Stoke Therapeutics Highlights Strategic Priorities and Anticipated Milestones for 2023

January 9, 2023

– Additional safety and seizure frequency data from patients treated with multiple doses of STK-001 (45mg) anticipated in mid-2023 –

– Data from the highest dose cohort (70mg) anticipated in the second half of 2023 –

– Company expects to complete Phase 1/2a in 2023 in order to initiate a Phase 3 program in 2024 –

– As of September 30, 2022, Company had $252.2 million in cash, cash equivalents, marketable securities, and restricted cash, anticipated to fund operations into 2025 –

BEDFORD, Mass.--(BUSINESS WIRE)--Jan. 9, 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 outlined its expected milestones and the following strategic priorities for 2023:

- Complete Phase 1/2a studies of STK-001 for Dravet syndrome in 2023 in order to initiate a Phase 3 program in 2024;
- Continue to advance STK-002 for autosomal dominant optic atrophy (ADOA) toward the clinic; and
- Develop and expand the pipeline with a focus on the central nervous system and the eye.

“Our recent data showed the first evidence that upregulating protein expression with STK-001 to target the underlying cause of Dravet syndrome can reduce seizure frequency in children and adolescents who are already taking several anti-seizure medicines, including fenfluramine,” said Edward M. Kaye, M.D., Chief Executive Officer of Stoke Therapeutics. “These data support our belief that we are entering a new era in the treatment of this disease – a shift from seizure management to syndrome management – one that could have a profound impact for patients and caregivers. With additional data anticipated in 2023, we expect to be in a position to select a dose level and dose frequency in order to initiate a Phase 3 program in 2024.”

“In recent years our understanding of Dravet syndrome has improved dramatically. We now know what causes it and the effects it has on patients as they age. Even though three new medications have been approved by the FDA in the last five years for the treatment of seizures associated with Dravet syndrome, none of them address the full scope of the syndrome," said Joseph Sullivan, M.D., 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 into Dravet Syndrome. "That leaves a significant gap in our ability to effectively care for our patients. By restoring native gene expression, potential disease-modifying approaches are positioned to improve seizure control and address the non-seizure aspects of the disease that negatively impact health and quality of life for people living with this disease.”

Updates and Anticipated Milestones

STK-001: Dravet Syndrome

- Dosing is ongoing in the expanded 45mg multiple dose cohort of MONARCH in the US.
- Dosing is ongoing in the 70mg dose cohort of ADMIRAL in the UK, which was recently expanded to evaluate more patients.
- Data from patients treated with multiple doses of 45mg are expected in mid-2023.
- Data from patients treated with multiple doses of 70mg are expected in the second half of 2023.
- Company expects to initiate Phase 3 program of STK-001 in 2024.

STK-002: Autosomal Dominant Optic Atrophy (ADOA)

- Clinical Trial Application (CTA) submission in the UK for planned Phase 1/2 study in patients with ADOA is expected in the first half of 2023.
- Phase 1/2 study of STK-002 expected to start in 2024.

Cash Position and Financial Guidance

Stoke ended the third quarter of 2022 with $252.2 million in cash, cash equivalents, marketable securities, and restricted cash anticipated to fund operations into 2025.

Stoke’s Presentation at the 41 st Annual J.P. Morgan Healthcare Conference

Dr. Edward M. Kaye will discuss Stoke’s strategic priorities and key milestones in a presentation at the 41st Annual J.P. Morgan Healthcare Conference on Tuesday, January 10, 2023, at 2:15 p.m. ET (11:15 a.m. PT).

A live audio webcast of the presentation will be available on the Investors & News section of Stoke’s website at https://investor.stoketherapeutics.com/

and can be accessed by following this Link. A replay of the webcast will be available for 30 days following the presentation.

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 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 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 for STK-001 and STK-002. 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 of data readouts and interim and final results of preclinical and clinical trials; 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; 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 into 2025; 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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