Stoke Therapeutics Reports Third Quarter Financial Results and Provides Business Updates

November 14, 2022

– Company announces positive interim data from the ongoing Phase 1/2a clinical studies of STK-001 in children and adolescents with Dravet syndrome –

– Single and multiple doses of STK-001 up to 45mg were well-tolerated –

– 55% median reduction from baseline in convulsive seizure frequency was observed among patients treated with three doses of 45mg –

– In 2023 the Company plans to report data from more patients treated with multiple doses of 45mg as well as those treated with multiple doses of 70mg –

– As of September 30, 2022, Company had $252.2 million in cash, cash equivalents, marketable securities, and restricted cash, anticipated to fund operations into 2025 –

– Management will host a webinar and conference call for analysts and investors at 8:30 a.m. Eastern Time today –

BEDFORD, Mass.--(BUSINESS WIRE)--Nov. 14, 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 third quarter of 2022 and provided business updates, including positive data from a planned interim analysis of the ongoing Phase 1/2a MONARCH and ADMIRAL clinical studies of STK-001 in children and adolescents with Dravet syndrome. In addition to positive safety, pharmacokinetic (PK) and cerebrospinal fluid (CSF) exposure data, median reductions in seizure frequency were observed among patients who were treated with multiple doses of STK-001 (20mg, 30mg and 45mg). Management will host a webinar and conference call today at 8:30 a.m. Eastern Time.

Dravet syndrome is a severe and progressive genetic epilepsy characterized by frequent, prolonged and refractory seizures beginning within the first year of life. Complications of the disease often contribute to poor quality of life for patients and their caregivers. Despite available anti-seizure medicines, seizures are not adequately controlled for more than 90% of patients. STK-001 is a proprietary antisense oligonucleotide (ASO) being developed by Stoke as the first potential new medicine to address the genetic cause of Dravet syndrome.

“We are encouraged by the data from our ongoing studies of STK-001, which continue to demonstrate favorable safety findings and reductions in seizure frequency among a highly refractory group of patients,” said Barry Ticho, M.D., Ph.D., Chief Medical Officer of Stoke Therapeutics. “Half of the patients in these studies were taking four or more anti-seizure medicines, including fenfluramine, setting a high bar for STK-001 to demonstrate additional benefit. Even so, 74% of patients experienced a reduction in seizure frequency following three doses of STK-001. Most notable is the 55% median reduction observed among the small group of patients treated with three doses of 45mg. Based on these data, we believe we have entered the therapeutic range, which is translating to a clinical benefit for patients. We look forward to additional data in 2023.”

Study Design

MONARCH and ADMIRAL are multi-center, Phase 1/2a studies of children and adolescents who have an established diagnosis of Dravet syndrome. The primary objectives for MONARCH in the United States and ADMIRAL in the United Kingdom 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 of STK-001 as an adjunctive antiepileptic treatment with respect to the percentage change from baseline in convulsive seizure frequency.

Key safety findings from the interim analysis include:

The interim safety analysis reported today was based on data from 55 patients who were treated with single or multiple doses of STK-001 (10mg, 20mg, 30mg, 45mg) and followed for up to six months after their last dose.

- Single and multiple doses of STK-001 up to 45mg were found to be well-tolerated.
- 27% (15/55) of patients experienced a treatment-emergent adverse event (TEAE) that was related to study drug. All adverse events related to study drug were mild to moderate in severity. No TEAEs led to study drug withdrawal.

Key efficacy findings from the interim analysis include:

The interim efficacy analysis was based on data from 27 patients who were treated with multiple doses (20mg, 30mg, 45mg) and followed for three months after their last dose.

- Median reductions from baseline in convulsive seizure frequency of 55% (45mg, n=6), 20% (30mg, n=17), 41% (20mg, n=4) were observed in patients treated with three doses of STK-001 as measured from Day 29 after their first dose to three months after receiving their last dose.
- 74% (20/27) of patients treated with three doses of STK-001 (20mg, 30mg or 45mg) experienced a reduction from baseline in convulsive seizure frequency.
- A preliminary analysis from a small cohort of patients treated in the SWALLOWTAIL open-label extension study showed

reductions in seizure frequency were maintained with ongoing treatment. In addition, there was an early indication of improvements in some non-seizure comorbidities as measured by the BRIEF-P, an assessment of executive function.

Key PK and CSF exposure findings:

- A dose-dependent increase in study drug exposure was observed in plasma. A greater increase was observed between 30mg and 45mg than between 20mg and 30mg. The plasma PK profile was consistent across ADMIRAL and MONARCH patients who were treated at the same dose level.
- CSF exposure was measurable up to six months following single and multiple intrathecal doses of STK-001, indicating sustained exposure of STK-001 in the brain.

The Company expects to provide more detail on data from the ongoing clinical studies at the American Epilepsy Society annual meeting December 2-6, 2022 in Nashville, TN.

Stoke Webinar and Conference Call for Analysts and Investors

Stoke will host a webinar and conference call for analysts and investors at 8:30 a.m. Eastern Time on Monday, November 14, 2022, to present the interim data from the ongoing Phase 1/2a clinical studies of STK-001. To participate in the call, please dial (800) 715-9871, or (646) 307-1963 for international callers and provide conference call ID number 2168761. The webinar will be broadcast live on the Investors & Media section of Stoke's website at https://investor.stoketherapeutics.com/ and can be accessed by following this Link. An archived replay of the webinar will be available for at least 90 days following the event.

