Stoke Therapeutics Highlights Strategic Priorities and Anticipated Milestones for 2024

January 8, 2024

– Data anticipated in Q1 2024 from studies of STK-001 for the treatment of Dravet syndrome –

– End of Phase 1/2a study results and OLE data from patients receiving ongoing treatment; Analyses to include effects of STK-001 on seizure frequency, cognition and behavior –

– Pending Q1 data, Company to request Phase 3 planning meetings with regulators –

– As of September 30, 2023, Company had $214.7 million in cash, cash equivalents and marketable securities, anticipated to fund operations to the end of 2025 –

BEDFORD, Mass.--(BUSINESS WIRE)--Jan. 8, 2024-- 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 strategic priorities and anticipated milestones for 2024.

"Over the last three years we have generated a comprehensive set of data from 81 patients that support STK-001 as potentially the first disease-modifying medicine for Dravet syndrome. 2024 is all about advancing this potential new medicine toward a registrational study," said Edward M. Kaye, M.D., Chief Executive Officer of Stoke Therapeutics. "The recent 2-year data from our BUTTERFLY natural history study make it clear that even the best available anti-seizure medicines are inadequate. These data show continued high seizure burden and stagnation of neurodevelopment, which are in stark contrast to the improvements we see across the studies of STK-001. Results from clinical studies anticipated in the first quarter are expected to give us the data necessary to request meetings with regulators to discuss our Phase 3 plans."

Updates and Anticipated Milestones

STK-001: Dravet Syndrome

- In December, at the American Epilepsy Society annual meeting, the Company presented data supporting the continued advancement of STK-001 as a disease-modifying potential new medicine for the treatment of Dravet syndrome. Two-year natural history study data showed a lack of improvement among patients who are taking the best available anti-seizure medicines. In contrast, substantial and sustained reductions in seizure frequency and improvements in cognition and behavior were observed in clinical studies of STK-001. Modeling data suggest that higher STK-001 drug exposure in brain leads to greater seizure reductions. Single and multiple doses of STK-001 up to 70mg have been generally well tolerated to date.
- In the first quarter of 2024, the Company plans to report additional clinical and modeling data from 81 patients treated in the Phase 1/2a studies of STK-001 (MONARCH and ADMIRAL) and the two ongoing open-label extension studies (OLE) (SWALLOWTAIL and LONGWING), including:
    - Safety, pharmacokinetic (PK) modeling, and cerebrospinal fluid (CSF) results;
    - Seizure frequency data from ~20 patients who received 1, 2, or 3 initial doses of 70mg of STK-001 and were followed for six months;
    - The effects of repeat doses of STK-001 (30mg, 45mg) on seizure frequency and cognition and behavior from patients treated in the SWALLOWTAIL and LONGWING OLE studies.
- Pending the results of the Q1 data readout, the Company plans to proceed with Phase 3 preparation activities, including discussions with global regulatory agencies, availability of chronic toxicology data, preparation of the investigator brochure, submission of a final protocol to regulatory agencies and institutional review boards (IRB).

Pipeline

- STK-002: Autosomal Dominant Optic Atrophy (ADOA): FALCON natural history study is fully enrolled. Phase 1 study (OSPREY) of STK-002 is expected to start in the UK in 2024.
- The Company's collaboration with Acadia Pharmaceuticals to discover, develop and commercialize novel RNA-based medicines for the potential treatment of severe and rare genetic neurodevelopmental diseases of the central nervous system (CNS) is ongoing. The collaboration includes Rett syndrome (*MECP2*), SYNGAP1, and an undisclosed neurodevelopmental target of mutual interest.

Cash Position and Financial Guidance

- Stoke ended the third quarter of 2023 with $214.7 million in cash, cash equivalents and marketable securities, anticipated

to fund operations to the end of 2025.

Stoke's Presentation at the 42nd Annual J.P. Morgan Healthcare Conference

Dr. Edward Kaye will discuss Stoke's strategic priorities and anticipated milestones in a presentation at the 42nd Annual J.P. Morgan Healthcare Conference on Wednesday, January 10, 2024, at 6:45 p.m. ET (3:45 p.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 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.

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.

Dosing in SWALLOWTAIL is ongoing.

About the Phase 1/2a ADMIRAL Study (United Kingdom)

The ADMIRAL study was 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 were 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 was 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 measured 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 met study entry criteria were 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.

Dosing in LONGWING is ongoing.

About the BUTTERFLY Observational Study

The BUTTERFLY study was 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 Autosomal Dominant Optic Atrophy (ADOA)

Autosomal dominant optic atrophy (ADOA) is the most common inherited optic nerve disorder. It is a rare disease that causes progressive and irreversible vision loss in both eyes starting in the first decade of life. Severity can vary and the rate of vision loss can be difficult to predict. Roughly half of people with ADOA fail driving standards and up to 46% are registered as legally blind. More than 400 *OPA1* mutations have been reported in people diagnosed with ADOA. Currently there is no approved treatment for people living with ADOA. ADOA affects approximately one in 30,000

people globally with a higher incidence in Denmark of one in 10,000 due to a founder effect. For more information about ADOA, visit https://www.stoketherapeutics.com/disease-areas/adoa/.

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/.

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 behavior or cognition at the indicated dosing levels or at all; the timing and expected progress of clinical trials, data readouts and presentations for STK-001 and STK-002; the timing of regulatory interactions or the outcome thereof; and the Company's cash runway. Statements including words such as "anticipate," "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 or indirect impact of global business, political and macroeconomic conditions, including inflation, interest rate volatility, cybersecurity events, uncertainty with respect to the federal budget, instability in the global banking system and volatile market conditions, and global events, including public health crises, and ongoing geopolitical conflicts, such as the conflicts in Ukraine and the Middle East; 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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