Sionna Therapeutics Announces Initiation of PreciSION CF Phase 2a Trial Evaluating NBD1 Stabilizer, SION-719, When Added to Standard of Care in Participants with Cystic Fibrosis

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SION-719 is the first NBD1 stabilizer being evaluated in people living with cystic fibrosis

Topline data expected in mid-2026

WALTHAM, Mass., Oct. 21, 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 initiation of the PreciSION CF Phase 2a proof-of-concept (POC) trial evaluating SION-719, a first-in-class nucleotide binding domain 1 (NBD1) stabilizer, when added to Trikafta® (elexacaftor/tezacaftor/ivacaftor), the current standard of care (SOC) in CF.

"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 none of the currently approved CF therapies directly stabilize NBD1. We are thrilled to initiate the first clinical trial to evaluate an NBD1 stabilizer in people living with CF," said Charlotte McKee, M.D., Chief Medical Officer of Sionna. "We are confident in the potential of NBD1 and believe that adding SION-719 to the standard of care could demonstrate clinically meaningful improvement in CFTR function. If the trial is successful, we believe it would represent an important step in validating the NBD1 mechanism and would provide evidence that NBD1 stabilization is mechanistically unique from, and synergistic with, the components of standard of care."

The PreciSION CF Phase 2a trial is a randomized, double-blind, placebo-controlled, crossover POC study that is enrolling adult CF patients homozygous for F508del on a stable dose of physician-prescribed Trikafta. The objectives of the trial are to evaluate the safety, tolerability, and pharmacokinetics (PK) of SION-719 when administered with SOC and to assess change in CFTR function as measured by sweat chloride levels, an important measure of CFTR function. The PreciSION CF trial is being conducted at multiple sites, including sites in the CF Foundation-supported Therapeutics Development Network (TDN), the largest CF clinical trials network in the world. Topline data are anticipated in mid-2026.

In its recent Phase 1 trial in healthy volunteers, SION-719 was generally well tolerated and exceeded PK concentration targets that, based on Sionna's preclinical cystic fibrosis human bronchial epithelial (CFHBE) assay, indicate that SION-719 when added to SOC has the potential to provide clinically meaningful improvement over the SOC, including the potential to restore CFTR function up to wild-type levels. Sionna also recently completed a successful drug-drug interaction study with midazolam, a sensitive CYP3A4 substrate, that confirmed SION-719 can be dosed in combination with Trikafta according to its label.

For more information about the PreciSION CF Phase 2a trial, visit ClinicalTrials.gov.

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 timing, progress, objectives and results of the development of its clinical and preclinical pipeline, including the therapeutic potential, clinical benefits and safety thereof; the timing of topline data from the Phase 2a trial; the ability of clinical trials to demonstrate safety and efficacy of Sionna's product candidates, including the potential of SION-719 when added to SOC to provide clinically meaningful benefit, including restoration of CFTR function up to wild-type

levels; the ability of Sionna's earlier clinical trials or preclinical studies to predict later clinical trial results; the ability of the Phase 2a clinical trial to validate the NBD1 mechanism and provide evidence of its synergy with the components of SOC; 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, including, without limitation, risks associated with: uncertainties inherent in the development of product candidates, including concerning the initiation, timing, design, progress, and results of current and future clinical trials; the company's ability to replicate positive results from earlier preclinical studies or clinical trials in current or future clinical trials; the company's ability to demonstrate that its product candidates are safe and effective for their proposed indications; the timing and outcome of interactions with regulatory authorities, and any regulatory developments in the United States and foreign countries; the availability of funding sufficient for the company's operating expenses and capital expenditure requirements; 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.

Media Contact
Adam Daley
CG Life
212.253.8881
adaley@cglife.com

Investor Contact
Juliet Labadorf
ir@sionnatx.com