Stoke Therapeutics Reports Third Quarter Financial Results and Provides Business Updates

November 12, 2020

- Company nominates OPA1 as the next preclinical target for its proprietary TANGO approach to treating the underlying cause of severe genetic diseases –

- OPA1 protein deficiency is the leading cause of autosomal dominant optic atrophy (ADOA), the most common inherited optic nerve disorder –

- Enrollment and dosing in Phase 1/2a MONARCH study of STK-001 in children and adolescents with Dravet syndrome is ongoing; Preliminary data still anticipated in 2021 –

– As of September 30, 2020, Company has $191.7 million in cash, cash equivalents and restricted cash, anticipated to fund operations into 2023 –

BEDFORD, Mass.--(BUSINESS WIRE)--Nov. 12, 2020-- Stoke Therapeutics, Inc. (Nasdaq: STOK), a biotechnology company pioneering a new way to treat the underlying cause of genetic diseases by precisely upregulating protein expression, today reported financial results for the third quarter of 2020 and provided business updates.

"We have made important progress in recent months that includes the continued enrollment and dosing of children and adolescents in our MONARCH study, reaching agreement with the FDA to evaluate an additional higher dose of STK-001 in this study and submitting a plan to the Agency that also would allow us to evaluate multiple ascending doses. We remain on track for preliminary data from this Phase 1/2a study in 2021," said Edward M. Kaye, M.D., Chief Executive Officer of Stoke Therapeutics. "In addition, based on new preclinical data, we are announcing today the expansion of our pipeline with the nomination of *OPA1* as our next preclinical target. Consistent with our strategy, we believe our approach has the potential to be a first-in-class, disease modifying treatment for autosomal dominant optic atrophy, the most common inherited optic nerve disorder. There are currently no treatments available for this disease, which causes progressive and irreversible vision loss in both eyes starting in the first decade of life."

The nomination of *OPA1* as the Company's next preclinical target is supported by preclinical data that demonstrated *in vitro* and *in vivo* target engagement and protein upregulation in *OPA1* protein-deficient cells. In these studies, TANGO antisense oligonucleotides (ASOs) demonstrated:

- Dose-dependent decreases in non-productive OPA1 mRNA and increases in OPA1 protein expression *in vitro* and *in vivo*.
- An increase in OPA1 protein expression to approximately 75% of wild-type levels in an OPA1 haploinsufficient (OPA1 +/-) cell line.
- *In vivo* increases in OPA1 protein levels in the retina of wild-type rabbits that correlated with increases in the level of the test ASO.
- The test ASO was well tolerated for up to 29 days (maximum days evaluated) after intravitreal injection.

Recently completed preclinical studies have now demonstrated the ability of TANGO ASOs targeting the *OPA1* gene to upregulate adenosine triphosphate production (ATP) levels in the mitochondria. These new data showed that in haploinsufficient cells where half the amount of OPA1 is present and mitochondrial function is impaired, our ASOs demonstrated an ability to increase OPA1 protein levels and also partially restore mitochondrial function as measured by an increase in ATP production. *OPA1* expression is essential to retinal ganglion cell survival and visual signal transmission. Retinal ganglion cells have high energy needs making them particularly susceptible to losses in ATP production due to *OPA1* haploinsufficiency.

"The ATP finding is significant because in patients with autosomal dominant optic atrophy (ADOA), the retinal ganglion cells are not producing enough ATP and have defective mitochondrial function, which leads to cell death and progressive vision loss. These new data suggest that our ASO approach can restore mitochondrial function to potentially address the underlying cause of autosomal dominant optic atrophy," said Gene Liau Ph.D., Executive Vice President, Head of Research and Preclinical Development of Stoke Therapeutics. "Our goal is to advance an ASO that would delay, or potentially even prevent, vision loss for people living with ADOA. We aim to complete our lead optimization studies by the end of 2021 so that we can advance the most promising potential new medicine into human studies."

OPA1 protein deficiency is the primary cause of ADOA, the most common inherited optic nerve disorder. ADOA typically presents in the first decade of life and 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 loss of function mutations in one allele (haploinsufficiency) in the *OPA1* gene. There are over 400 different mutations reported to date in ADOA patients. Similar to Stoke's Dravet syndrome program, Stoke's approach for ADOA leverages upregulation of the wild-type allele and can potentially be used to treat ADOA due to loss of OPA1 activity in a mutation-independent manner.

Third Quarter 2020 Business Highlights and Recent Developments

- On October 7, the Company announced plans to move forward with dosing of STK-001 in its ongoing Phase 1/2a MONARCH study for Dravet syndrome. The FDA will allow the Company to add an additional higher dose level to the single ascending dose portion of the study, which will now include a total of three dose levels (10 mg, 20 mg and 30 mg). In addition, the Company has submitted an amendment to the MONARCH protocol to add a multiple ascending dose portion to the study, pending FDA review.

