Stoke Therapeutics Presents Data from a Combined Interim Analysis of the Phase 1/2a MONARCH and ADMIRAL Studies of STK-001 in Children and Adolescents with Dravet Syndrome at the American Epilepsy Society (AES) 2022 Annual Meeting

December 2, 2022

– Single and multiple doses of STK-001 up to 45mg were well-tolerated –

– 55% median reduction from baseline in convulsive seizure frequency was observed among patients treated with three doses of 45mg (n=6) –

– Benefits of treatment with STK-001 were observed on top of standard anti-seizure medicines, including fenfluramine –

– Data from the SWALLOWTAIL open-label extension study showed that reductions in seizure frequency were maintained with ongoing treatment; trend toward improvement in non-seizure measures of disease also observed –

BEDFORD, Mass.--(BUSINESS WIRE)--Dec. 2, 2022--

Stoke Therapeutics, Inc. (Nasdaq: STOK), a biotechnology company dedicated to addressing the underlying cause of severe diseases by upregulating protein expression with RNA-based medicines, today announced highlights from presentations related to the ongoing clinical development of STK-001, the first potential new medicine to treat the underlying cause of Dravet syndrome. A total of seven posters will be presented at the American Epilepsy Society (AES) 2022 Annual Meeting, December 2-6. Dravet syndrome is a severe and progressive genetic epilepsy characterized by frequent, prolonged and refractory seizures beginning 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.

“Dravet syndrome is a complex and devastating disease that presents challenges for clinicians, patients and their caregivers,” said Barry Ticho, Ph.D., M.D., Chief Medical Officer of Stoke Therapeutics. “To curb the seizures, patients typically take multiple anti-seizure medicines which often produce additional challenges and side effects that impact their quality of life and overall health. STK-001 represents an entirely new approach to treatment, one that aims to treat the syndrome, not just the seizures. At the highest dose level, we observed a 55% median reduction in convulsive seizure frequency, with all but one patient responding to treatment with STK-001. Demonstrating this level of effect in highly refractory patients, who have already taken multiple standard anti-seizure medicines, including fenfluramine, has not been seen before.”

Topline data from a combined interim analysis of the Phase 1/2a MONARCH and ADMIRAL studies showed single and multiple doses of STK-001 up to 45mg were well-tolerated. Reductions in seizure frequency were observed among patients who received multiple doses of STK-001 (20mg, 30mg, 45mg). The effects were more evident at the highest dose (45mg) and in younger patients and were observed on top of standard treatments. Half of the patients in these studies were taking four or more anti-seizure medicines, including fenfluramine.

An interim analysis of six patients treated with three doses of 45mg was presented and showed:

- A 55% median reduction from baseline in convulsive seizure frequency from Day 29 after the first dose to three months after receiving the last dose.
- Reductions from baseline in convulsive seizure frequency in 5/6 (83%) patients.
- A greater than 50% reduction in convulsive seizure frequency in 4/6 (67%) patients.
- Reductions in seizure frequency began after the first dose and continued with additional treatment, consistent with the anticipated mechanism of action of STK-001.

The interim safety analysis of patients treated in MONARCH and ADMIRAL showed that 27% (15/55) of patients experienced a treatment-emergent adverse event (TEAE) that was related to study drug. All adverse events related to study drug were mild to moderate in severity. No TEAEs led to study drug withdrawal.

Preliminary data from a small cohort of patients in the open-label SWALLOWTAIL study showed the effects of ongoing treatment with STK-001 (30mg), including:

- Reductions in convulsive seizure frequency that were observed in MONARCH were maintained with ongoing treatment in the SWALLOWTAIL open-label extension study.
- A trend toward improvement in non-seizure comorbidities as measured by the BRIEF-P, an assessment of executive function, was observed among patients in the SWALLOWTAIL open-label extension study. One-year data from the BUTTERFLY observational study, which did not include treatment with STK-001, showed little change from baseline to 12 months in the mean BRIEF-P scores and other commonly used cognition assessments.
- Safety profile consistent with MONARCH and ADMIRAL.

