Stoke Therapeutics Reports First Quarter Financial Results and Provides Business Updates

May 10, 2022

– 2H 2022 clinical data readout on track for patients with Dravet syndrome who received multiple doses of STK-001 (30mg) in Phase 1/2a clinical studies MONARCH, ADMIRAL, and SWALLOWTAIL –

– Recent preclinical data support ongoing development of STK-002 as the first potential disease-modifying approach for the treatment of Autosomal Dominant Optic Atrophy (ADOA), the most common inherited optic nerve disorder –

– As of March 31, 2022, Company had $293.8 million in cash, cash equivalents, marketable securities, and restricted cash, anticipated to fund operations into 2025 –

BEDFORD, Mass.--(BUSINESS WIRE)--May 10, 2022-- 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 2022 and provided business updates.

“We have demonstrated continued progress with STK-001 in the first part of 2022, advancing multiple clinical trials, including the Phase 1/2a studies, MONARCH in the U.S. and ADMIRAL in the U.K., as well as their respective open-label extension studies, SWALLOWTAIL and LONGWING,” said Edward M. Kaye, M.D., Chief Executive Officer of Stoke Therapeutics. “The Stoke team is continuing to work with a sense of urgency to advance STK-001 as a potential new medicine for people living with Dravet syndrome who do not have adequate treatment options to control their seizures or to address the many non-seizure comorbidities associated with this disease. We look forward to our readout of data from patients treated with multiple doses of 30mg in the second half of 2022.”

“In addition to our progress in the clinic, we continue to deepen our understanding of STK-002 as the first potential disease modifying approach for the treatment of ADOA,” continued Kaye. “We believe we are in a strong financial position with sufficient capital to support our current research and clinical development efforts into 2025.”

First Quarter 2022 Business Highlights and Recent Developments

- Today, the Company announced continued clinical progress in the Phase 1/2a studies of STK-001. Dosing is complete in the initial 30mg multiple dose cohorts of MONARCH and ADMIRAL. The 30mg multiple dose cohort of MONARCH was expanded, per protocol, to provide additional patient data for the planned readout in the second half of 2022. Dosing is ongoing in this expanded cohort. The first patients have been dosed with 45mg in the multiple dose portion of MONARCH. Dosing is ongoing in the 45mg multiple dose portion of ADMIRAL.
- Dosing is ongoing in SWALLOWTAIL, an open label extension (OLE) study designed to evaluate the long-term safety and tolerability of repeat doses of STK-001 in patients who participated in the Phase 1/2a MONARCH study. Currently, patients are being treated with 30mg of STK-001 in SWALLOWTAIL.
- The European Medicines Agency (EMA) granted orphan drug designation for STK-001 as a potential new treatment for Dravet syndrome.
- On May 2, 2022, the Company presented new preclinical data for STK-002 at The Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting. The new data demonstrated *in-vivo*, dose-related target engagement and OPA1 protein upregulation with sustained effect in non-human primate (NHP) retinal tissue following intravitreal (IVT) administration of STK-002. Dose-related OPA1 upregulation in NHP retinal ganglion cells following IVT administration of STK-002 was also detected.

Upcoming Anticipated Milestones

- In the second quarter of 2022, the Company expects to dose the first patient in LONGWING, an OLE study designed to evaluate the long-term safety and tolerability of repeat doses of STK-001 in patients who participated in the Phase 1/2a ADMIRAL study.
- On May 16, 2022, the Company expects to present preclinical data supporting its approach to treating ADOA with STK-002 at the American Society of Gene and Cell Therapy (ASGCT) Annual Meeting, at 10:30am ET.
- In the second quarter of 2022, the Company expects to initiate a prospective natural history study (FALCON) of people living with ADOA.
- In the second half of 2022, the Company plans to report data from patients treated with multiple doses of STK-001 (30mg). The analyses will include data from patients treated in the ongoing Phase 1/2a MONARCH, ADMIRAL, and SWALLOWTAIL studies, including those who were treated in the expanded 30mg multiple dose cohort of MONARCH.

