Stoke Therapeutics Presents Data Showing Single Dose of ASO Therapy Restores Normal Protein Levels in Animal Model of Genetic Epilepsy

Stoke's antisense oligonucleotide reduces seizures and increases survival in mouse models of Dravet Syndrome

BEDFORD, Mass., December 1, 2018 – Stoke Therapeutics and research collaborators from the University of Michigan today present data demonstrating the efficacy of Stoke's proprietary antisense oligonucleotide (ASO) technology in treating Dravet Syndrome in mouse models. The data are being presented at the American Epilepsy Society 2018 conference in New Orleans.

Stoke's Targeted Augmentation of Nuclear Output (TANGO) technology is used to increase the expression of a target gene. In the case of Dravet Syndrome, up to 85 percent of patients have variant mutations of *Scn1a* that result in insufficient production of the $Na_v1.1$ protein. Stoke's ASO therapy is designed to raise the protein to normal levels.

Stoke's lead therapeutic:

- Successfully increased *Scn1a* mRNA expression and $Na_v1.1$ protein levels in a mouse model of Dravet Syndrome;
- Selectively upregulated *Scn1a* but did not affect other sodium channel genes;
- Through a single dose, restored $Na_v1.1$ expression to normal levels, reduced generalized seizures and increased survival by preventing Sudden Unexplained Death in Epilepsy (SUDEP);
- Resulted in effects that persisted at least up to 14 weeks.

"These data are particularly exciting because this approach could lead to the first disease-modifying treatment for patients with Dravet Syndrome. Stoke is also working on applying this technology to develop precision medicines for other genetic epilepsies," said Edward M. Kaye, M.D., Stoke's chief executive officer. "Dr. Lori Isom and her team at the University of Michigan have brought outstanding expertise on inherited epilepsies and the mutations that cause them, and we are delighted to achieve this early milestone for Dravet patients together."

"These results in the Dravet mouse model using Stoke's ASO technology have been quite remarkable," said Lori Isom, Ph.D., Maurice H. Seevers professor and chair of pharmacology at the University of Michigan Medical School. "We're hopeful we'll see the same results in the clinic."

"We're entering a new era for precision medicines in genetic epilepsies. These data are exciting for Dravet patients, their families and physicians," said Amy Brooks-Kayal, M.D., chief and Ponzio Family Chair in pediatric neurology at Children's Hospital Colorado, professor of pediatrics, neurology and pharmaceutical sciences, and co-director of the translational epilepsy research program at University of Colorado, and a past president of the American Epilepsy Society.

Stoke's lead program to target Dravet Syndrome applies their TANGO technology to leverage non-productive *Scn1a* mRNA splicing events to increase protein levels. Stoke is rapidly advancing this

program to the clinical stage, with plans to reach the clinic by 2020. TANGO can also be applied to other therapeutic areas, including disorders of the central nervous system, eye, liver and kidney.

Dr. Isom will host a podium presentation at AES 2018 on Monday, Dec. 3, at 3:30 p.m. CT.

About Stoke Therapeutics
Launched in 2018, Stoke Therapeutics is a biotechnology company working to increase gene expression to treat a wide array of severe genetic diseases, including genetic conditions affecting the central nervous system, eye, liver and kidney. Stoke has raised $130 million in funding from two rounds of financing; investors include RTW Investments, RA Capital Management, Cormorant Asset Management, Perceptive Advisors, funds managed by Janus Henderson Investors, Redmile Group, Sphera Funds Management, and Alexandria Venture Investments, as well as founding investor Apple Tree Partners. For more information, visit www.StokeTherapeutics.com and follow Stoke on Twitter @StokeTx.

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