Stoke Therapeutics Presents Data Related to the Ongoing Clinical Development of STK-001 for the Treatment of Dravet Syndrome at the 35th International Epilepsy Congress

September 5, 2023

– Data from multiple ongoing clinical studies of STK-001 show reductions in convulsive seizure frequency and improvements in cognition and behavior in children and adolescents with Dravet syndrome –

– Data support the potential for STK-001 to be the first disease-modifying treatment for Dravet syndrome –

– New pharmacokinetic (PK) modeling of clinical data from ongoing studies demonstrate that higher STK-001 drug exposures in brain correlate with greater reductions in seizure frequency –

DUBLIN--(BUSINESS WIRE)--Sep. 5, 2023-- 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. Four posters from the Company's work in Dravet syndrome are being presented at the International Epilepsy Congress (IEC) 2023, September 2-6, in Dublin, Ireland. Data from the recently announced analysis of results from the ongoing Phase 1/2a studies (MONARCH & ADMIRAL) and the SWALLOWTAIL open-label extension study are being presented in a scientific forum for the first time. In addition, a new pharmacokinetic (PK) analysis of 61 patients treated in STK-001 clinical trials is being presented for the first time, and demonstrates a correlation between higher STK-001 drug exposure in brain and greater reductions in seizure frequency over time.

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.

"The data from ongoing studies of STK-001 provide the first evidence of a disease modifying medicine for Dravet syndrome," said Helen Cross, MB ChB, Ph.D., Professor, The Prince of Wales's Chair of Childhood Epilepsy and Director of University College London Great Ormond Street Institute of Child Health, Honorary Consultant in Paediatric Neurology, and the ADMIRAL study lead investigator. "The primary goal of these studies is to assess safety and tolerability as well as to inform dose selection for future studies. Importantly, within these data we can now see a differentiated pattern of response emerging among the 11 patients treated with an initial two or three doses of 70mg. Additionally, data from the open-label extension study that is evaluating ongoing dosing at lower levels showed, for the first time, improvements in multiple measures of cognition and behavior among patients who have been highly refractory to standard anti-seizure medicines."

The potential of STK-001, a proprietary antisense oligonucleotide (ASO), to be the first disease-modifying medicine for Dravet syndrome is supported by multiple presentations of clinical and other data at IEC.

- MONARCH and ADMIRAL Interim Analyses: Single and multiple doses of STK-001 up to 70mg were generally well tolerated. Patients treated with 2 or 3 initial doses of 70mg experienced substantial and sustained reductions in convulsive seizure frequency with median reductions of 80% (n=6) at 3 months and 89% (n=3) at 6 months after last dose, compared to baseline.

- SWALLOWTAIL open label extension (OLE): Safety findings among patients, who are continuing to be dosed with STK-001, were consistent with the findings from MONARCH and ADMIRAL with the exception of a greater incidence of CSF protein elevation. Durable reductions in convulsive seizure frequency were observed throughout the course of treatment in SWALLOWTAIL. Additionally, data indicated substantial improvements from baseline through 12 months of continued STK-001 dosing in multiple assessments of cognition and behavior.

- BUTTERFLY (natural history study): Small but significant improvements in receptive communication were observed at Month 12; however, little to no change was observed across other measures of cognition and behavior. Data from this study will inform future Dravet syndrome studies.

- PK Model for STK-001: A relationship between STK-001 brain exposure and convulsive seizure frequency was evaluated based on patients treated in the two ongoing Phase 1/2a studies (MONARCH and ADMIRAL) and the SWALLOWTAIL OLE study in children and adolescents with Dravet syndrome. The exposure-seizure relationship showed a significant negative trend based on simulated brain Cavg ($R=-0.23$, $P<0.001$) demonstrating that higher STK-001 brain exposure leads to greater reductions in convulsive seizure frequency. This PK model is anticipated to help identify an optimal dosing regimen for a Phase 3 study.

"Our clinical findings to date show that patients treated with STK-001 experienced substantial and sustained reductions in seizures and importantly, improvements in cognition and behavior," said Barry Ticho, M.D., Ph.D., Chief Medical Officer of Stoke Therapeutics. "The new data from our

pharmacokinetic model provide additional confidence in the observed effects of STK-001 and provide helpful information as we design the pivotal program for STK-001. We look forward to sharing additional data in the first quarter of 2024 that are anticipated to provide greater clarity on dose and dose regimen, and to updating the Dravet community on our Phase 3 plans in the first half of 2024."

Details of the Company's four presentations can be found in the table below. All presentations are available for download on the Stoke Therapeutics website under the Investors & News tab.

Title	Presenter	Date
Utilization of a Pharmacokinetic (PK) Model for STK-001, an antisense oligonucleotide (ASO), in Patients with Dravet Syndrome (DS) To Predict Pharmacologically Active Doses in Clinic	Meena, Ph.D., Senior Vice President of Translational DMPK and Clinical Pharmacology at Stoke Therapeutics	Sunday, Sept. 3 9:00 AM ET (2:00 PM BST) **Location:** Digital Poster Presentation - Station B **Poster Number:** P913
MONARCH and ADMIRAL Interim Analyses: Ongoing Open-label, Phase 1/2a Studies in US and UK 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	Tuesday, Sept. 5 8:00 AM ET (1:00 PM BST) **Location:** Poster Hall **Poster Number:** P287
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	M. Scott Perry, M.D., Head of Neurosciences and Director of the Genetic Epilepsy Clinic at the Jane and John Justin Neurosciences Center of Cook Children's Medical Center	Tuesday, Sept. 5 8:00 AM ET (1:00 PM BST) **Location:** Poster Hall **Poster Number:** P286
Twelve-month Analysis of BUTTERFLY: An Observational Study to Investigate Cognition and Other Non-seizure Comorbidities in Children and Adolescents with Dravet Syndrome (DS)	Elaine Wirrell, M.D., Director of Pediatric Epilepsy atMayo Clinic, Director of the Child and Adolescent Neurology Residency Training Program at Mayo Clinic	Tuesday, Sept. 5 2:00 PM ET (7:00 PM BST) **Location:** Digital Poster Presentation - Station A **Poster Number:** P169

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, and sleep abnormalities. 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. 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 the 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 ongoing.

About the 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.

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 ongoing.

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, resulting in disease. 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 functional (or wild-type) genes produce more protein. TANGO aims to restore missing proteins by increasing – or stoking – protein output from healthy genes, thus compensating for the mutant copy of the gene.

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 X @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; 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, 2022, 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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