# Stoke Therapeutics Presents Data from the Phase 1/2a MONARCH Study of STK-001 in Children and Adolescents with Dravet Syndrome at the American Epilepsy Society (AES) 2021 Annual Meeting

December 3, 2021

*– Single doses of STK-001 up to 30mg and multiple doses of 20mg were well tolerated with no safety concerns related to study drug –*

*– 70.6% (12/17) of patients treated with STK-001 experienced a reduction from baseline in convulsive seizure frequency measured from Day 29 to Day 84 –*

*– All patients ages 2-12 (n=7) experienced reductions in seizure frequency –*

*– Additional data to be presented include pharmacokinetic (PK) modeling data of STK-001, initial safety data from the SWALLOWTAIL open-label extension study and three-month data from the BUTTERFLY observational study –*

BEDFORD, Mass.--(BUSINESS WIRE)--Dec. 3, 2021-- 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 five presentations related to the ongoing clinical development of STK-001 being made at the American Epilepsy Society (AES) 2021 Annual Meeting, December 3 – 7. STK-001 has the potential to be the first disease-modifying therapy to target the underlying cause of Dravet syndrome, which 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.

**Interim Safety, PK, and CSF Exposure Data from the Phase 1/2a MONARCH Study of STK-001, an Antisense Oligonucleotide (ASO), in Children and Adolescents with Dravet Syndrome (DS)**
**Session Date & Time:** Sunday, December 5 at12:00 p.m. CT
**Presenter:** Linda Laux, M.D., Associate Professor of Pediatrics (Neurology and Epilepsy) atNorthwestern University Feinberg School of Medicine and Attending Physician at Ann & Robert H. Lurie Children's Hospital of Chicago
**Poster Number:** 2.405

Highlights include:

- Single doses of STK-001 up to 30mg, and three 20mg doses of STK-001 given every four weeks, were found to be well tolerated with no safety concerns related to the study drug.
- The most common treatment-emergent adverse events (TEAE) were headache, vomiting, seizure, irritability, and back pain.
- 18.2% (4/22) of patients experienced a TEAE that was related to study drug, none of which were severe.
- 22.7% (5/22) of patients had a serious treatment-emergent adverse event (SAE), none of which were related to study drug.
- 70.6% (12/17) of patients treated with single doses (10mg, 20mg, 30mg) or multiple doses (20mg) of STK-001 experienced a reduction from baseline in convulsive seizure frequency measured from Day 29 to Day 84 after receiving their first dose of STK-001.
- All patients ages 2-12 (n=7) experienced a reduction from baseline in convulsive seizure frequency measured from Day 29 to Day 84. Reductions in seizure frequency were also observed among patients ages 13-18.
- Across all cohorts median reductions of 17% to 37% from baseline in convulsive seizure frequency from Day 29 to Day 84 were observed.

“Dravet syndrome is characterized by frequent, prolonged and intractable seizures, but some of the most devastating effects relate to non-seizure comorbidities such as developmental delays and cognitive impairment,” said Linda Laux, M.D., Associate Professor of Pediatrics (Neurology and Epilepsy) at Northwestern University Feinberg School of Medicine, Attending Physician at Ann & Robert H. Lurie Children's Hospital of Chicago, and the MONARCH study lead investigator. “Seeing an early trend toward reduction in seizure frequency at these relatively low dose levels is very encouraging, especially given that more than 90 percent of patients were taking three or more concomitant anti-seizure medications as maintenance therapy during the study.”

“STK-001 is designed to target the underlying cause of Dravet syndrome to potentially address both seizures and non-seizure comorbidities,” said Barry Ticho, M.D., Ph.D., Chief Medical Officer of Stoke Therapeutics. “These initial data give us confidence that STK-001 is having an effect on the disease. Based on our pharmacokinetic model, we believe that sustained higher exposure levels in the brain may lead to greater reductions in seizure frequency and potentially also improvements in some of the non-seizure comorbidities. We are pleased with the initial clinical findings from MONARCH, and the SWALLOWTAIL open-label extension study, and look forward to continuing our clinical progress in collaboration with the Dravet community.”

Additional posters include:

**SWALLOWTAIL: An Open-Label Extension (OLE) Study for Patients with Dravet Syndrome (DS) who Previously Participated in Studies of**

**STK-001**
**Session Date & Time:** Sunday, December 5 at12:00 p.m. CT
**Presenter:** Colin Roberts, M.D., Director of the Doernbecher Childhood Epilepsy Program atOregon Health & Science University
**Poster Number:** 2.22

Clinical data from the continued administration of STK-001 to patients previously treated in the Phase 1/2a MONARCH study demonstrated that multiple doses up to 30mg of STK-001 were well tolerated with no safety concerns related to the study drug. Additionally, dosing of STK-001 intrathecally (IT) every four months appears to be well tolerated. No patients have discontinued treatment in SWALLOWTAIL.

