Stoke Therapeutics Announces Presentations Related to the Company's Work in Dravet Syndrome at the American Epilepsy Society 2020 Virtual Annual Meeting

November 25, 2020

BEDFORD, Mass.--(BUSINESS WIRE)--Nov. 25, 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 that four abstracts related to the Company's work in Dravet syndrome have been selected for presentation at the upcoming American Epilepsy Society (AES) 2020 Virtual Annual Meeting, taking place December 4 – 8, 2020. Dravet syndrome is a severe and progressive genetic epilepsy characterized by frequent, prolonged and refractory seizures that usually begin within the first year of life. The disease is classified as a developmental and epileptic encephalopathy due to the developmental delays and cognitive impairment associated with the disease.

Highlights from the Company's presentations include:

- Baseline data from children and adolescents with Dravet syndrome enrolled in the Company's BUTTERFLY study, an ongoing, multicenter, longitudinal, prospective study designed to evaluate neurodevelopmental status using several scales assessing cognition. Secondary and exploratory endpoints in the study will evaluate changes in disease measures including seizures and additional non-seizure comorbidities. Patients enrolled to date are representative of patients with Dravet syndrome, and data collected indicate that the selected cognition measures are valid and appropriate for use in patients with Dravet syndrome.
- A review of the study design for MONARCH, the Company's ongoing Phase 1/2a study of STK-001, the first potential disease-modifying therapy to address the genetic cause of Dravet syndrome. Following a recent protocol amendment, the study is designed to evaluate both single ascending dose levels and multiple ascending doses of up to 30 mg of STK-001 in children and adolescents with Dravet syndrome. The primary endpoints are safety, tolerability and pharmacokinetic profile of STK-001 in Dravet syndrome patients. The impact of STK-001 on frequency of convulsive seizures and quality of life are secondary endpoints of this study. Preliminary safety and PK data are anticipated in 2021.
- New preclinical data further support the ability of a TANGO antisense oligonucleotides (ASO) to decrease seizures and death in a Dravet syndrome mouse model and, for the first time, provide evidence this is likely due to restoration of excitability of parvalbumin (PV) expressing interneurons. In this study, 50% of control animals developed seizures between P16-19 while ASO-treated mice were seizure free. Consistent with a previous study of STK-001, the ASO also greatly decreased seizure frequency and death post-weaning. Associated with this, ASO-treatment restored Dravet syndrome mouse PV interneurons firing frequency to that of wild type mice PV interneurons.
- Data generated from a no-cost epilepsy genetic testing program co-sponsored by Stoke demonstrate that this program can reduce the time to diagnosis and increase the detection of individuals with SCN1A-related disease.

"Our understanding of the diagnosis, progression and effects of Dravet syndrome continues to expand and everything we are learning reinforces the urgent need for a medicine that treats the underlying cause of the disease," said Barry Ticho, M.D., Ph.D., Chief Medical Officer of Stoke Therapeutics. "The data from our BUTTERFLY study give us a strong foundational understanding of the course of the disease and validate the applicability of several measures of cognition and other non-seizure comorbidities that will be helpful in evaluating potential disease-modifying medicines like STK-001."

Details for the AES presentations are as follows:

Title: Observational Study to Investigate Cognition and Other Non-seizure Comorbidities in Children and Adolescents with Dravet Syndrome: Patient Analysis of the BUTTERFLY Study
Session Date & Time: Available on-demand December 4
Presenter: Joseph Sullivan, M.D., Professor of Neurology at the University of California San Francisco and Director of the Benioff Children's Hospital Pediatric Epilepsy Center of Excellence
Abstract Number: 81

Title: Reducing the Time to Diagnosis and Increasing the Detection of Individuals with *SCN1A*-Related Disease Through a No-cost, Sponsored Epilepsy Genetic Testing Program
Session Date & Time: Available on-demand December 4
Presenter: Dianalee McKnight,Ph.D., Director, Medical Affairs, Invitae
Abstract Number: 392

Title: Safety and Pharmacokinetics of Antisense Oligonucleotide STK-001 in Children and Adolescents with Dravet Syndrome: Single Ascending Dose Design for the Open-Label Phase 1/2a MONARCH Study
Session Date & Time: Available on-demand December 4
Presenter: Linda Laux, M.D, Associate Professor of Pediatrics (Neurology and Epilepsy) at Northwestern University Feinberg School of Medicine and Attending Physician, Neurology and Epilepsy Center, Ann & Robert H. Lurie Children's Hospital of Chicago

Abstract Number: 344

Title: Targeted Augmentation of Nuclear Gene Output (TANGO) of SCN1A Reduces Seizures and Rescues Parvalbumin Positive Interneuron Firing Frequency in a Mouse Model of Dravet Syndrome
Session Date & Time: Available on-demand December 4
Presenter: Eric Wengert, Researcher, Department of Anesthesiology, University of Virginia
Abstract Number: 236

About STK-001

STK-001 is an investigational new medicine for the treatment of Dravet syndrome currently being evaluated in a Phase 1/2a clinical trial. 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. Enrollment and dosing are ongoing in MONARCH and Stoke plans to enroll approximately 48 patients in the study across 20 sites in the United States.

Additional information about the MONARCH study can be found at https://www.monarchstudy.com/.

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 severe intellectual disabilities, severe developmental disabilities, motor impairment, speech impairment, autism, behavioral difficulties and sleep abnormalities. 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: preclinical data and study results regarding OPA1, future operating results, financial position and liquidity, the direct and indirect impact of COVID-19 on our business, financial condition and operations, including on our expenses, supply chain, strategic partners, research and development costs, clinical trials and employees; our expectation about timing and execution of anticipated milestones, responses to regulatory authorities, expected nomination of future product candidates and timing thereof, our ability to complete lead optimization of ASOs for ADOA, the timing and results of ADOA preclinical studies, our ability to develop ASOs treat the underlying causes of ADOA, our ability to advance OPA1 as our next preclinical target, and 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, OPA1 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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