



Sionna Therapeutics Announces Initiation of Two Phase 1 Clinical Trials of SION-719 and SION-451, in Development for Cystic Fibrosis

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– SION-719 and SION-451 are candidates from Sionna’s next generation series of highly potent NBD1 stabilizers –

Boston, MA, August 13, 2024 — Sionna Therapeutics, a clinical-stage life sciences company dedicated to developing highly effective and differentiated treatments for cystic fibrosis (CF), today announced that the first subjects have been dosed in two separate Phase 1 clinical trials evaluating the safety, tolerability, and pharmacokinetics of SION-719 and SION-451 in healthy volunteers. SION-719 and SION-451 are product candidates from the company’s next generation series of highly potent nucleotide-binding domain 1 (NBD1) stabilizers. The trials are being conducted in Australia under the Clinical Trial Notification (CTN) process.

“We are pleased with the Company’s strong execution and the progress these first-in-class programs have made in entering the clinic,” said Mike Cloonan, President and Chief Executive Officer of Sionna. “We have a novel ability to target NBD1, which we believe could be the key to raising the efficacy bar and unlocking improved clinical benefits for CF patients. We expect that the data from these single and multiple ascending dose trials will inform our decision about a lead NBD1 stabilizer to bring forward into the next stages of clinical development.”

CF is caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, which codes for an epithelial ion channel that is essential for producing healthy, freely flowing mucus in the airways, digestive system, and other organs. The most common mutation in CFTR, F508del, causes NBD1 to unfold at body temperature and severely impairs CFTR function.

Sionna has presented preclinical data, including data from the clinically predictive human bronchial epithelial cell (CFHBE) model, that show its NBD1 stabilizers, SION-719 and SION-451, when combined with complementary modulators, significantly improve *in vitro* CFTR protein activity and demonstrate the potential to achieve superior clinical outcomes. Sionna is developing the first-ever clinical-stage NBD1 stabilizers, and is also developing complementary modulators with the goal of advancing differentiated combination therapies for CF.

About Sionna Therapeutics

Sionna Therapeutics is a clinical-stage life sciences company dedicated to developing highly effective and differentiated treatments for cystic fibrosis (CF) by normalizing the function of CFTR, the key protein associated with disease progression in CF. Building on over a decade of extensive research on the genetic mutations associated with CF and founded in 2019, Sionna is advancing a pipeline of small molecules engineered to correct the protein defects caused by F508del, the most common CF genetic mutation, which resides in the nucleotide-binding domain 1 (NBD1) of CFTR. The company has a portfolio of first-in-class programs designed to directly stabilize NBD1, which the company believes is the key mechanism to potentially achieving clinically meaningful and superior results. Sionna is also developing a portfolio of complementary CFTR modulators targeting ICL4 and TMD1 that are designed to work synergistically with its NBD1 stabilizers to improve CFTR function. For information about Sionna visit <https://www.sionnatx.com/>.

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