Biogen and Stoke Therapeutics Announce Publication of Two-Year Natural History Data Demonstrating the Severity of Dravet Syndrome, Including Frequent Seizures and Significant Cognitive and Behavioral Impairments

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– Despite treatment with standard-of-care anti-seizure medicines, children with Dravet syndrome experienced high seizure burden and plateaued in neurodevelopment, resulting in a widening gap relative to children with typical development –

– Findings underscore the urgent need for new medicines that target the underlying genetic cause of Dravet syndrome to improve long-term outcomes –

CAMBRIDGE, Mass. and BEDFORD, Mass., Nov. 17, 2025 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) and Stoke Therapeutics, Inc. (Nasdaq: STOK), a biotechnology company dedicated to restoring protein expression by harnessing the body's potential with RNA medicine, today announced the publication of final data from the BUTTERFLY study, a prospective, two-year natural history study in people with Dravet syndrome. Dravet syndrome is a severe developmental and epileptic encephalopathy (DEE) characterized by recurrent seizures and significant cognitive and behavioral impairments. There are currently no approved disease-modifying medicines to treat Dravet syndrome.

The BUTTERFLY study evaluated the impact of Dravet syndrome on adaptive functioning and neurodevelopment over two years in children and adolescents ages 2 to 18 years old. Major motor seizure frequency was evaluated as a secondary outcome measure. In the study, patients were treated with standard-of-care, including anti-seizure medicines (ASMs). Highlights from the research, published November 14, 2025, in *Neurology*®, [1] the medical journal of the American Academy of Neurology, include:

- Regardless of the age at which patients with Dravet syndrome entered the study, neurodevelopment plateaued at the developmental age of approximately two years old. This created a gap that widened over time versus what would be expected for children with typical development.
- Results showed that over the course of the two-year study, patients experienced minimal changes in cognition and behavior, including communication, motor skills and personal skills, compared to typical neurodevelopment expected for children of the same age.
    - Assessments of cognition and behavior used in BUTTERFLY were pre-determined endpoints that were incorporated into this natural history study to support use in future clinical studies of Dravet syndrome. They included the Vineland Adaptive Behavior Scale, Third Edition (Vineland-3); Bayley Scales of Infant Development, Third Edition (BSID-III); and Wechsler Preschool and Primary Scale of Intelligence, Fourth Edition (WPPSI-IV). These assessments, as well as other outcome measures used in BUTTERFLY, are consistent with the primary and secondary endpoints of the pivotal, global Phase 3 EMPEROR study evaluating zorevunersen as a potential disease-modifying medicine for the treatment of Dravet syndrome.
- Major motor seizure frequency increased by 10.6 percent over two years (average of 14.3 seizures/28 days at baseline; p=0.63; n=23).

"These natural history data confirm that the life-altering effects of Dravet syndrome extend well beyond seizures, resulting in significant deficits in patients' functioning and development despite treatment with the best available medicines," said Joseph Sullivan, M.D., FAES, lead author of the *Neurology* publication and Professor of Neurology and Pediatrics at the University of California San Francisco. "The findings make clear that as children with Dravet syndrome grow up, they experience a widening gap in their cognitive and behavioral development compared to a neurotypical child of the same age. By giving us a baseline characterization of what current treatments can do for patients, these data become increasingly important in helping us understand how potential disease-modifying medicines might change the trajectory of Dravet syndrome. I'd like to extend my deep appreciation to the families who participated in BUTTERFLY and made significant sacrifices to help us more fully comprehend the debilitating effects of this disease."

