Stoke Therapeutics Announces Presentations Related to the Company's Work to Advance STK-001, the First Potential New Medicine to Target the Underlying Cause of Dravet Syndrome at the American Epilepsy Society (AES) 2020 Annual Meeting

December 4, 2020

– Baseline data from the BUTTERFLY observational study provide initial validation of standard measures of cognition (BSID-III and WPPSI-IV) for use in evaluating non-seizure comorbidities in people with Dravet syndrome –

– The current design for the ongoing MONARCH Phase 1/2a study to assess both single and multiple ascending doses of STK-001 in children and adolescents with Dravet syndrome will be presented –

– New data in a mouse model of Dravet syndrome demonstrate that TANGO ASOs can help restore normal function of nerve cells which correlate to reductions in seizure frequency and extended survival –

BEDFORD, Mass.--(BUSINESS WIRE)--Dec. 4, 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 highlights from presentations being made at the American Epilepsy Society (AES) 2020 Virtual Annual Meeting December 4-8, 2020 related to the Company's work to advance STK-001, the first potential new medicine to target the underlying cause of Dravet syndrome. 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:

BUTTERFLY Observational Study – Baseline Analysis

Abst. 81. Observational Study to Investigate Cognition and Quality of Life in Children and Adolescents with Dravet Syndrome: Baseline Analysis of the BUTTERFLY Study

December 5, 2020 9:00 AM – 10:30 AM; Track: 4. Clinical Epilepsy / 4B. Clinical Diagnosis

22 children and adolescents with Dravet syndrome were enrolled in the Company's BUTTERFLY observational study and included in a baseline analysis.

All study participants evaluated are representative of patients with Dravet syndrome. The majority of patients were able to complete commonly used cognition assessments including either the BSID-III (Bayley Scales of Infant and Toddler Development) or the WPPSI-IV (Wechsler Preschool and Primary Scale of Intelligence Fourth Edition), indicating that these measures are valid and appropriate for use in patients with Dravet syndrome. An initial analysis of data from 17/22 patients who completed one of these assessments showed substantially decreased neurocognitive abilities compared to children of the same age level despite the use of multiple anti-epileptic therapies. The assessment also demonstrated an apparent widening in overall intellectual development that increases with age. In addition, a gap in adaptive functioning was noted using the Vineland Adaptive Behavior Scales.

"We have long known that Dravet syndrome is far more than seizures and the BUTTERFLY study is providing quantifiable information on cognition and quality of life that fill gaps in our understanding of this disease and its progression as children age," said Joseph Sullivan, M.D., Professor of Neurology at UCSF Benioff Children's Hospitals and Director of the UCSF Pediatric Epilepsy Center of Excellence. "Initial results from the study show significantly diminished neurocognitive abilities in children with Dravet syndrome such that 10 year-olds are functioning below the level of a healthy 1 year-old even while they are being treated with available anti-epileptic medicines. The fact that the majority of patients in this study were able to complete standard assessments of neurocognition gives us confidence that we can objectively assess whether potential new disease-modifying medicines have an effect on the non-seizure comorbidities that make Dravet so devastating."

"Dravet syndrome is characterized by an array of effects that go beyond seizures and include motor and speech impairment, intellectual and developmental disabilities, behavioral deficits and abnormal sleep patterns," said Barry Ticho, M.D., Ph D., Chief Medical Officer of Stoke Therapeutics. "We continue to generate strong preclinical evidence supporting the potential for STK-001 to address the underlying cause of Dravet syndrome and reduce seizure frequency. Our goal is to develop a medicine that goes beyond seizure control to address many of the other comorbidities associated with Dravet syndrome. As we look to future clinical studies of STK-001, we are encouraged by data showing the ability to diagnose children earlier as well as the validation of tools that will help us measure the potential impact of STK-001 on cognition and quality of life."

