Stoke Therapeutics Reports First Quarter Financial Results and Provides Business Updates

May 10, 2021

– Enrollment complete in single ascending dose (SAD) portion (10mg, 20mg, 30mg) of Phase 1/2a MONARCH study of STK-001 in children and adolescents with Dravet syndrome; Interim analysis planned for the third quarter –

– Enrollment and dosing ongoing in the 20mg multiple ascending dose (MAD) portion of MONARCH –

– Company on-track to identify a clinical candidate for the treatment of autosomal dominant optic atrophy by year end –

– As of March 31, 2021, Company has $267.7 million in cash, cash equivalents and restricted cash, anticipated to fund operations into 2024 –

BEDFORD, Mass.--(BUSINESS WIRE)--May 10, 2021-- Stoke Therapeutics, Inc. (Nasdaq: STOK), a biotechnology company dedicated to addressing the underlying cause of severe diseases by up-regulating protein expression with RNA-based medicines, today reported financial results for the first quarter of 2021 and provided business updates.

"The momentum we are seeing with STK-001 in the clinic is driven by high levels of interest from the Dravet community and our shared sense of urgency to advance a potential disease-modifying approach for the treatment of this devastating disease. The single dose portion of our Phase 1/2a MONARCH study in the U.S. is now fully enrolled up to the 30mg dose level and based on our progress, we now anticipate our first data readout from this single dose portion of MONARCH in the third quarter. We are also well underway with preparation to initiate a complementary study of STK-001 in the United Kingdom in the coming months. Together, we believe these studies will provide meaningful data to inform future development of STK-001," said Edward M. Kaye, M.D., Chief Executive Officer of Stoke Therapeutics. "In addition to clinical progress, we continue to advance our pipeline. We recently presented new preclinical data that provide additional confidence in our ability to upregulate OPA1 protein expression to treat the underlying cause of autosomal dominant optic atrophy (ADOA), the most common inherited optic nerve disorder. We are on track with lead optimization efforts for the ADOA program and expect to demonstrate proof of mechanism for a third preclinical target using our TANGO approach by year end."

First Quarter 2021 Business Highlights and Recent Developments

- The Company announced today, the completion of patient enrollment in the 10mg, 20mg, and 30mg single ascending dose (SAD) portion of the Phase 1/2a MONARCH study of STK-001 in children and adolescents with Dravet syndrome.
- Enrollment and dosing in the multiple ascending dose (MAD) portion of MONARCH is ongoing.
- On March 30, 2021, the Company announced the authorization of its Clinical Trial Application (CTA) by the United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA) to initiate a Phase 1/2a study (ADMIRAL) of STK-001 for the treatment of Dravet syndrome in the United Kingdom. The planned ADMIRAL study complements the ongoing MONARCH study by evaluating multiple doses of up to 70mg of STK-001 and represents a first step in the global clinical development of STK-001.
- Dosing of patients 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.
- On May 4, 2021, the Company presented new preclinical efficacy data for TANGO antisense oligonucleotides (ASO) at The Association for Research in Vision and Ophthalmology (ARVO). The new data demonstrated, for the first time, both OPA1 protein upregulation and improved mitochondrial function in human cells derived from autosomal dominant optic atrophy (ADOA) patients with different *OPA1* mutations. OPA1 protein deficiency is the primary cause of ADOA, the most common inherited optic nerve disorder.

Upcoming Anticipated Milestones

- Enrollment and dosing in the Phase 1/2a study (ADMIRAL) of STK-001 for the treatment of Dravet syndrome across multiple sites in the United Kingdom are expected to begin in the second half of 2021.
- As part of a planned interim analysis, the Company expects to report preliminary safety, pharmacokinetic, and cerebrospinal fluid (CSF) drug exposure data from the SAD portion of the Phase 1/2a MONARCH study of STK-001 in the third quarter of 2021.
- A presentation of preclinical data supporting the Company's approach to treating ADOA with a TANGO ASO will be presented on May 11, 2021 during the American Society of Gene and Cell Therapy (ASGCT) Annual Meeting.
- In the second half of 2021, the Company plans to initiate natural history data collection of people living with ADOA to better understand the natural progression of this disease and to support future clinical development of a TANGO ASO for the treatment of ADOA.
- The Company remains on track to identify a clinical candidate for the treatment of ADOA by the end of 2021.
- The Company expects to demonstrate *in vivo* proof of mechanism and safety for a third TANGO ASO program by the end

of 2021.

First Quarter 2021 Financial Results

- Net loss for the quarter ended March 31, 2021 was $16.8 million, or $0.46 per share compared to $11.0 million or $0.34 per share for the same period in 2020.
- Research and development expenses for the quarter ended March 31, 2021 were $9.9 million, compared to $7.2 million for the same period in 2020.
- General and administrative expenses for the quarter ended March 31, 2021 were $6.9 million, compared to $4.5 million for the same period in 2020.
- The increase in expenses for 2021 over the same periods in 2020 primarily relate to increases in costs associated with personnel, third party contracts, consulting, facilities, and other expenses associated with development activities for STK-001 and research on additional therapeutics and growing a public corporation.
- As of March 31, 2021, Stoke had approximately $267.7 million in cash, cash equivalents and restricted cash, which is anticipated to fund operations into 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, so the body does not function normally. 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 target genes produce more protein. TANGO aims to restore missing proteins by increasing – or stoking – protein output from healthy genes, thus compensating for the non-functioning copy of the gene.