About Dravet Syndrome
Dravet syndrome is a severe developmental and epileptic encephalopathy (DEE) characterized by recurrent seizures as well as significant cognitive and behavioral impairments. Most cases of Dravet are caused by mutations in one copy of the *SCN1A* gene, leading to insufficient levels of NaV1.1 protein in neuronal cells in the brain. More than 90 percent of patients continue to experience seizures despite treatment with the best available anti-seizure medicines. Complications of the disease often contribute to a poor quality of life for patients and their caregivers. Developmental and cognitive impairments 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. Compared with the general epilepsy population, people living with Dravet syndrome have a higher risk of sudden unexpected death in epilepsy, or SUDEP; up to 20 percent of children and adolescents with Dravet syndrome die before adulthood due to SUDEP, prolonged seizures, seizure-related accidents or infections.[2] Dravet syndrome occurs globally and is not concentrated in a particular geographic area or ethnic group. Currently, it is estimated that up to 38,000 people are living with Dravet syndrome in the U.S. (~16,000), UK, EU-4 and Japan.[3] There are no approved disease-modifying therapies for people living with Dravet syndrome.

About the BUTTERFLY Study
The BUTTERFLY study was a multicenter, longitudinal, prospective, observational study of children and adolescents ages 2 to 18 who have been diagnosed with Dravet syndrome as a result of an *SCN1A* gene mutation. The study was designed to evaluate neurodevelopmental status and change from baseline to 24 months. Secondary and exploratory endpoints in the study evaluated changes in other disease measures, including seizures and additional measures of cognition, behavior and overall functioning. No investigational medications or other treatments were provided. Participants

continued to receive optimized standard of care, including anti-seizure medications, and were observed for up to two years. The study was conducted at approximately 20 sites in the U.S.

About Biogen
Founded in 1978, Biogen is a leading biotechnology company that pioneers innovative science to deliver new medicines to transform patients' lives and to create value for shareholders and our communities. We apply deep understanding of human biology and leverage different modalities to advance first-in-class treatments or therapies that deliver superior outcomes. Our approach is to take bold risks, balanced with return on investment to deliver long-term growth.

We routinely post information that may be important to investors on our website at www.biogen.com. Follow us on social media - Facebook, LinkedIn, X, YouTube.

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 naturally-occurring protein levels. Stoke's first medicine in development, zorevunersen, has demonstrated the potential for disease modification in patients with Dravet syndrome and is currently being evaluated in a Phase 3 study. Stoke's initial focus are diseases of the central nervous system and the eye that are caused by a loss of ~50% of normal protein levels (haploinsufficiency). Proof of concept has been demonstrated in other organs, tissues, and systems, supporting broad potential for Stoke's proprietary approach. Stoke is headquartered in Bedford, Massachusetts. For more information, visit https://www.stoketherapeutics.com/.

Biogen Cautionary Note Regarding Forward-Looking Statements
This news release contains forward-looking statements, including 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 design, timing and results of the Phase 3 EMPEROR study. These forward-looking statements may be accompanied by such words as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "estimate," "expect," "forecast," "goal," "guidance," "hope," "intend," "may," "objective," "outlook," "plan," "possible," "potential," "predict," "project," "prospect," "should," "target," "will," "would" or the negative of these words or other words and terms of similar meaning. Drug development and commercialization involve a high degree of risk, and only a small number of research and development programs result in commercialization of a product. Results in early-stage clinical trials may not be indicative of full results or results from later stage or larger scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on these statements. Given their forward-looking nature, these statements involve substantial risks and uncertainties that may be based on inaccurate assumptions and could cause actual results to differ materially from those reflected in such statements.

