Stoke Therapeutics Announces Plans to Move Forward With Dosing of STK-001 in Children and Adolescents in its Ongoing Phase 1/2a MONARCH Study for Dravet Syndrome

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- FDA to Allow an Additional Higher Dose Level in the Single Ascending Dose Portion (Formerly, Part A) of the Study –

- New Preclinical Repeat-Dose Data Support Company Plans to Evaluate Multiple Ascending Dose Levels in MONARCH, Subject to FDA Review -

- Enrollment and Dosing in MONARCH is Ongoing; Preliminary Data Still Anticipated in 2021 -

BEDFORD, Mass.--(BUSINESS WIRE)--Oct. 7, 2020-- Stoke Therapeutics, Inc., (Nasdaq: STOK), a clinical-stage biotechnology company pioneering a new way to treat the underlying cause of genetic diseases by precisely upregulating protein expression, today announced plans to move forward with dosing of STK-001 in children and adolescents in its ongoing Phase 1/2a MONARCH study for Dravet syndrome. Following recent interactions with the U.S. Food and Drug Administration (FDA) related to the partial clinical hold on higher dose levels in the MONARCH study, the FDA will allow the Company to add an additional higher dose level to the single ascending dose (SAD) portion of the study (previously Part A). A total of three dose levels will now be evaluated in this portion of the study: 10 mg, 20 mg and 30 mg. Dosing above 30 mg in this study remains on FDA partial clinical hold.

In addition, subject to FDA review, the Company is preparing to add a multiple ascending dose (MAD) portion to the MONARCH study, replacing Part B. This decision is based on new preclinical repeat-dose toxicology data, which were reviewed by the FDA as part of ongoing discussions with the Company. There were no adverse effects observed in the non-human primate (NHP) repeat dose study. The Company plans to submit a protocol amendment to the FDA, which will reflect these changes to the SAD and MAD portions of the study.

“There is an urgent need for more effective medicines for people who are living with Dravet syndrome, so we are pleased to be moving ahead quickly with our plans to continue dosing children and adolescents in this important Phase 1/2a study of STK-001,” said Edward M. Kaye, M.D., Chief Executive Officer of Stoke Therapeutics. “We appreciate the FDA’s timely review of our additional data and look forward to evaluating a total of three individual dose levels in the single ascending dose portion of the study. In addition, we are encouraged by preclinical data that demonstrated the ability to safely achieve greater exposure levels with multiple doses of STK-001. Based on these data, we plan to also evaluate multiple ascending doses of up to 30 mg in this ongoing study. Our team is working diligently to submit a revised protocol to the FDA in the coming days.”

In March 2020, the Company announced the FDA had placed a partial clinical hold on higher doses of STK-001 in the MONARCH study, pending additional preclinical testing to determine the safety profile of doses higher than the current no observed adverse effect level (NOAEL). When intrathecal doses above the NOAEL were administered to NHPs, adverse hind limb paresis was observed. This finding is known to occur following intrathecal delivery of antisense oligonucleotides (ASOs) to NHPs and is not known to translate to the human experience. When extremely high dose levels were administered, acute convulsions were observed immediately following STK-001 administration. The dose levels were well above the range of corresponding human doses that would ever be administered in the clinic, and were delivered in a formulation that was at a higher concentration than would be administered in the clinic. There is no apparent correlation of these acute adverse events with the mechanism of action of STK-001.

Enrollment and dosing in MONARCH is ongoing. Preliminary safety and pharmacokinetic data are still anticipated in 2021.

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 Phase 1/2a Clinical Study (MONARCH)

The MONARCH study is a Phase 1/2a open-label study of children and adolescents ages 2 to 18 who have an established diagnosis of Dravet syndrome and have evidence of a pathogenic genetic mutation in the *SCN1A* gene. The primary objectives for the study will be to assess the safety and tolerability of STK-001, as well as to characterize human pharmacokinetics. A secondary objective will be to assess the efficacy as an adjunctive antiepileptic treatment with respect to the percentage change from baseline in convulsive seizure frequency over a 12-week treatment period. Stoke also intends to measure non-seizure aspects of the disease, such as quality of life, as secondary endpoints. Stoke plans to enroll approximately 48 patients across 20 sites in the United States.

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 intellectual disability, developmental delays, movement and balance issues, language and speech disturbances, growth defects, sleep abnormalities, chronic infections, disruptions of the autonomic nervous system and mood disorders. 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 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 the dosing, timing and execution of our Phase 1/2a MONARCH study of STK-001, including our ability to include a multiple ascending dose portion in the study and the partial clinical hold on Part B of the study; 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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