Stoke Therapeutics Reports First Quarter Financial Results and Provides Business Updates

May 4, 2023

– Company on-track to report new data from the ongoing Phase 1/2a clinical studies of STK-001 in children and adolescents with Dravet syndrome in mid-2023 –

– Data readout will focus on safety and seizure frequency results for up to 16 patients who received three doses of 45mg of STK-001 –

– Company plans to initiate a pivotal study in 2024, pending additional data from the Phase 1/2a studies –

– Company received authorization to initiate a Phase 1/2 study in the UK of STK-002, an investigational new treatment for Autosomal Dominant Optic Atrophy (ADOA) –

– As of March 31, 2023, Company had $254.2 million in cash, cash equivalents, marketable securities, and restricted cash, anticipated to fund operations to the end of 2025 –

BEDFORD, Mass.--(BUSINESS WIRE)--May 4, 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 reported financial results for the first quarter of 2023 and provided business updates including those related to STK-001, the company's proprietary antisense oligonucleotide (ASO) being developed by Stoke as the first potential new medicine to address the genetic cause of 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. Complications of the disease often contribute to poor quality of life for patients and their caregivers. Despite available anti-seizure medicines, seizures are not adequately controlled for more than 90% of patients.

"In the coming months, Stoke will report new safety and seizure frequency data from the ongoing clinical studies of STK-001, the first potential new medicine to treat the underlying cause of Dravet syndrome," said Edward M. Kaye, M.D., Chief Executive Officer of Stoke Therapeutics. "Last year we showed the first evidence that increasing protein expression with STK-001 led to improvements in patient outcomes, including reductions in convulsive seizure frequency of up to 55% and an early trend toward improvements in certain non-seizure aspects of the disease. This is the first time a gene-based approach has demonstrated a clinical effect in patients with Dravet syndrome, and it is particularly compelling given that these patients were experiencing numerous seizures despite use of the best available anti-seizure medicines. While we await the new data, we are moving forward with our Phase 3 planning, including seeking advice from outside experts so that we are in a position to move quickly if the early effects we observed are replicated in a larger patient group."

"We continue to make progress with our pipeline and anticipate starting a Phase 1/2 study of STK-002 in early 2024, which is designed to upregulate protein expression to address the underlying cause of autosomal dominant optic atrophy (ADOA), the most common inherited optic nerve disorder."

First Quarter 2023 Business Highlights and Recent Developments

- Today, the Company provided the following updates from the Phase 1/2a studies of STK-001 in children and adolescents with Dravet syndrome:
  - In the U.S., dosing is complete in the 45mg multiple dose cohort and dosing is underway in the 70mg single dose cohort of MONARCH.
  - In the U.K., dosing is ongoing in the 70mg multiple dose cohort of ADMIRAL.
- In April, the Company received authorization of its Clinical Trial Application (CTA) by the United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA) to initiate a Phase 1/2 study (OSPREY) of STK-002 for the treatment of autosomal dominant optic atrophy (ADOA), the most common inherited optic nerve disorder. The Phase 1/2 study of STK-002 is expected to start in early 2024.

Upcoming Anticipated Milestones

- In mid-2023, the Company plans to report additional clinical data from patients in the ongoing MONARCH, ADMIRAL and SWALLOWTAIL studies of STK-001 in children and adolescents with Dravet syndrome.
  - The analysis will include safety, pharmacokinetic (PK), and cerebrospinal fluid (CSF) drug exposure data from the MONARCH and ADMIRAL studies.
  - Also included will be seizure frequency data from up to 16 patients in the MONARCH and ADMIRAL studies who received three doses of 45mg of STK-001 and were followed for three months.
  - The effects of repeat doses of STK-001 (30mg) on seizure frequency from patients treated in the SWALLOWTAIL open-label extension study will also be provided.
  - The Company expects to initiate a Phase 3 program in 2024, pending additional data from the phase 1/2a studies.
- Data from patients treated with 70mg of STK-001 in MONARCH (single dose) and ADMIRAL (multiple doses) are

anticipated in the second half of 2023.

First Quarter 2023 Financial Results

- As of March 31, 2023, Stoke had $254.2 million in cash, cash equivalents, marketable securities, and restricted cash, which is anticipated to fund operations to the end of 2025.
- Revenue recognized for upfront license fees and services provided from a License and Collaboration Agreement for the three months ended March 31, 2023 was $5.2 million, compared to $3.0 million for the same period in 2022.
- Net loss for the three months ended March 31, 2023 was $22.5 million, or $0.53 per share, compared to $24.6 million, or $0.66 per share, for the same period in 2022.
- Research and development expenses for the three months ended March 31, 2023 were $19.6 million, compared to $18.3 million for the same period in 2022.
- General and administrative expenses for the three months ended March 31, 2023 were $10.2 million, compared to $9.5 million for the same period in 2022.
- The increase in expenses for the three months ended March 31, 2023 as compared to the same period in 2022 primarily relate to increases in costs associated with personnel, third party contracts, consulting, facilities and other costs associated with development activities for STK-001 and STK-002, research on additional therapeutics and growing a public corporation.

