Sionna Therapeutics Announces Presentation of SION-719 and SION-451 Phase 1 Data and Poster of New Preclinical Data on the Impact of NBD1 Stabilizers on F508del-CFTR Half-Life at the 2025 North American Cystic Fibrosis Conference

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Phase 1 data of first-in-class NBD1 stabilizers, SION-719 and SION-451, demonstrated they were generally well tolerated and exceeded desired pharmacokinetic targets

New preclinical data show that NBD1 stabilizers restored the half-life of F508del-CFTR up to wild-type levels

WALTHAM, Mass., Oct. 24, 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 data presented at the 2025 North American Cystic Fibrosis Conference (NACFC) being held in Seattle, Washington October 22-25.

“We are focused on advancing therapies that have the potential to make a meaningful difference for people living with CF, a mission underscored by the data presented this week at NACFC,” said Mike Cloonan, President and Chief Executive Officer of Sionna. “With multiple nucleotide binding domain 1 (NBD1) programs in the clinic, and the recent initiation of our Phase 2a proof-of-concept study in CF patients, we are at an important stage for our company and for people living with CF. The Phase 1 data highlighted at NACFC provides tremendous momentum as we continue to advance our NBD1 stabilizers to the next phases of development, with read-outs from our ongoing trials expected in mid-2026.”

SION-719 and SION-451 Phase 1 Data

Jason H. Maley, M.D., MS, Senior Director of Clinical Development at Sionna, presented data from the two Phase 1 clinical trials of SION-719 and SION-451, the company’s first-in-class nucleotide-binding domain 1 (NBD1) stabilizers. The randomized, double-blind, placebo-controlled Phase 1 trials enrolled over 200 healthy volunteers and evaluated each compound’s safety, tolerability, and pharmacokinetics (PK) across single and multiple ascending dose cohorts.

As previously disclosed, Sionna’s two Phase 1 trials demonstrated that both SION-719 and SION-451 were generally well tolerated and exceeded target exposure levels. Based on these Phase 1 data and its cystic fibrosis human bronchial epithelial (CFHBE) model, Sionna believes that its NBD1 stabilizers have the potential to deliver clinically meaningful benefit when SION-719 is added to the standard of care (SOC) or when SION-451 is used in proprietary dual combinations with one of Sionna’s complementary modulators. The Phase 1 data also supported the use of a tablet formulation in future trials and indicated that both compounds can be dosed in a fed or fasted state.

New Preclinical Data show NBD1 Stabilizer Impact on F508del-CFTR Half-Life

In a poster presented by Greg Hurlbut, Ph.D., Co-Founder and Senior Vice President of Discovery Research at Sionna, new preclinical data from metabolic pulse-chase labeling studies show the impact of Sionna’s NBD1 stabilizers on the half-life of F508del-CFTR protein, in the presence and absence of Sionna’s complementary CFTR modulators. In these studies, NBD1 stabilizers SION-719 and SION-451 increased the half-life of mature F508del-CFTR protein to levels seen with wild-type CFTR. This effect was apparent even when NBD1 stabilizers were used as single agents.

“The most common CFTR mutation that causes CF is F508del, which results in the destabilization of CFTR’s NBD1 domain and impaired CFTR folding, trafficking, half-life, and function,” said Dr. Hurlbut. “The minimal amount of F508del-CFTR protein that does reach the apical cellular membrane exhibits a dramatically increased rate of degradation and decreased half-life relative to wild-type CFTR. We have previously presented preclinical data which showed that Sionna’s NBD1 stabilizers offer a unique mechanism and have the potential to restore CFTR function up to wild-type levels when combined with complementary modulators. Based on these new preclinical data that further differentiate NBD1’s mechanism of action, we believe that our NBD1 stabilizers also have the potential to improve CFTR half-life up to wild-type levels.”

The presentation and posters are available under the “Scientific Presentations” section within the Science page of Sionna’s website at https://www.sionnatx.com/our-science/.

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 more 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 therapeutic potential of its product candidates, including their potential to make a meaningful difference for people living with 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 company's ongoing trials; the ability of clinical trials to demonstrate safety and efficacy of Sionna's product candidates, including the potential of an NBD1 stabilizer product candidate added to the SOC or used in a proprietary dual combination to provide clinically meaningful benefit, including up to wild-type levels of CFTR function and half-life; 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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