Stoke Therapeutics Reports Second Quarter Financial Results and Provides Business Updates

August 8, 2022

– In the fourth quarter, the Company plans to announce interim safety, pharmacokinetic (PK), and cerebrospinal fluid (CSF) drug exposure data from approximately 40 patients in the ongoing clinical studies of STK-001 in children and adolescents with Dravet syndrome –

– Analysis will also include seizure frequency data, including preliminary 3-month results from a subset of patients who received three doses of STK-001 (30mg or 45mg) –

– Company was granted FDA orphan drug designation for STK-002, an investigational new treatment for Autosomal Dominant Optic Atrophy (ADOA) –

– As of June 30, 2022, Company had $276.2 million in cash, cash equivalents, marketable securities, and restricted cash, anticipated to fund operations into 2025 –

BEDFORD, Mass.--(BUSINESS WIRE)--Aug. 8, 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 second quarter of 2022 and provided business updates.

“The Stoke team continues to execute and we look forward to our next readout of data from our ongoing clinical studies of STK-001 in children and adolescents with Dravet syndrome,” said Edward M. Kaye, M.D., Chief Executive Officer of Stoke Therapeutics. “These initial studies of STK-001 are designed primarily to evaluate safety, but we are also looking to these data to guide our understanding of the optimal dose level and administration frequency for this potential new medicine.”

“Dravet syndrome is characterized by frequent, prolonged and intractable seizures,” continued Kaye. “Despite being treated with multiple anti-seizure medicines, most patients continue to experience a high seizure burden. As part of our readout in the fourth quarter, we look forward to seeing the first seizure frequency data from the group of patients in our MONARCH and ADMIRAL studies who were treated with multiple doses of 30mg or 45mg of STK-001 on top of their existing anti-seizure regimen.”

Second Quarter 2022 Business Highlights and Recent Developments

- Today, the Company provided updates from the ongoing clinical studies of STK-001. In the U.S., dosing is ongoing in the 45mg multiple dose cohort of MONARCH. In the U.K., dosing is complete in the 45mg multiple dose cohort, and the first patients have now been dosed in the 70mg multiple dose cohort of ADMIRAL.
- Dosing is ongoing in SWALLOWTAIL, an open-label extension study of STK-001. Patients in this study are now eligible to receive 45mg doses of STK-001.
- In May 2022, the Company began dosing patients in LONGWING, an open-label extension 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.
- In May 2022, the Company presented new preclinical data for STK-002 that 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. A dose-related increase in OPA1 protein was also detected in retinal ganglion cells (RGCs) of NHPs treated with STK-002.
- In July 2022, the U.S. Food and Drug Administration (FDA) granted orphan drug designation to STK-002 for the potential treatment of patients with ADOA.

Upcoming Anticipated Milestones

- In the fourth quarter, the Company plans to report preliminary clinical data from approximately 40 patients in the ongoing MONARCH, ADMIRAL and SWALLOWTAIL studies of STK-001 in children and adolescents with Dravet syndrome. The focus of the interim analysis will be on safety, pharmacokinetic (PK), and cerebrospinal fluid (CSF) drug exposure data from these studies. In addition, the Company plans to report seizure frequency data, including preliminary results from up to 24 patients in the MONARCH and ADMIRAL studies who received three doses of STK-001 (up to 18 patients at 30mg and up to 6 patients at 45mg) and were followed for three months.
- In 2023, the Company expects to share additional data from patients who were treated in the 45mg and the 70mg dose cohorts in the ongoing clinical studies of STK-001.
- In the second half of 2022, the Company expects to begin enrollment in a prospective natural history study (FALCON) of people living with ADOA.