Third Quarter 2022 Business Highlights and Recent Developments

- Today, the Company provided topline results from the ongoing Phase 1/2a MONARCH and ADMIRAL studies of STK-001.
- Dosing is ongoing in MONARCH at 45mg and ADMIRAL at 70mg. Dosing is also ongoing in the open-label extension studies, SWALLOWTAIL and LONGWING. Following recent interactions with regulatory agencies, the Company agreed to limit chronic dosing in SWALLOWTAIL to 30mg and in LONGWING to 45mg.
- The 45mg multiple dose cohort of MONARCH was recently expanded to evaluate up to 10 additional patients, per protocol. Pending a safety review, an expansion of the 70mg cohort of ADMIRAL is planned.
- In October 2022, the U.S. Food and Drug Administration (FDA) granted Rare Pediatric Disease Designation to STK-001 for the potential treatment of patients with Dravet syndrome.
- In August 2022, the Company announced enrollment of the first patient in the FALCON natural history study of people ages 8 to 60 who are living with autosomal dominant optic atrophy (ADOA).

Third Quarter 2022 and Year-to-Date Financial Results

- Revenue recognized for upfront license fees and services provided from a License and Collaboration Agreement for the three months ended September 30, 2022, was $2.9 million, and for the nine months ended September 30, 2022 was $9.1 million. There was no revenue in the same periods in 2021.
- As of September 30, 2022, Stoke had approximately $252.2 million in cash, cash equivalents, marketable securities and restricted cash, which is anticipated to fund operations into 2025.
- Net loss for the three months ended September 30, 2022 was $26.1 million, or $0.66 per share, compared to $22.6 million, or $0.61 per share, for the same period in 2021.
- Research and development expenses for the three months ended September 30, 2022 were $20.1 million, compared to $14.4 million for the same period in 2021.
- General and administrative expenses for the three months ended September 30, 2022 were $9.9 million, compared to $8.3 million for the same period in 2021.
- Net loss for the nine months ended September 30, 2022 was $75.4 million, or $1.95 per share, compared to $61.4 million, or $1.67 per share, for the same period in 2021.
- Research and development expenses for the nine months ended September 30, 2022 were $56.8 million, compared to $38.4 million for the same period in 2021.
- General and administrative expenses for the nine months ended September 30, 2022 were $29.5 million, compared to $23.2 million for the same period in 2021.
- The increase in expenses for the three and nine month periods in 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, and rare pediatric disease 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 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 or show improvements in non-seizure comorbidities; 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 and preliminary interim data readouts of ongoing trials may show results that change when such trials are completed; 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 balance sheets
(in thousands, except share and per share amounts)
(unaudited)

	September 30, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 113,396	$ 144,895
Marketable securities	138,259	74,915
Prepaid expenses and other current assets	12,551	9,159
Deferred financing costs	—	117
Interest receivable	395	132
Total current assets	$ 264,601	$ 229,218
Restricted cash	569	569
Operating lease right-of-use assets	5,295	4,939
Property and equipment, net	7,161	4,139
Total assets	$ 277,626	$ 238,865
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,911	$ 2,385
Accrued and other current liabilities	14,046	14,754
Deferred revenue - current portion	12,838	—
Total current liabilities	$ 28,795	$ 17,139
Deferred revenue - net of current portion	41,078	—
Other long term liabilities	3,610	3,949
Total long term liabilities	44,688	3,949

Total liabilities	$ 73,483	$ 21,088
Commitments and contingencies		
Stockholders' equity		
Common stock, par value of $0.0001 per share; 300,000,000 shares authorized, 39,426,440 and 36,902,499 shares issued and outstanding as of September 30, 2022 and December 31, 2021, respectively	4	4
Additional paid-in capital	477,337	414,024
Accumulated other comprehensive loss	(1,703)	(168)
Accumulated deficit	(271,495)	(196,083)
Total stockholders' equity	$ 204,143	$ 217,777
Total liabilities and stockholders' equity	$ 277,626	$ 238,865

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,	
	2022	2021	2022	2021
Revenue	$ 2,905	$ —	$ 9,137	$ —
Operating expenses:				
Research and development	20,109	14,358	56,777	38,366
General and administrative	9,944	8,325	29,540	23,173
Total operating expenses	30,053	22,683	86,317	61,539
Loss from operations	(27,148)	(22,683)	(77,180)	(61,539)
Other income:				
Interest income (expense), net	995	44	1,643	84
Other income (expense), net	42	42	125	98
Total other income	1,037	86	1,768	182
Net loss	$ (26,111)	$ (22,597)	$ (75,412)	$ (61,357)
Net loss per share, basic and diluted	$ (0.66)	$ (0.61)	$ (1.95)	$ (1.67)
Weighted-average common shares outstanding, basic and diluted	39,420,310	36,759,319	38,716,615	36,706,647
Comprehensive loss:				
Net loss	$ (26,111)	$ (22,597)	$ (75,412)	$ (61,357)
Other comprehensive gain (loss):				
Unrealized gain (loss) on marketable securities	(427)	20	(1,535)	(22)
Total other comprehensive loss	$ (427)	$ 20	$ (1,535)	$ (22)
Comprehensive loss	$ (26,538)	$ (22,577)	$ (76,947)	$ (61,379)

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