Stoke Therapeutics Receives FDA Breakthrough Therapy Designation for Zorevunersen for the Treatment of Dravet Syndrome

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– Supported by evidence from clinical studies that indicate that zorevunersen may demonstrate substantial improvement over available therapies –

– Update on the company's plans for a global, randomized, controlled Phase 3 registrational study anticipated by year-end –

BEDFORD, Mass.--(BUSINESS WIRE)--Dec. 4, 2024-- Stoke Therapeutics, Inc. (Nasdaq: STOK), a biotechnology company dedicated to restoring protein expression by harnessing the body's potential with RNA medicine, today announced that it has received Breakthrough Therapy Designation from the U.S. Food and Drug Administration (FDA) for zorevunersen for the treatment of Dravet syndrome with a confirmed mutation, not associated with gain-of-function, in the *SCN1A* gene. Zorevunersen is being developed as potentially the first disease-modifying medicine for the treatment of Dravet syndrome.

Clinical data from the Phase 1/2a and open-label extension (OLE) studies of zorevunersen demonstrated substantial and sustained reductions in seizure frequency and continuous improvements in multiple measures of cognition and behavior. These effects were observed on top of the best available anti-seizure medicines, the current standard of care. Zorevunersen was generally well tolerated across the studies. To date, more than 600 doses of zorevunersen have been administered to patients, some of whom have been on treatment for more than three years.

Discussions with the FDA and other global regulatory agencies regarding a global, randomized, controlled Phase 3 registrational study of zorevunersen continue to progress. The Company plans to provide an update on its Phase 3 registrational plans by the end of the year.

"The FDA's Breakthrough Therapy designation for zorevunersen is supported by promising clinical data that suggest that zorevunersen has the potential to demonstrate substantial improvement over current treatments for Dravet syndrome," said Shamim Ruff, Chief Regulatory Affairs Officer, Stoke Therapeutics. "By helping the body restore naturally occurring NaV1.1 protein levels, zorevunersen is designed to treat the underlying cause of the disease. We thank the FDA for their support and look forward to continuing to work together closely to efficiently advance zorevunersen into a registrational Phase 3 study."

"This designation brings new hope to the many patients with Dravet syndrome who continue to experience treatment-resistant seizures and a myriad of health and quality of life complications despite the availability of symptomatic treatments," said Mary Anne Meskis, Executive Director, Dravet Syndrome Foundation. "Our organization has been engaging with the FDA to ensure greater awareness and understanding of Dravet syndrome. We are encouraged by the Agency's shared sense of urgency for the development of innovative new medicines that could help address the gaps left by current treatments by treating the underlying cause of the disease."

Breakthrough Therapy designation is a process designed to expedite the development and review of drugs that are intended to treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically-significant endpoint(s). This designation grants zorevunersen access to all Fast Track designation features, intensive guidance on an efficient drug development program and an organizational commitment involving senior FDA managers.

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 Zorevunersen (STK-001)

Zorevunersen is an investigational new medicine for the treatment of Dravet syndrome currently being evaluated in ongoing clinical trials. Stoke believes that zorevunersen, a proprietary antisense oligonucleotide (ASO), has the potential to be the first disease-modifying therapy to address the genetic cause of Dravet syndrome. Zorevunersen is designed to upregulate NaV1.1 protein expression by leveraging the non-mutant (wild-type) copy of the *SCN1A* gene to restore physiological NaV1.1 levels, thereby reducing both occurrence of seizures and significant non-seizure comorbidities. Zorevunersen 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 Stoke Therapeutics

Stoke Therapeutics (Nasdaq: STOK), is a biotechnology company dedicated to restoring protein expression by harnessing the body's potential with RNA medicine. 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, zorevunersen, 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/.

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 ability of zorevunersen to treat the underlying causes of Dravet syndrome and reduce seizures or show improvements in behavior and cognition at the indicated dosing levels or at all; and the timing and expected progress of clinical trials, data readouts, regulatory meetings, regulatory decisions and other presentations. Statements including words such as "expect," "plan," "will," "continue," 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, obtain regulatory approval of, and ultimately commercialize its product candidates, including zorevunersen; fast track or breakthrough designations by the FDA may not lead to faster development or regulatory review or approval process and do not increase the likelihood that zorevunersen will receive marketing approval; the timing of data readouts and interim and final results of preclinical and clinical trials; the receipt and timing of potential regulatory decisions; 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, including expectations regarding its collaboration with Acadia Pharmaceuticals; the Company's ability to protect its intellectual property; the direct or indirect impact of global business, political and macroeconomic conditions, including inflation, interest rate volatility, cybersecurity events, uncertainty with respect to the federal budget, instability in the global banking system and volatile market conditions, and global events, including public health crises, and ongoing geopolitical conflicts, such as the conflicts in Ukraine and the Middle East; 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, 2023, its quarterly reports on Form 10-Q, and the other documents it 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.

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