Stoke Therapeutics Reports Third Quarter Financial Results and Provides Business Updates

November 8, 2021

– Company nominates STK-002 as clinical candidate for the treatment of autosomal dominant optic atrophy (ADOA), the most common inherited optic nerve disorder –

– Additional data from an interim analysis of the Phase 1/2a MONARCH study of STK-001 including 20mg multiple ascending dose (MAD) seizure data submitted for presentation at the American Epilepsy Society (AES) 2021 Annual Meeting –

– Phase 1/2a studies MONARCH in the U.S. and ADMIRAL in the UK are ongoing; enrollment and dosing continues in the MAD portion (30mg) of both studies –

– As of September 30, 2021, Company has $236.9 million in cash, cash equivalents, marketable securities, and restricted cash, anticipated to fund operations until the end of 2023 –

BEDFORD, Mass.--(BUSINESS WIRE)--Nov. 8, 2021-- 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 third quarter of 2021 and provided business updates.

"The recent positive interim data from the Phase 1/2a MONARCH study in patients with Dravet syndrome continue to support our efforts to develop STK-001 as the first potential new medicine to target the underlying cause of this severe and progressive genetic epilepsy," said Edward M. Kaye, M.D., Chief Executive Officer of Stoke Therapeutics. "Today, we are announcing continued pipeline progress with the nomination of STK-002 as a clinical candidate for the treatment of autosomal dominant optic atrophy, the most common inherited optic nerve disorder. Like Dravet syndrome, ADOA is caused by insufficient protein production and there is a need for a treatment option that addresses the underlying cause of the disease. By leveraging RNA splicing with our TANGO approach, we believe we are uniquely positioned to treat this disease by restoring protein levels to near normal. We look forward to initiating preclinical studies in 2022 to support future clinical trial applications."

Third Quarter 2021 Business Updates

- The Company announced positive interim data from the Phase 1/2a MONARCH study of STK-001 in children and adolescents with Dravet syndrome.
- The Phase 1/2a studies MONARCH and ADMIRAL continue to progress with enrollment and dosing of patients ongoing in the 30mg MAD cohorts.
- The FDA will allow the evaluation of an additional higher dose level of STK-001 (45mg) in the MONARCH study.

Recent Developments

- The Company has nominated STK-002 as the clinical candidate for the treatment of ADOA, a severe and progressive optic nerve disorder. There are currently no approved treatments for ADOA, which is primarily caused by loss-of-function mutations in the *OPA1* gene, resulting in 50% OPA1 protein expression and disease manifestation. STK-002, a proprietary antisense oligonucleotide (ASO), is designed to upregulate OPA1 protein expression by leveraging the non-mutant (wild-type) copy of the *OPA1* gene. Based on preclinical data generated to date, the Company believes that STK-002 has the potential to be a disease-modifying therapy for people living with ADOA.

Upcoming Anticipated Milestones

- Additional data from an interim analysis of the Phase 1/2a MONARCH study of STK-001, including 20mg MAD seizure data, were submitted for presentation at the American Epilepsy Society (AES) 2021 Annual Meeting, December 3-7, 2021 in Chicago.
- The Company is on track to initiate the collection of natural history data of people living with ADOA by year-end. The data will be used to better understand the natural progression of this disease and to support future clinical development of STK-002 for the treatment of ADOA.
- The Company is on track to demonstrate *in vivo* proof of mechanism and safety for a third TANGO ASO program by the end of 2021.
- The Company plans to initiate preclinical studies in 2022 to support future clinical trial applications.
- The Company expects to share preliminary clinical data on 30mg MAD doses of STK-001 in the second half of 2022.

