# ACADIA Pharmaceuticals and Neuren Pharmaceuticals Announce Exclusive License Agreement for the North American Development and Commercialization of Trofinetide in Rett Syndrome

August 6, 2018

*-ACADIA plans to initiate a Phase 3 study of trofinetide for the treatment of Rett syndrome, a rare neurodevelopmental congenital CNS disorder, in the second half of 2019*

*-Neuren retains all rights to trofinetide outside of North America*

*-Neuren to receive US $10 million upfront plus potential milestones of up to US $455 million and royalties*

SAN DIEGO & MELBOURNE, Australia--(BUSINESS WIRE)--Aug. 6, 2018-- ACADIA Pharmaceuticals Inc. (NASDAQ: ACAD) and Neuren Pharmaceuticals Limited (ASX: NEU) announced today that they have entered into an exclusive North American License Agreement for the development and commercialization of trofinetide for Rett syndrome and other indications. Neuren retains rights to develop and commercialize trofinetide for all indications outside of North America.

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ACADIA plans to initiate a Phase 3 randomized, double-blind placebo-controlled study evaluating trofinetide in the second half of 2019 following completion of additional manufacturing activities. This study will evaluate trofinetide and placebo in approximately 180 girls with Rett syndrome and will measure the Rett Syndrome Behavior Questionnaire (RSBQ), a caregiver assessment, and the Clinical Global Impression of Improvement (CGI-I), a physician assessment, as co-primary efficacy endpoints.

“A potential treatment for Rett syndrome is a perfect fit with ACADIA’s mission to develop novel therapies to improve the lives of patients with central nervous system disorders,” said Serge Stankovic, M.D., M.S.P.H, Executive Vice President, Head of Research and Development at ACADIA. “Today there are no approved treatments for the girls and women suffering from Rett syndrome. We look forward to initiating a Phase 3 study in the second half of 2019 to further explore the potential benefits of trofinetide for patients and their caregivers.”

Neuren Executive Chairman Dr. Richard Treagus commented, “We are delighted to be partnering with ACADIA in North America. ACADIA’s team has a proven record in developing and commercializing medicines in central nervous system disorders with no approved therapies and high unmet needs. ACADIA’s additional capabilities and resources will immediately make a very significant difference, enabling us to advance our shared goal of developing this novel treatment option for Rett syndrome patients.”

Steve Kaminsky, Ph.D., Chief Science Officer of Rettsyndrome.org, commented, “Rettsyndrome.org is grateful to Neuren for their dedication to the development of trofinetide. ACADIA’s commitment to advance trofinetide to Phase 3 brings us closer to the first potential treatment for Rett syndrome with a drug designed to address the underlying biology and improve the lives of those suffering from the condition.”

Trofinetide is a novel synthetic analog of the amino-terminal tripeptide of IGF-1 designed to treat the core symptoms of Rett syndrome by reducing neuroinflammation and supporting synaptic function. 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[1,2]. Trofinetide has been granted U.S. Food and Drug Administration (FDA) Fast Track Status and Orphan Drug Designation in the U.S. and Europe.

Neuren conducted a Phase 2 double-blind placebo-controlled dose ranging study in girls aged 5 to 15 years with Rett syndrome, in which statistically significant and clinically meaningful improvement was demonstrated on the RSBQ and the CGI-I. This followed positive trends observed in an earlier Phase 2 trial in adolescents and adults aged 16 to 45 years with Rett syndrome[3]. In addition, Neuren has completed an exploratory study in Fragile X syndrome.

Dr. Daniel Glaze, Medical Director at the Blue Bird Circle Rett Center, Texas Children’s Hospital commented, “The trofinetide Phase 2 results in Rett syndrome are very promising in terms of both safety and clinical benefit. For many families, these improvements would provide meaningful improvement in their child’s quality of life.”

Under the terms of the License Agreement, Neuren is eligible to receive US $10 million upfront plus potential milestone payments of up to US $455 million. In addition, Neuren is eligible to receive tiered, escalating, double-digit percentage royalties on net sales of trofinetide in North America and one third of the market value of any Rare Pediatric Disease Priority Review Voucher, if awarded by the U.S. FDA upon approval of a New Drug Application for trofinetide. The potential milestone payments to Neuren consist of US $105 million subject to achievement of development milestones in Rett syndrome and Fragile X syndrome and up to US $350 million subject to achievement of thresholds of annual net sales of trofinetide in North America. ACADIA will fund and execute the remaining development for trofinetide in Rett syndrome in North America, except for the completion by Neuren of certain in-progress preparatory activities. ACADIA and Neuren will form a Joint Steering Committee to direct the development of trofinetide in all indications, including the next clinical trial for Fragile X syndrome. Any data and regulatory filings generated by ACADIA or Neuren may be used by either party for the development and commercialization of trofinetide in their respective territories. ACADIA has a right of first negotiation to acquire a license to develop and commercialize trofinetide outside North America. Neuren has an obligation not to develop a competing product in indications for which ACADIA develops and commercializes trofinetide.

