Stoke Therapeutics Announces Publication of Preclinical Data on STK-001 in the Journal Science Translational Medicine that Demonstrate Significant Improvements in Survival and Reductions in Seizure Frequency in a Dravet Syndrome Mouse Model

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STK-001 has the potential to be the first disease-modifying therapy to address the genetic cause of Dravet syndrome

A Phase 1/2a study of STK-001 in children and adolescents ages 2 to 18 years old is now underway

BEDFORD, Mass.--(BUSINESS WIRE)--Aug. 26, 2020-- Stoke Therapeutics, Inc., (Nasdaq: STOK), a biotechnology company pioneering a new way to treat the underlying cause of genetic diseases by precisely upregulating protein expression, today announced the publication of preclinical data from studies of STK-001 that demonstrated significant improvements in survival and reductions in seizure frequency in a mouse model of Dravet syndrome. Data published today in the journal *Science Translational Medicine* also showed that STK-001 achieved target engagement, pharmacologic activity and efficacy by selectively increasing *Scn1a* gene and $Na_V1.1$ protein expression. STK-001 is an antisense oligonucleotide (ASO) that was created using Stoke's proprietary Targeted Augmentation of Nuclear Gene Output (TANGO) approach. The company announced on August 10, 2020 that the first patient was dosed in Part A of its Phase 1/2a study of STK-001.

"These preclinical studies are foundational to our understanding of STK-001 and belief in its potential to be the first disease-modifying treatment for Dravet syndrome by precisely targeting the *SCN1A* gene to increase protein production," said Gene Liau, Ph.D., Executive Vice President, Head of Research and Preclinical Development at Stoke Therapeutics and senior Stoke author on the paper. "We recently advanced STK-001 into the clinic with the dosing of the first patient in Part A of our Phase 1/2a MONARCH study and we look forward to learning more about the translatability of our preclinical findings to the human experience."

"Dravet syndrome is usually caused by insufficient $Na_V1.1$ protein levels in the brain, which leads to intractable seizures, cognitive impairments and a high risk of sudden death," said Lori I. Isom, Ph.D., Chair, Department of Pharmacology and Professor of Molecular and Integrative Physiology and Neurology at the University of Michigan Medical School and corresponding author on the paper. "In these studies, we observed that when Dravet syndrome mice were treated with a single dose of STK-001 at postnatal Day 2, 97 percent survived to Day 90 compared to 23 percent in the placebo treated group. In contrast to other emerging gene-based treatments, the ASO approach is designed to be precise, reversible and not limited by the size of a target gene, which makes it particularly promising as a future treatment for this devastating disease."

"Antisense Oligonucleotides Increase *Scn1a* Expression and Reduce Seizures and SUDEP Incidence in a Mouse Model of Dravet Syndrome," is now available online at: https://stm.sciencemag.org/lookup/doi/10.1126/scitranslmed.aaz6100.

About STK-001

STK-001 is an investigational new medicine for the treatment of Dravet syndrome. Stoke believes that STK-001, a proprietary antisense oligonucleotide (ASO), has the potential to be the first disease-modifying therapy to address the genetic cause of Dravet syndrome. STK-001 is designed to upregulate $Na_V1.1$ protein expression by leveraging the non-mutant (wild-type) copy of the *SCN1A* gene to restore physiological $Na_V1.1$ levels, thereby reducing both occurrence of seizures and significant non-seizure comorbidities. Stoke has generated preclinical data demonstrating proof-of-mechanism and proof-of-concept for STK-001. STK-001 has been granted orphan drug designation by the FDA as a potential new treatment for Dravet syndrome.

About Dravet Syndrome

Dravet syndrome is a severe and progressive genetic epilepsy characterized by frequent, prolonged and refractory seizures, beginning within the first year of life. Dravet syndrome is difficult to treat and has a poor long-term prognosis. Complications of the disease often contribute to a poor quality of life for patients and their caregivers. The effects of the disease go beyond seizures and often include cognitive regression or developmental stagnation, ataxia, speech impairment and sleep disturbances. Compared with the general epilepsy population, people living with Dravet syndrome have a higher risk of sudden unexpected death in epilepsy, or SUDEP. Dravet syndrome affects approximately 35,000 people in the United States, Canada, Japan, Germany, France and the United Kingdom, and it is not concentrated in a particular geographic area or ethnic group.

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, so the body does not function normally. 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 target genes produce more protein. TANGO aims to restore missing proteins by increasing – or stoking – protein output from healthy genes, thus compensating for the non-functioning copy of the gene.

About Stoke Therapeutics

Stoke Therapeutics (Nasdaq: STOK), is a clinical-stage biotechnology company pioneering a new way to treat the underlying causes of severe genetic diseases by precisely upregulating protein expression to restore target proteins to near normal levels. Stoke aims to develop the first precision medicine platform to target the underlying cause of a broad spectrum of genetic diseases in which the patient has one healthy copy of a gene and one

mutated copy that fails to produce a protein essential to health. These diseases, in which loss of approximately 50% of normal protein expression causes disease, are called autosomal dominant haploinsufficiencies. Stoke is headquartered in Bedford, Massachusetts with offices in Cambridge, Massachusetts. For more information, visit https://www.stoketherapeutics.com/ or follow the company on Twitter at @StokeTx.

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: our expectation about timing and execution of anticipated milestones and timing thereof, the expansion of our pipeline and the use of the TANGO platform to treat other genetic diseases; our ability to use study data to advance the development of STK-001; the ability of STK-001 to treat the underlying causes of Dravet syndrome; and the ability of TANGO to design medicines to increase protein production and the expected benefits thereof. These forward-looking statements may be accompanied by such words as “aim,” “anticipate,” “believe,” “could,” “estimate,” “expect,” “forecast,” “goal,” “intend,” “may,” “might,” “plan,” “potential,” “possible,” “will,” “would,” and other words and terms of similar meaning. 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. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including: our ability to develop, obtain regulatory approval for and commercialize STK-001 and future product candidates; the timing and results of preclinical studies and clinical trials; the risk that positive results in a clinical trial may not be replicated in subsequent trials or success in early stage clinical trials may not be predictive of results in later stage clinical trials; risks associated with clinical trials, including our ability to adequately manage clinical activities, unexpected concerns that may arise from additional data or analysis obtained during clinical trials, regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of our drug candidates; the occurrence of adverse safety events; failure to protect and enforce our intellectual property, and other proprietary rights; failure to successfully execute or realize the anticipated benefits of our strategic and growth initiatives; risks relating to technology failures or breaches; our dependence on collaborators and other third parties for the development, regulatory approval, and commercialization of products and other aspects of our business, which are outside of our full control; risks associated with current and potential delays, work stoppages, or supply chain disruptions caused by the coronavirus pandemic; risks associated with current and potential future healthcare reforms; risks relating to attracting and retaining key personnel; failure to comply with legal and regulatory requirements; risks relating to access to capital and credit markets; environmental risks; risks relating to the use of social media for our business; and the other risks and uncertainties that are described in the Risk Factors section of our most recent annual or quarterly report and in other reports we have filed with the U.S. Securities and Exchange Commission. These statements are based on our current beliefs and expectations and speak only as of the date of this press release. We do not undertake any obligation to publicly update any forward-looking statements.

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