- On August 26, the journal *Science Translation Medicine* published preclinical data from studies of STK-001 that demonstrated significant improvements in survival and reductions in seizure frequency in a mouse model of Dravet syndrome.
- On August 17, the Company appointed Gary E. Menzel, Ph.D., to both its Board of Directors and Compensation Committee. Dr. Menzel brings more than 25 years of executive management experience in the global healthcare sector and currently serves as President and Chief Executive Officer of TCR^2 Therapeutics Inc.
- On July 9, the journal *Nature Communications* published data that support the Company's proprietary TANGO approach to addressing severe genetic diseases by precisely upregulating protein expression.
- The BUTTERFLY observational study is ongoing. Despite experiencing a slowing in new patient enrollment earlier this year due to the impact of COVID-19, new patient enrollment continues, and we believe we have achieved sufficient participation in the study to provide informative data about the natural progression of Dravet syndrome.

Upcoming Anticipated Milestones

- Preliminary safety and pharmacokinetic data from the MONARCH study are still expected in 2021.
- Several abstracts related to Stoke's work in Dravet syndrome have been accepted for presentation at the American Epilepsy Society (AES) Annual Meeting, December 4-8, 2020.
- The Company expects to complete lead optimization for TANGO ASOs directed at OPA1 in 2021.

Third Quarter and Year-to-Date Results

- Net loss for the three months ended September 30, 2020 was $13.7 million, or $0.41 per share compared to $8.6 million or $0.26 per share for the same period in 2019.
- Research and development expenses for the three months ended September 30, 2020 were $8.1 million, compared to $6.5 million for the same period in 2019.
- General and administrative expenses for the three months ended September 30, 2020 were $5.6 million, compared to $3.3 million for the same period in 2019.
- Net loss for the first nine months of 2020 was $37.7 million or $1.14 per share, compared to net loss of $22.2 million or $1.71 per share for the same period in 2019.
- Research and development expenses for the nine months ended September 30, 2020 were $23.3 million, compared to $16.7 million for the same period in 2019.
- General and administrative expenses for the nine months ended September 30, 2020 were $15.2 million, compared to $7.9 million for the same period in 2019.
- The increase in expenses for the three and nine month periods in 2020 over the same periods in 2019 primarily relate to increases in costs associated with personnel, third party contracts, consulting, facilities and others associated with development activities for STK-001, research on additional therapeutics and growing a public corporation.
- As of September 30, 2020, Stoke had approximately $191.7 million in cash, cash equivalents and restricted cash, which is anticipated to fund operations into 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 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 Clinical Study (MONARCH)

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 will be to assess the safety and tolerability of STK-001, as well as to characterize human pharmacokinetics. A secondary objective will be 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/.

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 severe intellectual disabilities, severe developmental disabilities, motor impairment, speech impairment, autism, behavioral difficulties and sleep abnormalities. Compared with the general epilepsy population, people living with Dravet syndrome have a higher risk of sudden unexpected death in epilepsy, or SUDEP. 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, 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.

About Stoke Therapeutics

Stoke Therapeutics (Nasdaq: STOK) is a biotechnology company pioneering a new way to treat the underlying causes of severe genetic diseases by precisely upregulating protein expression to restore target proteins to near normal levels. Stoke aims to develop the first precision medicine platform to target the underlying cause of a broad spectrum of genetic diseases in which the patient has one healthy copy of a gene and one mutated copy that fails to produce a protein essential to health. These diseases, in which loss of approximately 50% of normal protein expression causes disease, are called autosomal dominant haploinsufficiencies. 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: preclinical data and study results regarding OPA1, 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, our ability to advance OPA1 as our next preclinical target, and 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, 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; 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)

	September 30, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 191,461	$ 222,471
Prepaid expenses and other current assets	3,615	3,281
Deferred financing costs	378	—
Interest receivable	2	281

Total current assets	$ 195,456	$ 226,033
Restricted cash	205	205
Operating lease right-of-use assets	1,381	—
Property and equipment, net	2,893	2,512
Total assets	$ 199,935	$ 228,750
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,095	$ 751
Accrued and other current liabilities	5,640	3,350
Total current liabilities	$ 6,735	$ 4,101
Long term liabilities	665	221
Total liabilities	$ 7,400	$ 4,322
Commitments and contingencies		
Stockholders' equity		
Common stock, par value of $0.0001 per share; 300,000,000 shares authorized, 33,361,188 and 32,861,842 shares issued and outstanding as of September 30, 2020 and December 31, 2019, respectively	3	3
Additional paid-in capital	288,249	282,460
Accumulated deficit	(95,717)	(58,035)
Total stockholders' equity	$ 192,535	$ 224,428
Total liabilities and stockholders' equity	$ 199,935	$ 228,750

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,	
	2020	2019	2020	2019
Revenue	$ —	$ —	$ —	$ —
Operating expenses:				
Research and development	8,109	6,518	23,293	16,675
General and administrative	5,602	3,324	15,165	7,935
Total operating expenses	13,711	9,842	38,458	24,610
Loss from operations	(13,711)	(9,842)	(38,458)	(24,610)
Other income:				
Interest income	11	1,236	734	2,447
Other income (expense), net	16	2	42	(2)
Total other income	27	1,238	776	2,445
Net loss and comprehensive loss	$ (13,684)	$ (8,604)	$ (37,682)	$ (22,165)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.41)	$ (0.26)	$ (1.14)	$ (1.71)
Weighted-average common shares outstanding, basic and diluted	33,273,597	32,707,647	32,954,727	12,991,672

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