These forward-looking statements are based on Biogen management's current beliefs and assumptions and on information currently available to Biogen management. Given their nature, Biogen cannot assure that any outcome expressed in these forward-looking statements will be realized in whole or in part. Biogen cautions that these statements are subject to risks and uncertainties, many of which are outside of Biogen's control and could cause future events or results to differ materially from those stated or implied in this document, including, among others, uncertainty of Biogen's long-term success in developing, licensing, or acquiring other product candidates or additional indications for existing products; expectations, plans, prospects and timing of actions relating to product approvals, approvals of additional indications for Biogen's existing products, sales, pricing, growth, reimbursement and launch of Biogen's marketed and pipeline products; the potential impact of increased product competition in the biopharmaceutical and healthcare industry, as well as any other markets in which Biogen competes, including increased competition from new originator therapies, generics, prodrugs and biosimilars of existing products and products approved under abbreviated regulatory pathways; Biogen's ability to effectively implement Biogen's corporate strategy; difficulties in obtaining and maintaining adequate coverage, pricing, and reimbursement for Biogen's products; the drivers for growing Biogen's business, including Biogen's dependence on collaborators and other third parties for the development, regulatory approval, and commercialization of products and other aspects of Biogen's business, which are outside of Biogen's full control; risks related to commercialization of biosimilars, which is subject to such risks related to Biogen's reliance on third-parties, intellectual property, competitive and market challenges and regulatory compliance; the risk that positive results in a clinical trial may not be replicated in subsequent or confirmatory trials or success in early stage clinical trials may not be predictive of results in later stage or large scale clinical trials or trials in other potential indications; risks associated with clinical trials, including Biogen's 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 Biogen's drug candidates; and the occurrence of adverse safety events, restrictions on use with Biogen's products, or product liability claims; and any other risks and uncertainties that are described in other reports Biogen has filed with the U.S. Securities and Exchange Commission, which are available on the SEC's website at www.sec.gov.

These statements speak only as of the date of this press release and are based on information and estimates available to us at this time. Should known or unknown risks or uncertainties materialize or should underlying assumptions prove inaccurate, actual results could vary materially from past results and those anticipated, estimated or projected. Investors are cautioned not to put undue reliance on forward-looking statements. A further list and description of risks, uncertainties and other matters can be found in Biogen's Annual Report on Form 10-K for the fiscal year ended December 31, 2024 and in Biogen's subsequent reports on Form 10-Q. Except as required by law, Biogen does not undertake any obligation to publicly update any forward-looking statements whether as a result of any new information, future events, changed circumstances or otherwise.

Digital Media Disclosure
From time to time, Biogen has used, or expect in the future to use, Biogen's investor relations website (investors.biogen.com), the Biogen LinkedIn account (linkedin.com/company/biogen-) and the Biogen X account (https://x.com/biogen) as a means of disclosing information to the public in a broad, non-exclusionary manner, including for purposes of the SEC's Regulation Fair Disclosure (Reg FD). Accordingly, investors should monitor Biogen's investor relations website and these social media channels in addition to Biogen's press releases, SEC filings, public conference calls and websites, as the information posted on them could be material to investors.

Stoke Therapeutics 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 design, timing and results of the Phase 3 EMPEROR study. Statements including words such as "anticipate," "could," "expect," "plan," "will," or "may" 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 Stoke's results to differ materially from those expressed or implied by such forward-looking statements, including, but not limited to, risks and uncertainties related to: Stoke's ability to advance, obtain regulatory approval and ultimately commercialize its product candidates; that if Stoke's collaborators were to breach or terminate their agreements, it would not obtain the anticipated financial or other benefits; the possibility that Stoke and Biogen may not be successful in their development of zorevunersen and that, even if successful, they may be unable to successfully commercialize zorevunersen; 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; Stoke's ability to protect its intellectual property; Stoke's ability to fund development activities and achieve development goals to mid-2028; and the other risks and uncertainties described under the heading "Risk Factors" in Stoke's Annual Report on

Form 10-K for the year ended December 31, 2024, its quarterly reports on Form 10-Q, and the other documents it files with the Securities and Exchange Commission. These forward-looking statements speak only as of the date of this press release, and Stoke undertakes no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date hereof.

References:

[1] Sullivan J, Wirrell E, Knupp K. et al. Natural history of children and adolescents with Dravet syndrome: a 24-month follow-up. Neurology. 2025;105:e214388

[2] Symonds, J. et al. Early childhood epilepsies: epidemiology, classification, aetiology, and socio-economic determinants. *Brain*. 2021;144(9):2879-2891.

[3] Based on Stoke Therapeutics' preliminary estimates, which scaled annual incidence to prevalence using country-specific live birth rates over the past 85 years and adjusted for Dravet-specific mortality. The estimate is based on incidence rates published by Wu et al., Pediatrics, 2015.

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