Sionna Therapeutics Announces First Subjects Dosed in Phase 1 Trial Evaluating NBD1 Stabilizer, SION-451, in Proprietary Dual Combinations in Development for the Treatment of Cystic Fibrosis

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Dosing initiated for SION-451 combined with SION-2222 and SION-451 combined with SION-109 in healthy volunteers; topline data anticipated in mid-2026

WALTHAM, Mass., Aug. 25, 2025 (GLOBE NEWSWIRE) -- Sionna Therapeutics, Inc. (Nasdaq: SION), a clinical-stage biopharmaceutical company on a mission to revolutionize the current treatment paradigm for cystic fibrosis (CF) by developing novel medicines that normalize the function of the cystic fibrosis transmembrane conductance regulator (CFTR) protein, today announced that the first subjects have been dosed in a Phase 1 trial evaluating SION-451, a first-in-class nucleotide binding domain 1 (NBD1) stabilizer, in proprietary dual combinations with SION-2222 (galicaftor), a transmembrane domain 1 (TMD1)-directed CFTR corrector, and with SION-109, an intracellular loop 4 (ICL4)-directed CFTR corrector.

This Phase 1 trial is a randomized, double-blind, placebo-controlled trial in healthy volunteers. It is designed to assess the safety, tolerability, and pharmacokinetics (PK) of varying doses of dual combinations of SION-451 with SION-2222 and SION-451 with SION-109. Topline data are anticipated in mid-2026, and will inform selection of a dual combination for a planned Phase 2b trial in people living with CF.

“I’ve spent many years as a pulmonary and critical care specialist caring for CF patients in the clinic, and I’ve been in a unique position to experience the evolution of treatment firsthand,” said Charlotte McKee, M.D., Chief Medical Officer of Sionna. “At Sionna, our research and understanding of the CFTR protein and the underlying causes of CF have led us to this exciting point, where we are taking the first ever NBD1-anchored dual combinations forward in clinical trials with the goal of revolutionizing the treatment paradigm for CF patients.”

CF is a progressive and life-threatening genetic disease that affects more than 100,000 people globally. While advances in the discovery and development of modulators have significantly improved the lives of people living with CF, at least two-thirds of patients on the current standard of care do not have normal CFTR function as measured by levels of sweat chloride. The NBD1 domain of the CFTR protein plays a critical role in the folding, stability and trafficking of CFTR to a cell’s surface, but no approved CF therapies directly stabilize NBD1.

Positive data from Phase 1 clinical trials and preclinical data support the mechanistic rationale and advancement of this dual combination trial. In its recent Phase 1 trial, SION-451 was generally well tolerated and exceeded PK concentration targets that Sionna believes, based on its preclinical CF human bronchial epithelial (CFHBE) model, indicate the potential to provide clinically meaningful benefit, including the potential for wild-type levels of CFTR function, in proprietary dual combinations with complementary modulators.

About Sionna Therapeutics
Sionna Therapeutics is a clinical-stage biopharmaceutical company on a mission to revolutionize the current treatment paradigm for cystic fibrosis (CF) by developing novel medicines that normalize the function of the cystic fibrosis transmembrane conductance regulator (CFTR) protein. Sionna’s goal is to deliver differentiated medicines for people living with CF that can restore their CFTR function to as close to normal as possible by directly stabilizing CFTR’s nucleotide binding domain 1 (NBD1), which Sionna believes is central to potentially unlocking dramatic improvements in clinical outcomes and quality of life for people with CF. Leveraging more than a decade of the co-founders’ research on NBD1, Sionna is advancing a pipeline of small molecules engineered to correct the defects caused by the F508del genetic mutation, which resides in NBD1. Sionna is also developing a portfolio of complementary CFTR modulators that are designed to work synergistically with its NBD1 stabilizers to improve CFTR function. For information about Sionna, visit www.sionnatx.com.

Sionna intends to use its Investor Relations website as a means of disclosing material nonpublic information and for complying with its disclosure obligations under Regulation FD. Accordingly, investors should monitor Sionna’s Investor Relations website, in addition to following Sionna’s press releases, SEC filings, public conference calls, presentations, and webcasts.

Cautionary Note Regarding Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, implied and express statements about Sionna’s beliefs and expectations regarding: its goal of transforming the treatment paradigm for CF, the initiation, timing, progress and results of Sionna’s research and development programs, preclinical studies and clinical trials, including the timing of topline data from the Phase 1 dual combination trial and a potential Phase 2b trial; the ability of clinical trials to demonstrate safety and efficacy of Sionna’s product candidates, including the potential of a dual combination product candidate to provide clinically meaningful benefit, including wild-type levels of CFTR function; the ability of Sionna’s earlier clinical trials or preclinical studies to predict later clinical trial results; and other

statements that are not historical facts. In some cases, the forward-looking statements can be identified by terms such as “may,” “will,” “should,” “would,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “believe,” “estimate,” “predict,” “potential” or “continue” or the negative of these terms or other similar expressions. Any forward-looking statements in this press release are based on management’s current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by the forward-looking statements contained in this press release. Factors that could cause actual results to differ include, but are not limited to, risks and uncertainties inherent in the development of product candidates, including uncertainties concerning the initiation, timing, progress, and results of Sionna’s planned and future clinical trials and studies; the company’s ability to replicate positive results from earlier preclinical studies or clinical trials in current or future clinical trials; Sionna’s ability to demonstrate that its NBD1 stabilizers, complementary CFTR modulators, and any potential future product candidates are safe and effective for their proposed indications; regulatory developments in the United States and foreign countries; and general economic, industry and market conditions. These risks and uncertainties are described in the section entitled “Risk Factors” in Sionna’s most recent Quarterly Report on Form 10-Q as well as any subsequent filings with the Securities and Exchange Commission. The events and circumstances reflected in the forward-looking statements may not be achieved or occur. In addition, any forward-looking statements represent Sionna’s views only as of today and should not be relied upon as representing its views as of any subsequent date. Sionna explicitly disclaims any obligation to update any forward-looking statements except as required by law. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

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