MONARCH Phase 1/2a Current Study Design

Abst. 344. Safety and Pharmacokinetics of Antisense Oligonucleotide STK-001 in Children and Adolescents with Dravet Syndrome: Single and Multiple Ascending Dose Design for the Open-Label Phase 1/2a MONARCH Study

December 6, 2020 12:00 PM – 1:30 PM; Track: 7. Antiepileptic Drugs / 7B. Clinical Trials

A review of the study design for MONARCH, the Company's ongoing Phase 1/2a study of STK-001 in children and adolescents with Dravet syndrome will be presented during a poster session by Linda Laux, M.D., Associate Professor of Pediatrics (Neurology and Epilepsy), Northwestern University Feinberg School of Medicine. Following a recent protocol amendment, MONARCH is designed to evaluate both single and multiple ascending doses

of up to 30mg of STK-001 in children and adolescents with Dravet syndrome. The primary endpoints are safety, tolerability and pharmacokinetic (PK) 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. Patient enrollment and dosing in MONARCH is ongoing and preliminary safety and PK data are anticipated in 2021.

Restoration of Interneuron Firing Frequency in a Dravet Mouse Model

Abst. 236. 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

December 5, 2:00 PM – 3:30 PM; Platform A: Translational Research / Genetics

December 6, 12:00 PM – 1:30 PM; Track: 2. Translational Research / 2B. Devices, Technologies, Stem Cells

New preclinical data provide additional evidence of the potential for TANGO antisense oligonucleotides (ASOs) to provide a gene-specific, disease-modifying treatment for Dravet syndrome. In this study, Dravet syndrome mice treated with a TANGO ASO had significantly decreased seizure frequency and increased survival. Data presented by Eric Wengert, graduate student at the University of Virginia, show that 100% of mice treated with a TANGO ASO were seizure free between postnatal day 16 and postnatal day 19 compared to 50% of vehicle-treated control mice. The data also provide evidence that decreases in seizures and mortality are, in part, due to restoration of excitability of parvalbumin (PV) expressing interneurons. PV interneurons are commonly hypoexcitable in Dravet syndrome. In this study, treatment with a TANGO ASO restored Dravet syndrome mouse PV interneuron firing frequency to that of wild-type mice.

Additional Work in a Dravet Mouse Model

Antisense Oligonucleotides Increase Scn1a Expression and Reduce Seizures and SUDEP Incidence in a Mouse Model of Dravet Syndrome

December 8, 1:30 PM – 4:00 PM; Annual Fundamentals Symposium: Fundamentally New Ideas in Epilepsy Treatment and Research

Lori Isom, Ph.D., Maurice H. Seevers Professor and Chair of Pharmacology, University of Michigan Medical School, will present a review of data from experiments conducted with TANGO ASOs in a mouse model of Dravet syndrome.

Early Diagnosis of Dravet Syndrome

Abst. 392. Reducing the Time to Diagnosis and Increasing the Detection of Individuals with *SCN1A*-related Disease Through a Sponsored Epilepsy Genetic Testing Program

December 6, 12:00- 1:30 PM; Track: 12. Genetics / 12A. Human Studies

Data from an analysis of 6,874 children who participated in a no-cost epilepsy genetic testing program co-sponsored by Stoke showed that 152 had a positive molecular diagnosis related to the *SCN1A* gene, accounting for 2.2% of all patients. Results demonstrated a substantial decrease in the time to diagnosis from >6 years of age (2011-2015) to <2 years of age (2019-2020).

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 the BUTTERFLY Observational Study

BUTTERFLY study, an ongoing, multicenter, longitudinal, prospective study of children and adolescents ages 2 to 18 who have been diagnosed with Dravet syndrome as a result of an *SCN1A* gene mutation. This observational study designed to evaluate neurodevelopmental status and change from baseline to 24 months. Secondary and exploratory endpoints in the study will evaluate changes in other disease measures, including seizures and additional non-seizure comorbidities. No investigational medications or other treatments will be provided. Participants continue to receive their usual care, and will be observed by a team of doctors and nurses over time for up to two years. The study is being conducted at approximately 20 sites in the United States.

About the 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 STK-001 and Dravet syndrome, including from the BUTTERFLY study; our 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, 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; 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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