Seven presentations related to the Company’s work in Dravet syndrome will be presented during the AES Annual Meeting and can be found on the Stoke Therapeutics website under the Investors & News tab.

Title	Presenter	Date
MONARCH and ADMIRAL Interim Analyses: Phase 1/2a Studies Investigating Safety and Drug Exposure of STK-001, an Antisense Oligonucleotide (ASO), in Children and Adolescents with Dravet Syndrome (DS)	Helen Cross, MB ChB, Ph.D., Professor, The Prince of Wales's Chair of Childhood Epilepsy and Head of the Developmental Neuroscience Programme at University College London Great Ormond Street Institute of Child Health, Honorary Consultant in Paediatric Neurology, President of the International League Against Epilepsy	**Poster Number:** 1.215 Saturday, Dec. 3 12:00 PM CST
MONARCH and ADMIRAL Interim Analyses: Phase 1/2a Studies Investigating Safety and Drug Exposure of STK-001, an Antisense Oligonucleotide (ASO), in Children and Adolescents with Dravet Syndrome (DS)	Linda Laux, M.D., Associate Professor of Pediatrics (Neurology and Epilepsy) at Northwestern University Feinberg School of Medicine and Attending Physician at Ann & Robert H. Lurie Children's Hospital of Chicago	**Poster Number:** 1.227 Saturday, Dec. 3 12:00 PM CST
SWALLOWTAIL: An Open-Label Extension (OLE) Study for Children and Adolescents with Dravet Syndrome (DS) who Previously Participated in a Study of Antisense Oligonucleotide (ASO) STK-001	Colin Roberts, M.D., Director of the Doernbecher Childhood Epilepsy Program at Oregon Health & Science University	**Poster Number:** 1.216 Saturday, Dec. 3 12:00 PM CST
Utilization of Pharmacokinetic (PK) Model for STK-001 in Patients with Dravet Syndrome (DS) to Predict Pharmacological Active Dose in Clinic	Meena, Ph.D., Senior Vice President of Bioanalytical, DMPK and Biomarker Development at Stoke Therapeutics	**Poster Number:** 1.134 Saturday, Dec. 3 12:00 PM CST
Twelve-month Analysis of BUTTERFLY: An Observational Study to Investigate Cognition and Other Non-seizure Comorbidities in Children and Adolescents with Dravet Syndrome (DS)	Joseph Sullivan, M.D., Professor of Neurology and Pediatrics and Director of the University of California San Francisco Pediatric Epilepsy Center of Excellence	**Poster Number:** 1.228 Saturday, Dec. 3 12:00 PM CST
Quantitative EEG Analysis Patients with Dravet Syndrome (DS) Treated in the Phase 1/2a MONARCH Study of STK-001, an Antisense Oligonucleotide (ASO)	Kimberly Parkerson, M.D., Ph.D., Vice President, Head of Neurology Clinical Development at Stoke Therapeutics	**Poster Number:** 3.225 Monday, Dec. 5 12:00 PM CST
STK-001 Surrogate Restores the Excitability of Parvalbumin-positive Fast-spiking Interneurons in a Mouse Model of Dravet Syndrome	Luis Lopez-Santiago, Ph.D., Associate Research Scientist at University of Michigan Medical School	**Poster Number:** 3.050 Monday, Dec. 5 12:00 PM CST

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, disruptions of the autonomic nervous system and mood disorders. The disease is classified as a developmental and epileptic encephalopathy due to the developmental delays and cognitive impairment associated with the disease. Compared with the general epilepsy population, people living with Dravet syndrome have a higher risk of sudden unexpected death in epilepsy, or SUDEP. There are no approved disease-modifying therapies for people living with Dravet syndrome. One out of 16,000 babies are born with Dravet syndrome, which is not concentrated in a particular geographic area or ethnic group.