**A Pharmacokinetic (PK) Model for STK-001, an Antisense Oligonucleotide (ASO), Based on Data from Non-human Primates (NHP) Enables Dose Selection in Patients with Dravet Syndrome (DS)**
**Session Date & Time:** Monday, December 6 at12:00 p.m. CT
**Presenter:** Meena, Ph.D., Vice President of Bioanalytical, DMPK and Biomarker Development at Stoke Therapeutics
**Poster Number:** 3.264

A population pharmacokinetic model for intrathecal STK-001 was developed using non-human primate data and was scaled and adjusted using clinical data to predict STK-001 concentrations in plasma, CSF and brain in pediatric patients with Dravet syndrome. STK-001 levels in plasma and CSF in patients treated with STK-001 correlated very well with model predictions, indicating that plasma and CSF levels observed in patients are good predictors of STK-001 brain levels in patients. Modeling of clinical data also suggest that more than 95% of patients are predicted to have pharmacologically active STK-001 brain levels following three doses of 30mg administered one month apart and half of all patients are anticipated to maintain greater than minimum pharmacologically active levels of STK-001 for approximately three months after their last dose.

**ADMIRAL: A UK Open-Label Study to Investigate the Safety and Pharmacokinetics (PK) of Multiple Ascending Doses of Antisense Oligonucleotide (ASO) STK-001 in Children and Adolescents with Dravet Syndrome**
**Session Date & Time:** Sunday, December 5 at 12:00 p.m. CT
**Presenter:** 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:** 2.219

Provides the trial design of the Company's ongoing Phase 1/2a study (ADMIRAL) in the United Kingdom. This study is evaluating multiple doses of up to 70mg of STK-001. The primary endpoints are safety and tolerability of STK-001 as well as to determine the PK in plasma and exposure in CSF. The impact of STK-001 on frequency of convulsive seizures and quality of life are secondary endpoints of this study. Enrollment and dosing in ADMIRAL is ongoing.

**BUTTERFLY, An Observational Study to Investigate Cognition and Other Non-seizure Comorbidities in Children and Adolescents with Dravet Syndrome**
**Session Date & Time:** Monday, December 6 at12:00 p.m. CT
**Presenter:** Elaine Wirrell, M.D., Director of Pediatric Epilepsy atMayo Clinic, Director of the Child and Adolescent Neurology Residency Training Program at Mayo Clinic
**Poster Number:** 3.278

Three-month data suggest that commonly used cognition assessments including the VABS-III (Vineland Adaptive Behavior Scales, Third Edition), BSID-III (Bayley Scales of Infant Development, Third Edition), and WPPSI-IV (Wechsler Preschool and Primary Scale of Intelligence, Fourth Edition) may be useful for clinical studies assessing neurodevelopment and adaptive behavior in patients with Dravet syndrome. All three assessments showed relatively low intra-patient variability and no significant change from baseline three months after baseline assessments for all 36 patients enrolled.

All Company posters presented at AES 2021 will be available on the Investors & News section of Stoke's website at https://investor.stoketherapeutics.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 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 $Na_V1.1$ 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 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 pathogenic 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 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. Stoke plans to enroll approximately 90 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/.

Patients who participated in the MONARCH study 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. 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 over a 24-week treatment period. Stoke also intends to measure non-seizure aspects of the disease, such as overall clinical status and quality of life, as secondary endpoints. Stoke plans to enroll up to 60 patients in the study across multiple sites in the United Kingdom. Additional information about the ADMIRAL study can be found at https://www.admiralstudy.com.

**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 the Company's proprietary TANGO (Targeted Augmentation of Nuclear Gene Output) approach, Stoke is developing antisense oligonucleotides (ASOs) to selectively restore protein levels. The Company'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. The Company is pursuing treatment for a second haploinsufficient disease, 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 the Company's 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 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: the ability of STK-001 to treat Dravet syndrome and reduce seizures, the timing and expected progress of clinical trials, data readouts and presentations, and the timing or receipt of regulatory approval. Statements including words such as "believe," "plan," "will," "continue," "expect," "may," 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 do not fully materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. Forward-looking statements are subject to risks and uncertainties that may cause the company's actual activities or results to differ significantly from those expressed in any forward-looking statement, including risks and uncertainties related to the Company's ability to advance its product candidates, obtain regulatory approval of and ultimately commercialize its product candidates, the timing and results of preclinical and clinical trials, the company's ability to fund development activities and achieve development goals, the company's ability to protect intellectual property and other risks and uncertainties described under the heading "Risk Factors" in 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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