Acadia Pharmaceuticals and Stoke Therapeutics Announce Collaboration to Pursue Multiple RNA-based Treatments for Severe and Rare Genetic Neurodevelopmental Diseases

January 10, 2022

– Establishes co-development and co-commercialization agreement for Stoke's SYNGAP1 preclinical program

– Acadia receives exclusive worldwide licenses for two additional preclinical programs: Rett syndrome (MECP2) and undisclosed neurodevelopmental target

– Combines Stoke's TANGO research platform with Acadia's expertise in neurology drug development and commercialization

– Stoke receives a $60 million upfront payment and potential milestone payments of up to $907 million and royalties on future sales

SAN DIEGO & BEDFORD, Mass.--(BUSINESS WIRE)--Jan. 10, 2022-- Acadia Pharmaceuticals Inc. (Nasdaq: ACAD) and Stoke Therapeutics, Inc. (Nasdaq: STOK) announced today that the companies have entered a collaboration to discover, develop and commercialize novel RNA-based medicines for the potential treatment of severe and rare genetic neurodevelopmental diseases of the central nervous system (CNS). The collaboration includes SYNGAP1 syndrome, Rett syndrome (*MECP2*), and an undisclosed neurodevelopmental target of mutual interest.

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"Stoke's RNA-based approach to upregulating healthy proteins offers very exciting new possibilities for the treatment of rare, neurodevelopmental diseases like Rett syndrome," said Steve Davis, Chief Executive Officer of Acadia Pharmaceuticals. "Combining Stoke's capabilities with Acadia's extensive expertise in neuroscience drug development and commercialization enables us to push harder and faster in exploring some of the new frontiers in rare central nervous system disorders. We are excited to have the opportunity to further build our Rett syndrome franchise and pursue treatments in SYNGAP1 syndrome and other neurodevelopmental disorders."

"Rett syndrome and SYNGAP1 syndrome are two severe, intractable diseases of the central nervous system and both are associated with developmental delays, motor function loss, autism, seizures and other comorbidities that impact quality of life for patients and their families," said Edward M. Kaye, M.D., Chief Executive Officer of Stoke Therapeutics. "Acadia shares our deep commitment to improving outcomes for people living with neurodevelopmental disorders. We believe their late-stage development and commercialization capabilities, in addition to their neuroscience expertise, complement our discovery research efforts and clinical learnings from our work in Dravet syndrome. Together, we believe we have a significant opportunity to improve treatment options by delivering new disease-modifying medicines to people who need them."

Terms of Collaboration
Under the terms of the agreement, Stoke will receive an upfront payment of $60 million from Acadia and is eligible to receive up to $907 million in milestones as well as royalties on future sales.

For the SYNGAP1 program, the two companies will jointly share global research, development and commercialization responsibilities and share 50/50 in all worldwide costs and future profits. In addition, Stoke is eligible to receive potential development, regulatory, first commercial sales and sales milestones.

For the Rett syndrome *(MECP2*) and the undisclosed neurodevelopmental program, Stoke will lead research and pre-clinical development activities, while Acadia will lead clinical development and commercialization activities. Acadia will fully fund the research and pre-clinical development activities related to these two targets and Stoke is eligible to receive potential development, regulatory, first commercial sales and sales milestones as well as tiered royalty payments on worldwide sales starting in the mid-single digit range and escalating to the mid-teens based on revenue levels.

About SYNGAP1 Syndrome
SYNGAP1 syndrome is a rare neurological disorder characterized by moderate to severe intellectual disability that is evident in early childhood. Mutations in the *SYNGAP1* gene (which produces the SynGAP protein) were first identified in 2009 and since then, an increasing number of children with SYNGAP1 syndrome have been identified. Normal levels of SynGAP protein are essential for proper brain function and development. Mutations in the *SYNGAP1* gene also play an important role in the development of epileptic encephalopathies (DEEs). The severity and onset of symptoms can vary from patient to patient. SYNGAP1 syndrome is characterized by developmental delay or intellectual disability, generalized epilepsy, and autism spectrum disorder (ASD) and other behavioral abnormalities. More than 80% of cases of SYNGAP1 syndrome are caused by a haploinsufficiency of the *SYNGAP1* gene. SYNGAP1 syndrome is estimated to account for 1% to 2% of all intellectual disability cases. There are currently no approved treatments for SYNGAP1 syndrome.