Third Quarter 2021 Financial Results

- Net loss for the three months ended September 30, 2021 was $22.6 million, or $0.61 per share, compared to $13.7 million,

or $0.41 per share, for the same period in 2020.
- Research and development expenses for the three months ended September 30, 2021 were $14.4 million, compared to $8.1 million for the same period in 2020.
- General and administrative expenses for the three months ended September 30, 2021 were $8.3 million, compared to $5.6 million for the same period in 2020.
- Net loss for the nine months ended September 30, 2021 was $61.4 million, or $1.67 per share, compared to $37.7 million, or $1.14 per share, for the same period in 2020.
- Research and development expenses for the nine months ended September 30, 2021 were $38.4 million, compared to $23.3 million for the same period in 2020.
- General and administrative expenses for the nine months ended September 30, 2021 were $23.2 million, compared to $15.2 million for the same period in 2020.
- The increase in expenses for the three and nine month periods in 2021 over the same periods in 2020 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.
- As of September 30, 2021, Stoke had approximately $236.9 million in cash, cash equivalents, marketable securities and restricted cash, which is anticipated to fund operations until the end of 2023.

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 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 that is 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 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 blood 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. Stoke plans to enroll approximately 90 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 blood 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 up to 60 patients in the study across multiple sites in the United Kingdom. Additional information about the ADMIRAL study can be found at https://www.admiralstudy.com.

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 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 reverse 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 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, our 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 do not fully materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. Forward-looking statements are subject to risks and uncertainties that may cause the company's actual activities or results to differ significantly from those expressed in any forward-looking statement, including 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 success 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 intellectual property, the risks associated with the direct and indirect impacts of the ongoing COVID-19 pandemic on our business, and other risks and uncertainties described under the heading "Risk Factors" in 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 balance sheets
(in thousands, except share and per share amounts)
(unaudited)

	September 30, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 149,038	$ 287,308
Marketable Securities	87,118	—
Prepaid expenses and other current assets	8,468	6,435
Restricted cash - short-term	147	—
Deferred financing costs	117	181
Interest receivable	45	6
Total current assets	$ 244,933	$ 293,930
Restricted cash	569	205
Operating lease right-of-use assets	5,326	1,115

Property and equipment, net	2,943	2,675
Total assets	$ 253,771	$ 297,925
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 655	$ 1,495
Accrued and other current liabilities	11,229	9,930
Total current liabilities	$ 11,884	$ 11,425
Long term liabilities	4,374	422
Total liabilities	$ 16,258	$ 11,847
Commitments and contingencies		
Stockholders' equity		
Common stock, par value of $0.0001 per share; 300,000,000 shares authorized, 36,780,393 and 36,577,149 shares issued and outstanding as of September 30, 2021 and December 31, 2020, respectively	4	4
Additional paid-in capital	409,166	396,352
Accumulated other comprehensive loss	(22)	—
Accumulated deficit	(171,635)	(110,278)
Total stockholders' equity	$ 237,513	$ 286,078
Total liabilities and stockholders' equity	$ 253,771	$ 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 September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Revenue	$ —	$ —	$ —	$ —
Operating expenses:				
Research and development	14,358	8,109	38,366	23,293
General and administrative	8,325	5,602	23,173	15,165
Total operating expenses	22,683	13,711	61,539	38,458
Loss from operations	(22,683)	(13,711)	(61,539)	(38,458)
Other income:				
Interest income (expense), net	44	(1)	84	703
Other income (expense), net	42	28	98	73
Total other income	86	27	182	776
Net loss	$ (22,597)	$ (13,684)	$ (61,357)	$ (37,682)
Net loss per share, basic and diluted	$ (0.61)	$ (0.41)	$ (1.67)	$ (1.14)
Weighted-average common shares outstanding, basic and diluted	36,759,319	33,273,597	36,706,647	32,954,727
Comprehensive loss:				
Net loss	$ (22,597)	$ (13,684)	$ (61,357)	$ (37,682)
Other comprehensive loss:				
Unrealized gain (loss) on marketable securities	20	—	(22)	—
Total other comprehensive loss	$ 20	$ —	$ (22)	$ —
Comprehensive loss	$ (22,577)	$ (13,684)	$ (61,379)	$ (37,682)

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