Windtree Announces Results from Its Phase 2 Study of Lucinactant for COVID-19 Associated Acute Respiratory Distress Syndrome (ARDS) and Lung Injury

March 22, 2022

Results support the feasibility for development of a potential treatment for critically ill patients with ARDS due to COVID-19 and other causes

WARRINGTON, Pa., March 22, 2022 (GLOBE NEWSWIRE) -- Windtree Therapeutics, Inc. (NasdaqCM: WINT), a biotechnology company focused on advancing multiple late-stage interventions for acute cardiovascular and pulmonary disorders, today announced results from its Phase 2 study of lucinactant (KL4 surfactant) for patients with severe COVID-19 associated acute respiratory distress syndrome (ARDS) and lung injury.

The rationale for the study was that the SARS-CoV-2 virus causing COVID-19 uses the angiotensin-converting enzyme 2 (ACE2) receptor for entry into host cells. The ACE2 receptor is found on alveolar Type 2 cells in the lung. Type 2 cells are the source of pulmonary surfactant production. When these cells are infected and damaged, surfactant production is impaired, increasing the risk for respiratory failure as surfactant is necessary for the lungs to stay inflated and for proper gas exchange. Surfactant deficiency is known to contribute to the pathophysiology of ARDS, respiratory failure, and lung injury in patients on mechanical ventilation.

The Phase 2 trial was designed to assess feasibility, safety, and tolerability of administration of reconstituted lyophilized lucinactant in these critically ill patients. The multicenter, single-arm study enrolled 20 critically ill patients who were intubated and on mechanical ventilation due to severe COVID-19 associated ARDS. Patients received lucinactant as a liquid via the endotracheal tube assessing safety and tolerability of the administration procedure and of the drug. Oxygenation and other physiological responses were also measured. Study sites were in the U.S. and Argentina.

Key findings from the study were:

- The trial demonstrated that intratracheal administration of reconstituted lyophilized lucinactant was generally safe and well tolerated and could be safely administered to critically ill, mechanically ventilated patients with severe COVID-19 associated ARDS.
- Compared to earlier trials in non-COVID-19 ARDS where patients were administered SURFAXIN®, a different formulation of lucinactant approved to treat premature neonates with RDS, it appeared reconstituted lyophilized lucinactant was easier and faster to administer and was associated with fewer peri-dosing side effects that commonly occur when liquid surfactants are administered in the airway. This apparent difference may be due to reconstituted lyophilized lucinactant having substantially lower viscosity than SURFAXIN®.
- Oxygenation and other physiological outcomes were generally stable or improved in these critically ill patients. Only a few patients received multiple doses of surfactant, suggesting that the amount of surfactant delivered was at the low end of the dose response curve.
- The results in this study support the feasibility of this treatment approach to develop a potential treatment for critically ill patients with severe ARDS due to COVID-19 or other causes.

“We are pleased to report these study results which demonstrate the feasibility of lucinactant delivered as a liquid via the endotracheal tube in treating critically ill patients who are intubated and mechanically ventilated due to severe COVID-19 associated ARDS,” said Steve Simonson, MD, Chief Medical Officer of Windtree Therapeutics. “The ease and speed of drug administration, along with the safety and tolerability profile, were important findings in this study. We believe the study provides the foundation upon which further development work in ARDS due to COVID-19 or other causes could be based. The Company and our investigators also believe there may be potential for lyophilized lucinactant to support severely injured lungs when extracorporeal membrane oxygenation (ECMO) is used to rest the lungs and oxygenate the blood outside the body in these critically ill patients.”

About KL4 Surfactant Platform Programs
The Company has been supporting Lee’s (HK) in its development of the KL4 surfactant platform in Asia. To support the future global development of our KL4 surfactant platform, including further development in pre-term infants experiencing respiratory distress syndrome (RDS) via aerosolized AEROSURF and/or instillate delivery and/or in other applications such as acute lung injury, in markets outside of Asia, we are pursuing one or more licensing transactions.