Second Quarter 2022 and Year-to-Date Financial Results

- As of June 30, 2022, Stoke had approximately $276.2 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 June 30, 2022, was $3.2 million. There was no revenue in the same period in 2021.
- Net loss for the three months ended June 30, 2022, was $24.7 million, or $0.63 per share, compared to $22.0 million, or $0.60 per share, for the same period in 2021.
- Research and development expenses for the three months ended June 30, 2022, were $18.4 million, compared to $14.1 million for the same period in 2021.
- General and administrative expenses for the three months ended June 30, 2022, were $10.1 million, compared to $7.9 million for the same period in 2021.
- Revenue recognized for upfront license fees and services provided from a License and Collaboration Agreement for the six months ended June 30, 2022, was $6.2 million. There was no revenue in the same period in 2021.
- Net loss for the six months ended June 30, 2022, was $49.3 million, or $1.29 per share, compared to $38.8 million, or $1.06 per share, for the same period in 2021.
- Research and development expenses for the six months ended June 30, 2022, were $36.7 million, compared to $24.0 million for the same period in 2021.
- General and administrative expenses for the six months ended June 30, 2022, were $19.6 million, compared to $14.8 million for the same period in 2021.
- The increase in expenses for the three and six month periods ending June 30, 2022 over the same periods 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.

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.

About the FALCON Study

FALCON is a multicenter, prospective natural history study of people ages 8 to 60 who have an established clinical diagnosis of ADOA that is caused by a heterozygous *OPA1* gene variant. No investigational medications or other treatments will be provided. The study is expected to enroll approximately 45 patients across 10 sites in the U.S., U.K., Italy and Denmark. Patients will undergo assessments at 6 months, 12 months, 18 months, and 24 months. There will be no additional follow-up period. For more information about enrolling in the study, please email Falconstudy@medpace.com.

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 June 30,		Six months ended June 30,	
	2022	2021	2022	2021
Revenue	$ 3,231	$ —	$ 6,232	$ —
Operating expenses:				
Research and development	18,358	14,095	36,668	24,008
General and administrative	10,111	7,934	19,596	14,848
Total operating expenses	28,469	22,029	56,264	38,856
Loss from operations	(25,238)	(22,029)	(50,032)	(38,856)
Other income:				
Interest income (expense), net	544	34	648	40
Other income (expense), net	42	28	83	56
Total other income	586	62	731	96
Net loss	$ (24,652)	$ (21,967)	$ (49,301)	$ (38,760)
Net loss per share, basic and diluted	$ (0.63)	$ (0.60)	$ (1.29)	$ (1.06)
Weighted-average common shares outstanding, basic and diluted	39,258,358	36,708,188	38,358,936	36,675,876
Comprehensive loss:				
Net loss	$ (24,652)	$ (21,967)	$ (49,301)	$ (38,760)
Other comprehensive loss:				
Unrealized loss on marketable securities	(592)	(42)	(1,108)	(42)
Total other comprehensive loss	$ (592)	$ (42)	$ (1,108)	$ (42)
Comprehensive loss	$ (25,244)	$ (22,009)	$ (50,409)	$ (38,802)

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

	June 30, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 67,754	$ 144,895
Marketable securities	207,876	74,915
Prepaid expenses and other current assets	13,179	9,159
Deferred financing costs	—	117
Interest receivable	350	132
Total current assets	$ 289,159	$ 229,218
Restricted cash	569	569
Operating lease right-of-use assets	5,831	4,939
Property and equipment, net	5,868	4,139
Total assets	$ 301,427	$ 238,865
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 3,602	$ 2,385
Accrued and other current liabilities	13,413	14,754
Deferred revenue - current portion	10,634	—
Total current liabilities	$ 27,649	$ 17,139
Deferred revenue - net of current portion	45,210	—
Other long term liabilities	4,247	3,949
Total long term liabilities	49,457	3,949
Total liabilities	$ 77,106	$ 21,088

Commitments and contingencies		
Stockholders' equity		
Common stock, par value of $0.0001 per share; 300,000,000 shares authorized, 39,382,467 and 36,902,499 shares issued and outstanding as of June 30, 2022 and December 31, 2021, respectively	4	4
Additional paid-in capital	470,977	414,024
Accumulated other comprehensive loss	(1,276)	(168)
Accumulated deficit	(245,384)	(196,083)
Total stockholders' equity	$ 224,321	$ 217,777
Total liabilities and stockholders' equity	$ 301,427	$ 238,865

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