About STK-001

STK-001 is an investigational new medicine for the treatment of Dravet syndrome currently being evaluated in a Phase 1/2a clinical trial. 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 characterize human pharmacokinetics. 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. Enrollment and dosing are ongoing in MONARCH and Stoke plans to enroll approximately 48 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 characterize human pharmacokinetics. 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 approximately 22 patients in the study across multiple sites in the United Kingdom.

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, chronic infections, 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. Dravet syndrome affects approximately 35,000 people in the United States, Canada, Japan, Germany, France and the United Kingdom, and it is not concentrated in a particular geographic area or ethnic group.

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. Symptoms typically begin between the ages of 4 and 6 years old, affecting males

and females equally. The severity of the condition by adolescence reflects the overall level of visual function to be expected throughout most of the individual's adult life. 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 Stoke Therapeutics

Stoke Therapeutics (Nasdaq: STOK), is a biotechnology company dedicated to addressing the underlying cause of severe diseases by up-regulating 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: our quarter-end results and cash runway; preclinical data and study results regarding OPA1 and STK-001; our future operating results, financial position and liquidity; the direct and indirect impact of COVID-19 on our business, financial condition and operations, including on our expenses, supply chain, strategic partners, research and development costs, clinical trials and employees; our expectation about timing and execution of anticipated milestones, responses to regulatory authorities, expected nomination of future product candidates and timing thereof; our ability to complete lead optimization of ASOs for ADOA, the timing and results of ADOA preclinical studies, our ability to develop ASOs treat the underlying causes of ADOA and our ability to advance OPA1 as our next preclinical target; our ability to use study data to advance the development of STK-001; the ability of STK-001 to treat the underlying causes of Dravet syndrome; and the ability of TANGO to design medicines to increase protein production and the expected benefits thereof. These forward-looking statements may be accompanied by such words as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "goal," "intend," "may," "might," "plan," "potential," "possible," "will," "would," and other words and terms of similar meaning. 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. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including: our ability to develop, obtain regulatory approval for and commercialize STK-001, any potential clinical candidate for OPA1 and future product candidates; the timing and results of preclinical studies and clinical trials; the risk that positive results in a clinical trial may not be replicated in subsequent trials or success in early stage clinical trials may not be predictive of results in later stage clinical trials; risks associated with clinical trials, including our ability to adequately manage clinical activities, unexpected concerns that may arise from additional data or analysis obtained during clinical trials, regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of our drug candidates; the occurrence of adverse safety events; failure to protect and enforce our intellectual property, and other proprietary rights; failure to successfully execute or realize the anticipated benefits of our strategic and growth initiatives; risks relating to technology failures or breaches; our dependence on collaborators and other third parties for the development, regulatory approval, and commercialization of products and other aspects of our business, which are outside of our full control; risks associated with current and potential delays, work stoppages, or supply chain disruptions caused by the coronavirus pandemic; risks associated with current and potential future healthcare reforms; risks relating to attracting and retaining key personnel; failure to comply with legal and regulatory requirements in the United States and abroad; risks relating to access to capital and credit markets; environmental risks; risks relating to the use of social media for our business; and the other risks and uncertainties that are described in the Risk Factors section of our most recent annual or quarterly report and in other reports we have filed with the U.S. Securities and Exchange Commission. These statements are based on our current beliefs and expectations and speak only as of the date of this press release. We do not undertake any obligation to publicly update any forward-looking statements.

Financial Tables Follow

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

	March 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 267,514	$ 287,308
Prepaid expenses and other current assets	7,511	6,435
Restricted cash - short-term	147	—
Deferred financing costs	117	181
Interest receivable	6	6
Total current assets	$ 275,295	$ 293,930

Restricted cash	58	205
Operating lease right-of-use assets	844	1,115
Property and equipment, net	2,711	2,675
Total assets	$ 278,908	$ 297,925
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,496	$ 1,495
Accrued and other current liabilities	4,614	9,930
Total current liabilities	$ 6,110	$ 11,425
Long term liabilities	333	422
Total liabilities	$ 6,443	$ 11,847
Commitments and contingencies		
Stockholders' equity		
Common stock, par value of $0.0001 per share; 300,000,000 shares authorized, 36,697,808 and 36,577,149 shares issued and outstanding as of March 31, 2021 and December 31, 2020, respectively	4	4
Additional paid-in capital	399,532	396,352
Accumulated deficit	(127,071)	(110,278)
Total stockholders' equity	$ 272,465	$ 286,078
Total liabilities and stockholders' equity	$ 278,908	$ 297,925

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,	
	2021	**2020**
Revenue	$ —	$ —
Operating expenses:		
Research and development	9,913	7,215
General and administrative	6,914	4,520
Total operating expenses	16,827	11,735
Loss from operations	(16,827)	(11,735)
Other income:		
Interest income	18	674
Other income (expense), net	16	22
Total other income	34	696
Net loss and comprehensive loss	$ (16,793)	$ (11,039)
Net loss per share, basic and diluted	$ (0.46)	$ (0.34)
Weighted-average common shares outstanding, basic and diluted	36,643,205	32,897,395

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Stoke Media & Investor Contacts:
Dawn Kalmar
Chief Communications Officer
dkalmar@stoketherapeutics.com
781-303-8302

Eric Rojas
Vice President, Investor Relations
IR@stoketherapeutics.com
617-312-2754

Source: Stoke Therapeutics, Inc.