First Quarter 2022 Financial Results

- As of March 31, 2022, Stoke had approximately $293.8 million in cash, cash equivalents, marketable securities and restricted cash, which is anticipated to fund operations into 2025.
- Revenue recognized for upfront license fees and services provided from a License and Collaboration Agreement for the three months ended March 31, 2022, was $3.0 million. There was no revenue in the same period in 2021.
- Net loss for the three months ended March 31, 2022, was $24.6 million, or $0.66 per share, compared to $16.8 million, or $0.46 per share, for the same period in 2021.
- Research and development expenses for the three months ended March 31, 2022, were $18.3 million, compared to $9.9 million for the same period in 2021.
- General and administrative expenses for the three months ended March 31, 2022, were $9.5 million, compared to $6.9 million for the same period in 2021.
- The increase in expenses for the three months ended March 31, 2022 over the same period in 2021 primarily relate to increases in costs associated with personnel, third party contracts, consulting, facilities and others associated with development activities for STK-001 and STK-002, research on additional therapeutics and growing a public corporation.

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 $Na_V1.1$ 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 and the EMA 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.

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. ADOA is considered a haploinsufficiency disease, as

most people living with ADOA have genetic mutations in the *OPA1* gene that result in only half the necessary OPA1 protein being produced. 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. 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.

About STK-002

STK-002 is a proprietary antisense oligonucleotide (ASO) in preclinical development for the treatment of Autosomal Dominant Optic Atrophy (ADOA). Stoke believes that STK-002 has the potential to be the first disease-modifying therapy for people living with ADOA. 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.

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; 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; 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; the Company's ability to fund development activities and achieve development goals; 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.

Financial Tables Follow

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

	Three Months Ended March 31,	
	2022	**2021**
Revenue	$ 3,000	$ —
Operating expenses:		
Research and development	18,309	9,913
General and administrative	9,486	6,914
Total operating expenses	27,795	16,827
Loss from operations	(24,795)	(16,827)
Other income:		
Interest income (expense), net	104	6
Other income (expense), net	42	28
Total other income	146	34
Net loss	$ (24,649)	$ (16,793)
Net loss per share, basic and diluted	$ (0.66)	$ (0.46)
Weighted-average common shares outstanding, basic and diluted	37,448,301	36,643,205
Comprehensive loss:		
Net loss	$ (24,649)	$ (16,793)
Other comprehensive loss:		

Unrealized gain (loss) on marketable securities	(516)	—
Total other comprehensive loss	$ (516)	$ —
Comprehensive loss	$ (25,165)	$ (16,793)

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

	March 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 84,111	$ 144,895
Marketable Securities	209,105	74,915
Prepaid expenses and other current assets	12,290	9,159
Deferred financing costs	—	117
Interest receivable	265	132
Total current assets	$ 305,771	$ 229,218
Restricted cash	569	569
Operating lease right-of-use assets	4,563	4,939
Property and equipment, net	5,035	4,139
Total assets	$ 315,938	$ 238,865
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 3,328	$ 2,385
Accrued and other current liabilities	11,108	14,754
Deferred revenue - current portion	8,469	—
Total current liabilities	$ 22,905	$ 17,139
Deferred revenue - net of current portion	49,545	—
Other long term liabilities	3,511	3,949
Total long term liabilities	53,056	3,949
Total liabilities	$ 75,961	$ 21,088
Commitments and contingencies		
Stockholders' equity		
Common stock, par value of $0.0001 per share; 300,000,000 shares authorized, 39,044,669 and 36,902,499 shares issued and outstanding as of March 31, 2022 and December 31, 2021, respectively	4	4
Additional paid-in capital	461,389	414,024
Accumulated other comprehensive loss	(684)	(168)
Accumulated deficit	(220,732)	(196,083)
Total stockholders' equity	$ 239,977	$ 217,777
Total liabilities and stockholders' equity	$ 315,938	$ 238,865

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