Stoke Therapeutics Presents Data From Multiple Studies of Children and Adolescents With Dravet Syndrome at the American Epilepsy Society (AES) 2023 Annual Meeting

December 1, 2023

– Data from clinical studies of STK-001 demonstrated clinical benefit for patients ages 2 to 18 years old, including reductions in seizures and improvements in cognition and behavior that support the potential for disease modification –

– Analysis of 72 patients treated in STK-001 clinical trials suggests that higher STK-001 drug exposure in brain leads to greater seizure reductions –

– Two-year data from the longest prospective natural history study of Dravet syndrome showed that, on average, patients experienced no meaningful improvement in convulsive seizure frequency and exhibited widening gaps in cognition and behavior despite treatment with the best available anti-seizure medicines –

BEDFORD, Mass.--(BUSINESS WIRE)--Dec. 1, 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 of clinical data at the American Epilepsy Society (AES) 2023 Annual Meeting December 1 – 5, in Orlando, Florida. Together, these data support the company's continued progress to develop STK-001 as the first disease-modifying medicine for the treatment of Dravet syndrome.

"The comprehensive set of data being presented at AES are giving us a very good understanding of how STK-001 works and its potential to address not only seizures, but many of the non-seizure effects of Dravet syndrome," said Barry Ticho, M.D., Ph.D., Chief Medical Officer of Stoke Therapeutics. "The substantial and sustained reductions in seizure frequency and improvements in cognition and behavior observed in our STK-001 clinical studies give us confidence that we are addressing the root cause of Dravet syndrome. In addition, the correlation between higher STK-001 exposure levels in brain and reductions in seizure frequency shown in our modeling data provides additional confidence in the clinical benefits observed among patients treated with STK-001 at higher doses and for longer periods of time. These findings are in stark contrast to the data from our two-year natural history study that show a lack of improvement among patients who are taking the best available anti-seizure medicines."

"Dravet syndrome goes far beyond seizures, and as children grow up, they experience a complex array of life-altering challenges, including developmental delays, movement and balance issues and delayed language and speech," said Joseph Sullivan, M.D., FAES, Professor of Neurology and Pediatrics and Director of the Pediatric Epilepsy Center of Excellence at the University of California San Francisco, and a prominent researcher in Dravet syndrome. "On average, patients enrolled in the BUTTERFLY natural history study were taking 3.5 anti-seizure medicines. Despite this, they continued to experience similarly high rates of seizure frequency throughout the study and fell further and further behind their neurotypical peers in aspects of cognition and behavior, including their ability to communicate and use gross motor and fine motor skills. These findings highlight the critical need for a new approach to treating this disease, one that can improve the treatment of seizures and go beyond that to address the debilitating cognitive and behavioral aspects of this disease."

Highlights from the Company's presentations of data at the meeting, include:

- BUTTERFLY Natural History Study of Patients with Dravet Syndrome Ages 2 to 18: Despite treatment with the best available anti-seizure medicines, on average, patients continued to experience convulsive seizures over 24 months at similar frequency to baseline. No statistically significant change from baseline in the majority of Vineland-III measures (an established instrument for assessing developmental disabilities) was observed and the rate of improvement on multiple clinical measures, including key domains of the Vineland-III, was substantially below neurotypical peers. Gaps in neurodevelopment continued to widen throughout the study among patients with Dravet syndrome compared to their age-matched neurotypical peers.

- MONARCH & ADMIRAL Interim Analyses: Single and multiple doses of STK-001 up to 70mg were generally well tolerated. The multiple dose 70mg cohort showed the greatest reductions in convulsive seizure frequency, outperforming all lower dose groups. Patients treated with 2 or 3 initial doses of 70mg experienced substantial and sustained reductions in convulsive seizure frequency.

- SWALLOWTAIL & LONGWING Open Label Extension (OLE) studies: Approximately 90% of patients who completed participation in Phase 1/2a studies of STK-001 enrolled in one of these OLE studies. Multiple doses of STK-001 up to 45mg given every 4 months were generally well tolerated. In addition to durable reductions in convulsive seizure frequency throughout the course of treatment, data indicated substantial improvements in multiple assessments of cognition and behavior over 12 months. These data support the potential for disease-modification with STK-001.

- PK Model for STK-001: A relationship between STK-001 brain exposures and convulsive seizure frequency was evaluated based on 72 patients treated in the Phase 1/2a studies (MONARCH and ADMIRAL) and the SWALLOWTAIL OLE study in children and adolescents with Dravet syndrome. The exposure-seizure analysis demonstrated that higher STK-001 brain exposure leads to greater reductions in convulsive seizure frequency ($R=-0.23$, $P<0.001$).

Details of the Company's 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
24-Month Analysis of BUTTERFLY: A Prospective, Observational Study to Investigate Cognition and Other Non-seizure Comorbidities in Children & Adolescents with Dravet Syndrome (DS)	Joseph Sullivan, M.D., FAES, Professor of Neurology and Pediatrics and Director of the Pediatric Epilepsy Center of Excellence at the University of California San Francisco	**Poster Number:** 1.233 Saturday, Dec. 2 12:00 PM EST **Oral Presentation:** Monday, Dec. 4 3:15 PM EST
MONARCH & ADMIRAL: Phase 1/2a Studies in US & UK Investigating Safety and Drug Exposure of STK-001, an Antisense Oligonucleotide (ASO), in Children & 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:** 1.276 Saturday, Dec. 2 12:00 PM EST
SWALLOWTAIL & LONGWING: Open-Label Extension (OLE) Studies for Children and Adolescents with Dravet Syndrome (DS) who Previously Participated in a Study of Antisense Oligonucleotide (ASO) STK-001	Archana Desurkar M.D., Consultant Paediatric Neurologist at Sheffield Children's Hospital National Health Service Foundation Trust	**Poster Number:** 1.279 Saturday, Dec. 2 12:00 PM EST
Utilization of a Pharmacokinetic (PK) Model for STK-001 in Patients with Dravet Syndrome (DS) To Support Selection of Dosing Regimens in Clinic	Meena, Ph.D., Senior Vice President of Translational DMPK and Clinical Pharmacology at Stoke Therapeutics	**Poster Number:** 3.110 Monday, Dec. 4 12:00 PM EST

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. 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 the BUTTERFLY Observational Study

The BUTTERFLY study is a multicenter, longitudinal, prospective, observational 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 was designed to evaluate neurodevelopmental status and change from baseline to 24 months. Secondary and exploratory endpoints in the study evaluated changes in other disease measures, including seizures and additional non-seizure comorbidities. No investigational medications or other treatments were provided. Participants continued to receive their usual care, including anti-seizure medications, and were observed by a team of doctors and nurses over time for up to two years. The study was conducted at approximately 20 sites in the United States.

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 presentation of data at AES 2023. 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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