About STK-001
STK-001 is an investigational new medicine for the treatment of Dravet syndrome currently being evaluated in ongoing clinical trials. 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 NaV1.1 protein expression by leveraging the non-mutant (wild-type) copy of the *SCN1A* gene to restore physiological NaV1.1 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 and the EMA, and rare pediatric disease designation by the FDA as a potential new treatment for Dravet syndrome.

About Phase 1/2a MONARCH Study (United States)
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 genetic mutation in the *SCN1A* gene. The primary objectives for the study are to assess the safety and tolerability of STK-001, as well as to determine the pharmacokinetics in plasma and exposure in cerebrospinal fluid. A secondary objective is to assess the efficacy as an adjunctive antiepileptic treatment with respect to the percentage change from baseline in convulsive seizure frequency. Stoke also intends to measure non-seizure aspects of the disease, such as quality of life, as secondary endpoints. Additional information about the MONARCH study can be found at https://www.monarchstudy.com/.

Patients who participated in the MONARCH study and meet study entry criteria are eligible to continue treatment in SWALLOWTAIL, an open-label extension (OLE) study designed to evaluate the long-term safety and tolerability of repeat doses of STK-001. We expect that SWALLOWTAIL will also provide valuable information on the preliminary effects of STK-001 on seizures along with non-seizure aspects of the disease, such as quality of life and cognition.
Enrollment and dosing in SWALLOWTAIL are underway.

About Phase 1/2a ADMIRAL Study (United Kingdom)
The ADMIRAL 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 genetic mutation in the *SCN1A* gene. The primary objectives for the study are to assess the safety and tolerability of multiple doses of STK-001, as well as to determine the pharmacokinetics in plasma and exposure in cerebrospinal fluid. A secondary objective is to assess the effect of multiple doses of STK-001 as an adjunctive antiepileptic treatment with respect to the percentage change from baseline in

convulsive seizure frequency. Stoke also intends to measure non-seizure aspects of the disease, such as overall clinical status and quality of life, as secondary endpoints. Additional information about the ADMIRAL study can be found at https://www.admiralstudy.com.

Patients who participated in the ADMIRAL study and meet study entry criteria are eligible to continue treatment in LONGWING, an open-label extension (OLE) study designed to evaluate the long-term safety and tolerability of repeat doses of STK-001. We expect that LONGWING will also provide valuable information on the preliminary effects of STK-001 on seizures along with non-seizure aspects of the disease, such as quality of life and cognition.
Enrollment and dosing in LONGWING are underway.

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 the development of STK-002 for the treatment of 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.

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 the ability of STK-001 to treat the underlying causes of Dravet syndrome and reduce seizures or show improvements in non-seizure comorbidities at the indicated dosing levels or at all, and the timing and expected progress of clinical trials, data readouts and presentations. Statements including words such as "plan," "will," "continue," "expect," or "ongoing" and statements in the future tense are forward-looking statements. These forward-looking statements involve risks and uncertainties, as well as assumptions, which, if they prove incorrect or do not fully materialize, could cause our results to differ materially from those expressed or implied by such forward-looking statements, including, but not limited to, risks and uncertainties related to: the Company's ability to advance, obtain regulatory approval of and ultimately commercialize its product candidates; the timing and results of preclinical and clinical trials; the risk that positive results in a clinical trial may not be replicated in subsequent trials or successes in early stage clinical trials may not be predictive of results in later stage trials and preliminary interim data readouts of ongoing trials may show results that change when such trials are completed; the Company's ability to fund development activities and achieve development goals; the Company's ability to protect its intellectual property; the direct and indirect impacts of the ongoing COVID-19 pandemic and its variants on the Company's business; and other risks and uncertainties described under the heading "Risk Factors" in the Company's Annual Report on Form 10-K for the year ended December 31, 2021, its quarterly reports on Form 10-Q, and the other documents the Company 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 the Company undertakes no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date hereof.

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