Sionna Therapeutics Announces Presentation of Preclinical Data that Demonstrate Proprietary Dual Combination Therapies Enable Full CFTR Correction in CFHBE Model

June 6, 2025

Data featured in oral presentation and poster session at 48th European Cystic Fibrosis Conference

WALTHAM, Mass., June 06, 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 the presentation of preclinical data that demonstrate that the company's nucleotide-binding domain 1 (NBD1) stabilizers, in dual combinations with proprietary complementary modulators, enable full CFTR correction in CF models. The data are featured in an oral presentation and poster session at the European Cystic Fibrosis Society (ECFS) 48th European Cystic Fibrosis Conference being held in Milan, Italy.

"NBD1 instability and defective CFTR domain-domain assembly are the central drivers of CFTR dysfunction that results from the most prevalent CF-causing mutation, F508del-CFTR," said Greg Hurlbut, Ph.D., Co-Founder and Senior Vice President, Discovery Research of Sionna. "Leveraging over 15 years of research, we've had unique success developing novel NBD1 stabilizers that target the NBD1 region of the CFTR protein, a mechanism previously deemed undruggable. We are also developing a portfolio of complementary CFTR modulators designed to work synergistically with our NBD1 stabilizers to address domain-domain assembly defects. Preclinical data suggest these compounds, when used in combination, have the potential to dramatically improve clinical outcomes and quality of life for people with CF."

Sionna has completed Phase 1 clinical trials evaluating two potent first-in-class small molecule NBD1 stabilizers, SION-719 and SION-451. The company is also developing modulators with mechanisms of action that are complementary to NBD1, including SION-2222 (galicaftor), a transmembrane domain 1 (TMD1)-directed CFTR corrector, and SION-109, an intracellular loop 4 (ICL4)-directed CFTR corrector.

At the ECFS conference, Sionna is presenting results from functional and biochemical preclinical studies that assessed dual combinations of NBD1 stabilizers SION-719 and SION-451 with SION-2222 and with SION-109. Key findings from Dr. Hurlbut and team include:

- Both SION-719 and SION-451 display high-affinity 1:1 NBD1 binding and can increase the stability of isolated ΔF508-NBD1 by 16°C, to levels higher than those observed with wild-type NBD1.
- SION-719 and SION-451 correct F508del-CFTR maturation to wild-type levels when either is combined with SION-2222 or SION-109 in CF-patient derived cells.
- SION-719 and SION-451 correct ΔF508-CFTR function to wild-type levels when either is combined with SION-2222 or SION-109 in cystic fibrosis human bronchial epithelial (CFHBE) assays at their highest effective doses (E_{max}).
- In the CFHBE model, SION-719 and SION-451 dual combinations also show potential for clinically meaningful improvement including to wild-type levels at concentrations below E_{max}.

Earlier this week, Sionna announced its plans to advance SION-719 and SION-451 to the next stage of clinical development. The company plans to evaluate SION-719 in a Phase 2a proof-of-concept (POC) trial in CF patients as an add-on to standard of care (SOC), and SION-451 in a Phase 1 healthy volunteer trial evaluating SION-451 in two dual combinations with SION-2222 and with SION-109. Both trials are expected to initiate in the second half of 2025, with data anticipated in mid-2026.

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 CF patients; the initiation, timing, progress and results of Sionna's research and development programs, preclinical studies and clinical trials and studies, 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; 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 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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