food and Drug Administration (FDA) has accepted for filing its New Drug Application (NDA) of trofinetide for the treatment of Rett syndrome. The FDA has granted a priority review and assigned a PDUFA (Prescription Drug User Fee Act) action date of March 12, 2023. The FDA has also informed the company that at this time they are not planning to hold an Advisory Committee meeting.

"We're pleased that the FDA has accepted our NDA filing and we will be working closely with them to facilitate completion of the review in a timely manner," said Steve Davis, Acadia's Chief Executive Officer. "If approved, trofinetide will be the first drug available for the treatment of Rett syndrome, a rare and devastating condition for patients and their families. This milestone reinforces Acadia's ongoing commitment to advancing research into high unmet needs in disorders affecting the central nervous system."

Rett syndrome is a complex, multisystem neurodevelopmental disorder that includes a period of normal development followed by significant developmental regression with loss of language and hand function skills, impaired gait and development of hand stereotypes.^{1,2} It occurs worldwide in approximately one of every 10,000 to 15,000 female births.³

"Rett is a complex disease that can present with a diverse array of symptoms. In clinical trials, trofinetide demonstrated a significant improvement in a range of Rett syndrome symptoms," said Jeffrey L. Neul, M.D., Ph.D., Annette Schaffer Eskind Chair and Director, Vanderbilt Kennedy Center, Professor of Pediatrics, Division of Neurology, Pharmacology, and Special Education, Vanderbilt University Medical Center and Phase 3 Lavender™ study investigator. "We look forward to the FDA's review of this submission and the prospect of having access to the first approved treatment for Rett syndrome."

The NDA 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) total score 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). 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 assessment of ability to communicate.

In 2018, Acadia entered into an exclusive license agreement with Neuren Pharmaceuticals Limited (ASX: NEU) for the development and commercialization of trofinetide for the treatment of Rett syndrome and other indications in North America. In addition to receiving priority review by the FDA, trofinetide has been granted Fast Track Status and Orphan Drug Designation for the treatment of Rett syndrome in the U.S. and has been granted Rare Pediatric Disease (RPD) designation by the FDA. Upon FDA approval of a product with RPD designation, the sponsor can receive a Priority Review Voucher, which can be used to obtain priority review for a subsequent application.

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 non-verbal 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*.⁴ 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.³ 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.^{1,2,4} Rett syndrome is diagnosed based on clinical evaluation, typically by about three years of age.^{2,5}

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 shown to inhibit the production of inflammatory cytokines, inhibit the overactivation of microglia and astrocytes, and increase the amount of available IGF-1 that can bind to IGF-1 receptors.

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 clinical-stage development efforts are focused on treating the negative symptoms of schizophrenia, Rett syndrome 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

- ¹ Fu et al. Consensus guidelines on managing Rett syndrome across the lifespan. *BMJ Paediatrics Open*. 2020;4:1-14.
- ² Neul JL, Kaufmann WE, Glaze DG, et al. Rett syndrome: revised diagnostic criteria and nomenclature. *Ann Neurol*. 2010;68(6):944-950.
- ³ U.S. prevalence estimate based on incidence rates from the National Institutes of Health – National Institute of Neurological Disorders and Stroke.
- ⁴ Amir RE, et al. Rett syndrome is caused by mutations in X-linked MECP2, encoding methyl-CpG-binding protein 2. *Nat Genet*. 1999;23:185-188.
- ⁵ Tarquinio. Age of Diagnosis in Rett Syndrome: Patterns of Recognition Among Diagnosticians and Risk Factors for Late Diagnosis. *Pediatric Neurology*. 2015;52:585-591.

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Source: Acadia Pharmaceuticals Inc.