About Lucinactant
Lucinactant is a synthetic surfactant that is structurally similar to human pulmonary surfactant and contains a proprietary synthetic peptide KL4 (sinapultide), a 21-amino acid peptide that is designed to imitate the essential attributes of the human surfactant protein B (SP-B). SP-B is one of four known surfactant proteins and is important for proper functioning of the respiratory system. Surfactant is a natural lubricant produced by specialized cells in the lung called alveolar Type 2 cells and is critical for proper lung function. Surfactant helps keep the lungs from collapsing when exhaling and improves oxygen transfer to the blood. Windtree’s lucinactant can be given either through an endotracheal tube or via a proprietary aerosolized delivery system. It has the potential to mitigate surfactant deficiency and inactivation that can occur because of infectious diseases and inflammation in the lung, such as COVID-19. Preclinical data demonstrated that lucinactant may possess other beneficial properties, including modulation of the

inflammatory process, antimicrobial properties, and lack of immunogenicity.

About Windtree Therapeutics
Windtree Therapeutics, Inc. is advancing multiple late-stage interventions for acute cardiovascular and acute pulmonary disorders to treat patients in moments of crisis. Using new scientific and clinical approaches, Windtree is developing a multi-asset franchise anchored around compounds with an ability to activate SERCA2a, with lead candidate, istaroxime, being developed as a first-in-class treatment for acute heart failure and for early cardiogenic shock. Windtree's heart failure platform includes follow-on oral pre-clinical SERCA2a activator assets as well. In pulmonary care, Windtree has focused on facilitating the transfer of the clinical development of AEROSURF®, to its licensee in Asia, Lee's HK. Windtree is also evaluating KL4 surfactant for the treatment of acute respiratory distress syndrome in COVID-19 patients. Included in Windtree's portfolio is rostafuroxin, a novel precision drug product targeting hypertensive patients with certain genetic profiles.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. The Company may, in some cases, use terms such as "predicts," "believes," "potential," "proposed," "continue," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Such statements are based on information available to the Company as of the date of this press release and are subject to numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from the Company's current expectations. Examples of such risks and uncertainties include: risks and uncertainties associated with the ongoing economic and social consequences of the COVID-19 pandemic, including any adverse impact on the Company's clinical trials, clinical trial timelines or disruption in supply chain; the success and advancement of the clinical development programs for istaroxime, KL4 surfactant and the Company's other product candidates; the impacts of political unrest, including as a result geopolitical tension, including escalation in the conflict between Russia and Ukraine and any additional resulting sanctions, export controls or other restrictive actions that may be imposed by the United States and/or other countries, which could have an adverse impact on the Company's operations, including through disruption in supply chain or access to potential international clinical trial sites, and through disruption, instability and volatility in the global markets, which could have an adverse impact on the Company's ability to access the capital markets; the Company's ability to secure significant additional capital as and when needed; the Company's ability to access the debt or equity markets; the Company's ability to manage costs and execute on its operational and budget plans; the results, cost and timing of the Company's clinical development programs, including any delays to such clinical trials relating to enrollment or site initiation; risks related to technology transfers to contract manufacturers and manufacturing development activities; delays encountered by the Company, contract manufacturers or suppliers in manufacturing drug products, drug substances, aerosol delivery systems (ADS) and other materials on a timely basis and in sufficient amounts; risks relating to rigorous regulatory requirements, including that: (i) the FDA or other regulatory authorities may not agree with the Company on matters raised during regulatory reviews, may require significant additional activities, may not accept or may withhold or delay consideration of applications, or may not approve or may limit approval of the Company's product candidates, and (ii) changes in the national or international political and regulatory environment may make it more difficult to gain regulatory approvals and risks related to the Company's efforts to maintain and protect the patents and licenses related to its product candidates; risks that the Company may never realize the value of its intangible assets and have to incur future impairment charges; risks related to the size and growth potential of the markets for the Company's product candidates, and the Company's ability to service those markets; the Company's ability to develop sales and marketing capabilities, whether alone or with potential future collaborators; and the rate and degree of market acceptance of the Company's product candidates, if approved. These and other risks are described in the Company's periodic reports, including the annual report on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, filed with or furnished to the Securities and Exchange Commission and available at www.sec.gov. Any forward-looking statements that the Company makes in this press release speak only as of the date of this press release. The Company assumes no obligation to update forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

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Source: Windtree Therapeutics