About Rett Syndrome
Rett syndrome is a rare, debilitating neurological disorder that occurs primarily in females following apparently normal development for the first six months of life. Rett syndrome is 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*. There are more than 200 different mutations found on the *MECP2* gene that interfere with its ability to generate a normal gene product. Rett syndrome occurs 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. Rett syndrome causes problems in brain function that are responsible for cognitive, sensory, emotional, motor and autonomic function. Typically, with symptoms presenting between 6 to 18 months of age, patients experience a period of rapid decline with loss of purposeful hand use (fine motor skills), development of hand stereotypies, absent or impaired mobility (gross motor skills), loss of communication skills (including eye contact) and inability to independently conduct activities of daily living. Symptoms also include seizures,

disorganized breathing patterns, an abnormal side-to-side curvature of the spine (scoliosis), and sleep disturbances. Currently, there are no FDA-approved medicines for the treatment of Rett syndrome.

About TANGO
TANGO (Targeted Augmentation of Nuclear Gene Output) is Stoke's proprietary research platform. Stoke's initial application for this technology are diseases in which one copy of a gene functions normally and the other is mutated, also called haploinsufficiencies. In these cases, the mutated gene does not produce its share of protein, resulting in disease. Using the TANGO approach and a deep understanding of RNA science, Stoke researchers design antisense oligonucleotides (ASOs) that bind to pre-mRNA and help the functional (or wild-type) genes produce more protein. TANGO aims to restore missing proteins by increasing – or stoking – protein output from healthy genes, thus compensating for the mutant copy of the gene.

About Stoke Therapeutics
Stoke Therapeutics (Nasdaq: STOK), is a biotechnology company dedicated to addressing the underlying cause of severe diseases by upregulating protein expression with RNA-based medicines. Using Stoke's proprietary TANGO (Targeted Augmentation of Nuclear Gene Output) approach, Stoke is developing antisense oligonucleotides (ASOs) to selectively restore protein levels. Stoke's first compound, STK-001, is in clinical testing for the treatment of Dravet syndrome, a severe and progressive genetic epilepsy. Dravet syndrome is one of many diseases caused by a haploinsufficiency, in which a loss of ~50% of normal protein levels leads to disease. Stoke is pursuing treatment for a second haploinsufficient disease, autosomal dominant optic atrophy (ADOA), the most common inherited optic nerve disorder. Stoke's initial focus is haploinsufficiencies and diseases of the central nervous system and the eye, although proof of concept has been demonstrated in other organs, tissues, and systems, supporting its belief in the broad potential for its proprietary approach. Stoke is headquartered in Bedford, Massachusetts with offices in Cambridge, Massachusetts. For more information, visit https://www.stoketherapeutics.com/ or follow Stoke on Twitter at @StokeTx.

About Acadia Pharmaceuticals
Acadia is advancing breakthroughs in neuroscience to elevate life. For more than 25 years Acadia has been working at the forefront of healthcare to bring vital solutions to people who need them most. Acadia developed and commercialized the first and only approved therapy for hallucinations and delusions associated with Parkinson's disease psychosis. Acadia's late-stage development efforts are focused on treating psychosis in patients with dementia, the negative symptoms of schizophrenia and Rett syndrome. Acadia's 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-pharm.com and follow us on LinkedIn and Twitter.

Stoke's Cautionary Note Regarding Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to, statements regarding: receipt of upfront payments; receipt of potential milestone payments under the SYNGAP1 collaboration; receipt of potential milestones and royalty payments under the MECP2 program and the third program; the ability to develop new treatments for neurodevelopmental disorders; and expectations regarding the proposed transaction with Acadia. Statements including words such as "believe," "will," "eligible," or "potential," and any other statements in the future tense are forward-looking statements. These forward-looking statements involve risks and uncertainties, as well as assumptions, which, if they do not fully materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. Forward-looking statements are subject to risks and uncertainties that may cause the company's actual activities or results to differ significantly from those expressed in any forward-looking statement, including risks and uncertainties related to: Stoke's ability to develop and identify potential product candidates; that if Acadia were to breach or terminate the collaboration, Stoke would not obtain the anticipated financial or other benefits; the possibility that Stoke and Acadia may not be successful in their development efforts under any of the collaborations and that, even if successful, Stoke and Acadia may be unable to successfully commercialize any resulting product candidates; and other risks and uncertainties described under the heading "Risk Factors" in documents Stoke files from time to time with the Securities and Exchange Commission. These forward-looking statements speak only as of the date of this press release and Stoke undertakes no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date hereof.

Acadia's Forward-Looking Statement
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, 2020 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.

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Source: Acadia Pharmaceuticals Inc.