Stoke Therapeutics Presents Preclinical Data on the Biodistribution, Target Engagement and Safety of STK-001 in Non-Human Primates That Support the Planned Clinical Development of STK-001 for the Treatment of Dravet Syndrome

December 8, 2019

STK-001 showed distribution throughout the brain after a single intrathecal injection; Target engagement and increased Nav1.1 protein expression were observed throughout the cortex

Safety findings showed STK-001 to be well-tolerated at both dose levels studied

IND submission on track for early 2020; Phase 1/2 study anticipated to start in 1H 2020

BEDFORD, Mass.--(BUSINESS WIRE)--Dec. 8, 2019-- Stoke Therapeutics, Inc. (Nasdaq: STOK), a biotechnology company pioneering a new way to treat the underlying cause of severe genetic diseases by precisely upregulating protein expression, today presented new preclinical data on STK-001, a potential new disease-modifying medicine for the treatment of Dravet syndrome. Data from studies in non-human primates (NHP) showed STK-001 distributed throughout the brain and achieved target engagement and increased $Na_v1.1$ protein expression throughout the cortex after a single intrathecal injection. Safety findings showed STK-001 to be well-tolerated at the two intrathecal dose levels studied. These data were presented today in a poster session at the American Epilepsy Society (AES) Annual Meeting in Baltimore.

"The effects of Dravet syndrome go beyond seizures and often include cognitive regression or developmental stagnation, ataxia, speech impairment and sleep disturbances. The disease is believed to affect multiple areas of the brain, with the cerebral cortex playing a particularly important role," said Edward M. Kaye, M.D., Chief Executive Officer of Stoke Therapeutics. "These new data are encouraging because they show the ability of STK-001 to broadly distribute in the brain and to elicit target engagement and increased $Na_v1.1$ throughout the cortex. These results will be included in our planned IND submission and provide additional confidence in our clinical plans for STK-001."

Dravet syndrome is a severe and progressive form of genetic epilepsy that affects approximately 35,000 people in the United States, Canada, Japan, Germany, France and the United Kingdom. Approximately 85% of Dravet syndrome cases are caused by spontaneous, heterozygous mutations in the *SCN1A* gene, resulting in 50% of normal $Na_v1.1$ protein expression.

Stoke selected two dose levels of STK-001 for this non-GLP study in order to evaluate safety, brain biodistribution, target engagement and $Na_v1.1$ protein expression. On day 1, treatment-naïve cynomolgus monkeys were administered a single, bolus intrathecal lumbar (IT-L) injection at one of two dose levels of STK-001. After dosing, the animals underwent standard clinical and neurological observation, and blood samples were collected. STK-001 concentration level, gene expression, and protein expression were assessed in the brain on day 3 and on day 29.

The following are highlights from today's poster presentation.

- Brain tissue exposure to STK-001 was observed on day 3 and day 29. In the high dose group, exposure of STK-001 was observed in all brain regions examined, except pons and thalamus. STK-001 levels in cortical brain regions were generally higher than in deeper structures and were also increased from day 3 to day 29.
- $Na_v1.1$ protein levels were observed to increase up to 3-fold in some regions of the cortex on day 29 in the high dose group. No or marginal changes in $Na_v1.1$ protein levels were observed on day 29 in the low dose group, or on day 3 in either dose group.
- Significant target engagement (*SCN1A* expression) was observed on day 29 throughout the cortex and the limbic lobe in the high dose group. No or marginal change in *SCN1A* levels in brain tissues were observed at the low dose of STK-001, or on day 3 in either dose group.
- A favorable safety profile was demonstrated for STK-001 at both dose levels with no change in neurological or physical measures, even in animals that overexpressed $Na_v1.1$ protein above wild type levels.

Stoke plans to submit an investigational new drug (IND) application to the U.S. Food and Drug Administration in early 2020 and, subject to acceptance of the IND, plans to initiate a Phase 1/2 single-ascending dose study in children and adolescents with Dravet syndrome in the first half of 2020.

Details of today's presentation are as follows:

Presentation Title: TANGO Oligonucleotides for the Treatment of Dravet Syndrome: Safety, Biodistribution and Pharmacology in the Non-Human Primate
Session Date & Time: Sunday, December 8, 2019, 10:00 a.m. – 4:00 p.m. ET
Session Title: Poster Session 2
Presenter: Anne Christiansen, Ph.D., Associate Director, Neuroscience, Stoke Therapeutics
Poster Number: 2.195
Location: The Baltimore Convention Center, Hall E

Data from preclinical studies of STK-001 in a Dravet syndrome mouse model were presented at AES on Saturday, December 7, 2019. (Poster Number 1.116)

The posters presented at AES are now available online on the Events and Presentations section of Stoke's website at https://investor.stoketherapeutics.com/.

About STK-001

STK-001 is an investigational new medicine for the treatment of Dravet syndrome. 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 U.S. Food and Drug Administration as a potential new treatment for Dravet syndrome. Stoke plans to submit an investigational new drug (IND) application to the U.S. Food and Drug Administration in early 2020.

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 cognitive regression or developmental stagnation, ataxia, speech impairment and sleep disturbances. 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 Stoke Therapeutics

Stoke Therapeutics, Inc. (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. The company's lead investigational new medicine is STK-001, a proprietary antisense oligonucleotide (ASO) that has the potential to be the first disease-modifying therapy to address the genetic cause of Dravet syndrome, a severe and progressive genetic epilepsy. 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.

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 ability of STK-001 to improve survival and reduce seizure frequency in mice, as well as its biodistribution, target engagement and ability to increase protein expression in non-human primates; 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. Statements including words such as "plan," "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 our 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 develop, obtain regulatory approval for and commercialize STK-001 and its future product candidates, the timing and results of preclinical studies and clinical trials, the company's ability to protect intellectual property; and other risks set forth in our filings with the Securities and Exchange Commission, including the risks set forth in our quarterly report on Form 10-Q for the three months ended September 30, 2019. These forward-looking statements speak only as of the date hereof and we specifically disclaim any obligation to update these forward-looking statements or reasons why actual results might differ, whether as a result of new information, future events or otherwise, except as required by law.

View source version on businesswire.com: https://www.businesswire.com/news/home/20191208005025/en/

Source: Stoke Therapeutics, Inc.

Stoke Media & Investor Contact:
Dawn Kalmar
Vice President, Head of Corporate Affairs
dkalmar@stoketherapeutics.com
781-303-8302