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 underway.

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. 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 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.

About STK-002

STK-002 is a proprietary antisense oligonucleotide (ASO) in preclinical development for the treatment of Autosomal Dominant Optic Atrophy (ADOA). Approximately 80% of individuals with ADOA experience symptoms before age 10, typically beginning between the ages of 4 and 6. Stoke believes that STK-002 has the potential to be the first disease-modifying therapy for people living with ADOA. An estimated 65% to 90% of cases are caused by mutations in the *OPA1* gene, most of which lead to a haploinsufficiency resulting in 50% OPA1 protein expression and disease manifestation. STK-002 is designed to upregulate OPA1 protein expression by leveraging the non-mutant (wild-type) copy of the *OPA1* gene to restore OPA1 protein expression with the aim to stop or slow vision loss in patients with ADOA. Stoke has generated preclinical data demonstrating proof-of-mechanism and proof-of-concept for STK-002. STK-002 has been granted orphan drug designation by the FDA as a potential new treatment for ADOA and the company has received authorization of its CTA from the MHRA.

About the Phase 1/2 OSPREY Study (United Kingdom)

The OSPREY study is a Phase 1/2 open-label study of children and adults ages 6 to 55 who have an established diagnosis of ADOA and have evidence of a genetic mutation in the *OPA1* gene. The primary objectives for the study are to assess the safety and tolerability of single ascending doses of STK-002, as well as to determine the exposure in blood A secondary objective is to assess efficacy following intravitreal (IVT) administration of STK-002 in one eye of each patient as measured by changes in visual function and ocular structure as well as quality of life in patients with ADOA. Enrollment and dosing are anticipated to begin in early 2024.

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 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 Company's quarterly results and cash runway; its future operating results, financial position and liquidity; the ability of STK-001 to treat the underlying causes of Dravet syndrome and reduce seizures or show improvements in non-seizure comorbidities; the ability of STK-002 to treat the underlying causes of ADOA; the timing and expected progress of clinical trials, data readouts and presentations; the timing or receipt of regulatory approvals; the ability of TANGO to design medicines to increase protein production and the expected benefits thereof. 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 its product candidates, obtain regulatory approval of and ultimately commercialize its product candidates; the timing and 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 to the end of 2025; the Company's ability to protect its intellectual property; the direct and indirect impacts of public health crises, including the COVID-19 pandemic, 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, 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.

Financial Tables Follow

Stoke Therapeutics, Inc.
Consolidated balance sheets
(in thousands, except share and per share amounts)
(unaudited)

	March 31,	December 31,

	2023	2022
Assets		
Current assets:		
Cash and cash equivalents	$ 190,339	$ 113,556
Marketable securities	63,334	116,039
Prepaid expenses	10,191	10,932
Other current assets	5,880	2,955
Interest receivable	492	588
Total current assets	$ 270,236	$ 244,070
Restricted cash	569	569
Operating lease right-of-use assets	4,202	4,753
Property and equipment, net	6,789	6,675
Total assets	$ 281,796	$ 256,067
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 4,299	$ 766
Accrued and other current liabilities	13,777	15,748
Deferred revenue - current portion	13,451	14,880
Total current liabilities	$ 31,527	$ 31,394
Deferred revenue - net of current portion	34,144	36,856
Other long term liabilities	2,303	2,968
Total long term liabilities	36,447	39,824
Total liabilities	$ 67,974	$ 71,218
Commitments and contingencies		
Stockholders' equity		
Common stock, par value of $0.0001 per share; 300,000,000 shares authorized, 44,175,089 and 39,439,575 shares issued and outstanding as of March 31, 2023 and December 31, 2022, respectively	4	4
Additional paid-in capital	534,111	483,170
Accumulated other comprehensive loss	(598)	(1,175)
Accumulated deficit	(319,695)	(297,150)
Total stockholders' equity	$ 213,822	$ 184,849
Total liabilities and stockholders' equity	$ 281,796	$ 256,067

Stoke Therapeutics, Inc.
Consolidated statements of operations and comprehensive loss
(in thousands, except share and per share amounts)
(unaudited)

	Three Months Ended March 31,	
	2023	2022
Revenue	$ 5,152	$ 3,000
Operating expenses:		
Research and development	19,631	18,309
General and administrative	10,211	9,486
Total operating expenses	29,842	27,795
Loss from operations	(24,690)	(24,795)
Other income:		
Interest income (expense), net	2,103	104
Other income (expense), net	42	42
Total other income	2,145	146
Net loss	$ (22,545)	$ (24,649)
Net loss per share, basic and diluted	$ (0.53)	$ (0.66)
Weighted-average common shares outstanding, basic and diluted	42,536,474	37,448,301
Comprehensive loss:		
Net loss	$ (22,545)	$ (24,649)
Other comprehensive gain (loss):		
Unrealized gain (loss) on marketable securities	577	(516)
Total other comprehensive loss	$ 577	$ (516)
Comprehensive loss	$ (21,968)	$ (25,165)

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