*About Trofinetide*

Trofinetide is a novel synthetic analog of the amino-terminal tripeptide of IGF-1 designed to treat the core symptoms of Rett syndrome by reducing neuroinflammation and supporting synaptic function. 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[1,2]. Trofinetide has been granted

U.S. FDA Fast Track Status and Orphan Drug Designation in the U.S. and Europe for both Rett syndrome and Fragile X syndrome.

*About Rett Syndrome*
Rett syndrome is a debilitating neurological disorder that occurs primarily in females following apparently normal development for the first six months of life. Rett syndrome has been most often misdiagnosed as autism, cerebral palsy, or non-specific developmental delay. Rett syndrome is caused by mutations on the X chromosome on a gene called MeCP2[4]. There are more than 200 different mutations found on the MeCP2 gene that interfere with its ability to generate a normal gene product[4]. Rett syndrome occurs worldwide in approximately one of every 10,000 to 15,000 female births[5] causing problems in brain function that are responsible for cognitive, sensory, emotional, motor and autonomic function. Typically, between six to eighteen months of age, patients experience a period of rapid decline with loss of purposeful hand use and spoken communication and inability to independently conduct activities of daily living[5]. Symptoms also include seizures, disorganized breathing patterns, an abnormal side-to-side curvature of the spine (scoliosis) and sleep disturbances. Currently, there are no approved medicines approved for the treatment of Rett syndrome[1].

*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[6]. 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 ACADIA Pharmaceuticals*
ACADIA is a biopharmaceutical company focused on the development and commercialization of innovative medicines to address unmet medical needs in central nervous system disorders. ACADIA has developed and is commercializing the first and only medicine approved for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis. In addition, ACADIA has ongoing clinical development efforts in additional areas with significant unmet need including dementia-related psychosis, schizophrenia inadequate response, schizophrenia-negative symptoms and major depressive disorder. This press release and further information about ACADIA can be found at: www.acadia-pharm.com.

*About Neuren Pharmaceuticals*
Neuren Pharmaceuticals Limited (Neuren) is a biopharmaceutical company developing new therapies for brain injury, neurodevelopmental and neurodegenerative disorders. Neuren has completed Phase 2 development of trofinetide for Rett syndrome and has completed a Phase 2 clinical trial in Fragile X syndrome.

*About Rettsyndrome.org*
Rettsyndrome.org is one of the leading private funders of Rett syndrome research. The organization hosts the largest global gathering of Rett researchers and clinicians to establish research direction for the future. The mission of the organization is to accelerate the full spectrum research to cure Rett syndrome and empower families with information, knowledge and connectivity. Further information about Rettsyndrome.org can be found at: rettsyndrome.org.

*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 the commencement of the Phase 3 clinical trial evaluating trofinetide; the likelihood of success of such clinical trial; the prospects for FDA approval of trofinetide for Rett syndrome and other indications; and the success of any efforts to commercialize trofinetide in North America. 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 discovery, 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, 2017 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.

This ASX-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.

*References*

[1]Tropea, D., et al. (2009). "Partial reversal of Rett Syndrome-like symptoms in MeCP2 mutant mice." Proc Natl Acad Sci U S A 106(6): 2029-2034.

[2]Vahdatpour, C., et al. (2016). "Insulin-Like Growth Factor 1 and Related Compounds in the Treatment of Childhood-Onset Neurodevelopmental Disorders." Front Neurosci 10: 450.

[3]Glaze, D. G., et al. (2017). "A Double-Blind, Randomized, Placebo-Controlled Clinical Study of Trofinetide in the Treatment of Rett Syndrome." Pediatr Neurol 76: 37-46.

[4]Chahrour, M. and H. Y. Zoghbi (2007). "The story of Rett syndrome: from clinic to neurobiology." Neuron 56(3): 422-437.

[5]Ip, J. P. K., et al. (2018). "Rett syndrome: insights into genetic, molecular and circuit mechanisms." Nat Rev Neurosci 19(6): 368-382.

[6]Hagerman, R.J., et al. (2017). "Fragile X syndrome." Nat Rev Disease Primers 3: 1-19.

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