Sionna Therapeutics Announces Positive Phase 1 Data for NBD1 Stabilizers SION-719 and SION-451 and Advances Both Programs in Clinical Development for Cystic Fibrosis

June 4, 2025

SION-719 and SION-451 were generally well tolerated and achieved desired pharmacokinetic targets that reinforce their potential as either an add-on to standard of care or in a Sionna dual combination

Sionna plans to advance SION-719 to a Phase 2a proof-of-concept add-on to standard of care trial in cystic fibrosis patients, and SION-451 to a Phase 1 healthy volunteer dual combination trial

Next trials to initiate in the second half of 2025 with topline data expected in mid-2026

Sionna to hold a conference call today at 8:00 a.m. ET

WALTHAM, Mass., June 04, 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 positive data from its Phase 1 clinical trials of SION-719 and SION-451, the company's first-in-class nucleotide-binding domain 1 (NBD1) stabilizers, in healthy volunteers. Both NBD1 stabilizers were generally well tolerated and achieved pharmacokinetic (PK) concentration targets established using Sionna's preclinical CF human bronchial epithelial (CFHBE) model. These data reinforce the potential of both NBD1 stabilizers to provide clinically meaningful benefit for CF patients, including the potential for wild-type CFTR function, either as an add-on to standard of care (SOC), or in a proprietary dual combination with complementary modulators. Sionna plans to advance both NBD1 stabilizers to the next stage of clinical development — SION-719 to a Phase 2a proof-of-concept (POC) trial in CF patients as an add-on to SOC, and SION-451 to a Phase 1 proprietary dual combination trial in healthy volunteers.

"Today's announcement brings us one step closer to our vision of developing novel NBD1-led proprietary dual combinations to transform the treatment paradigm for CF patients. The successful completion of two NBD1 Phase 1 trials and being the first company to bring NBD1 compounds into the clinic are important milestones," said Mike Cloonan, President and Chief Executive Officer of Sionna. "Based on these encouraging data, we are fortunate to have the option to advance the clinical development of both NBD1 stabilizers while maintaining our timelines and cash runway into 2028."

Positive Phase 1 Results for SION-719 and SION-451

The Phase 1 randomized, double-blind, placebo-controlled clinical trials evaluated the safety, tolerability, and PK profiles of single ascending doses (SAD) and multiple ascending doses (MAD) of SION-719 and SION-451 in healthy volunteers. The effect of food on the PK and the bioequivalence of a tablet formulation was also evaluated in Part C of each trial. 100 subjects were dosed in the SION-719 trial and 110 subjects were dosed in the SION-451 trial.

Both compounds were generally well tolerated in the Phase 1 trials. There were no serious adverse events, treatment emergent adverse events (TEAEs) that led to discontinuation of drug, or dose-limiting TEAEs observed. Most TEAEs were mild to moderate (Grade 1 or Grade 2). There was one Grade 1 TEAE related to liver function tests (LFTs) in a SION-451 treated subject who tested positive for influenza; no TEAEs related to LFTs were observed in the other cohorts of SION-451. There were no TEAEs related to LFTs in SION-719 treated subjects. The data from Part C of each trial support the use of a tablet formulation in future studies and indicate that both compounds can be dosed in a fed or fasted state.

SION-719 and SION-451 each achieved desired target PK concentrations at multiple dose levels in a twice daily regimen. Both stabilizers met exposure thresholds that, based on Sionna's preclinical CFHBE model, have the potential to provide clinically meaningful benefit if administered as an add-on to SOC or in a proprietary dual combination with complementary modulators.

"While advances in CF treatments have improved the lives of CF patients over the past decade, there still remains a large unmet need. The majority of CF patients on approved modulators do not have normal CFTR function and many patients discontinue or reduce dosages due to tolerability issues," said Patrick Flume, M.D., Professor of Medicine and Pediatrics at the Medical University of South Carolina. "It is exciting to hear that both NBD1 stabilizers will progress into the next stage of clinical development with the goal of providing new options for CF patients."

Next Phase of Clinical Development for NBD1 Stabilizers

SION-719 to Advance to Phase 2a Proof-of-concept in CF Patients as an Add-on to Standard of Care

Sionna is progressing SION-719 into a Phase 2a POC trial evaluating the compound as an add-on to SOC in CF patients. The

trial objectives will be to show an improvement in CFTR function as defined by sweat chloride reduction and to demonstrate that NBD1 is mechanistically unique from, and synergistic with, the components of SOC. Sionna is on track to initiate this trial in the second half of 2025 with topline data anticipated in mid-2026. The U.S. Food and Drug Administration (FDA) has cleared the Investigational New Drug (IND) application for SION-719, and the first subject has been dosed in a midazolam drug-drug interaction (DDI) study to confirm SION-719 can be dosed in combination with the SOC according to its label. This study will be completed prior to initiation of the Phase 2a trial.

SION-451 to Advance to Phase 1 Healthy Volunteer Dual Combination Trial with Complementary Modulators

Sionna plans to initiate a Phase 1 healthy volunteer dual combination trial evaluating SION-451 in combination with SION-2222 (galicaftor), a transmembrane domain 1 (TMD1)-directed CFTR corrector, and with SION-109, an intracellular loop 4 (ICL4)-directed CFTR corrector. The trial will assess the safety, tolerability, and PK of varying doses of the dual combinations, and will inform selection of a dual combination for a Phase 2b trial in CF patients. Sionna is on track to initiate the healthy volunteer trial in the second half of 2025 with topline data expected in mid-2026.

Conference Call
Sionna will host a conference call today, June 4, 2025, at 8:00 a.m. ET to discuss the positive Phase 1 results for SION-719 and SION-451 and the Company's development strategy. The conference call can be accessed via this link. A live and archived webcast of the conference call will be available on the "Events" page in the "Investors" section of Sionna's website at https://investors.sionnatx.com/news-events/events.

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 and providing clinically meaningful benefit to patients, including the potential for wild-type CFTR function; the initiation, timing, progress and results of Sionna's research and development programs, preclinical studies and clinical trials, including the timing of the planned initiation of a Phase 2a proof-of-concept trial and Phase 1 healthy volunteer combination trial and the timing of topline data from these trials and the ongoing DDI study; the ability of clinical trials to demonstrate safety and efficacy of Sionna's product candidates; the ability of Sionna's preclinical studies to predict later clinical trial results; and financial projections and expectations regarding the time period in which Sionna's capital resources will be sufficient to fund its anticipated operations, including cash runway, use of capital, expenses and other financial results. 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 ongoing, 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.

Media Contact
Adam Daley
CG Life

212.253.8881
adaley@cglife.com

Investor Contact
Juliet Labadorf
ir@sionnatx.com