Windtree Presents Data from its Positive SEISMiC Phase 2 Study of Istaroxime in Early Cardiogenic Shock in a Late-Breaker Presentation at the European Society of Cardiology Heart Failure Meeting in Madrid

May 23, 2022

The study met its primary endpoint of improved systolic blood pressure (SBP) profile at 6 hours with the istaroxime group performing significantly better than the control group
Increased SBP also persisted through 24 hours

The study also met several key secondary endpoints associated with improving cardiac function

Investor conference call and webcast to be held today, Monday May 23 at 4:30 pm EDT

WARRINGTON, Pa., May 23, 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 presented data from its positive Phase 2 study of istaroxime in early cardiogenic shock in a late-breaker presentation at the European Society of Cardiology Heart Failure Meeting in Madrid, Spain. The study met its primary endpoint of significantly improved SBP, the critical clinical objective in treating patients with cardiogenic shock, compared to the control group at 6 hours. The significant improvement in blood pressure profile persisted through 24 hours. The study met several other secondary endpoints including assessments of cardiac function.

The SEISMiC Phase 2 study is an international, randomized, double blind, placebo-controlled study that enrolled 60 patients with Society for Cardiovascular Angiography & Interventions (SCAI) Stage B early cardiogenic shock due to severe heart failure with SBP between 75-90 mmHg. Patients were randomized on a 1:1 basis (placebo versus treatment) with two istaroxime target doses utilized in the treatment arm: (1.5 µg/kg/min in the first 13 patients and 1.0 µg/kg/min in the next 17 patients). Patients were infused for 24 hours. The primary endpoint was the difference in SBP area under the curve over six hours after initiating the infusion. Secondary endpoints included characterization of blood pressure changes over 24 hours, echocardiographic assessments of systolic and diastolic cardiac function, assessment of renal function and measures associated with safety and tolerability.

Study results

- The study met its primary endpoint in SBP profile over six hours, with the istaroxime treated group performing significantly better compared to the control group (p =0.017). The improvement persisted through the 24-hour SBP profile measurement, which was also statistically significant (p=0.025).
- SBP increases were rapid within the first hour and sustained throughout the 96-hour post-infusion measure.
- Istaroxime treatment demonstrated improvement in cardiac index compared to the control (p = 0.016).
- Several other, key secondary measurements associated with cardiac function were significantly improved including left atrial area and left ventricular end systolic volume. Left ventricular end diastolic volume was also decreased with treatment. Patients treated with istaroxime also experienced a substantial increase in stroke volume (the amount of blood pumped from the heart with each contraction).
- Importantly, renal function was maintained, and treated patients tended to experience greater diuresis than placebo despite needing a lower cumulative dose of diuretics.
- Istaroxime was generally well tolerated with the 1.0 µg/kg/min dose group performing numerically better on efficacy and safety than the 1.5 µg/kg/min dose group.

Dr. Marco Metra, principal investigator of the study and Professor of Cardiology and Director of the Institute of Cardiology of the Civil Hospital and University of Brescia, Italy, put these results into context by stating, “These data indicating istaroxime can improve both blood pressure and cardiac function are very exciting. This is the first non-adrenergic agent to potentially do so and indicate that istaroxime has the potential to become a novel approach to patient care that fills an important gap in treating patients with cardiogenic shock as well as acute heart failure and hypotension.”

Dr. Steven Simonson, Chief Medical Officer at Windtree, stated: “We are very pleased with the results demonstrated in patients experiencing early cardiogenic shock due to acute heart failure. This study provides valuable information for advancement of the istaroxime program. The positive results from SEISMiC have helped to clarify the next steps in istaroxime development, and we look forward to expanding the shock population we are studying and evaluating the benefits of istaroxime with longer infusions in our planned extension study as we progress toward a potential new therapeutic innovation for treating cardiogenic shock due to heart failure.”

Craig Fraser, CEO of Windtree, stated, “Results from the study are consistent with and complement our prior Phase 2 data in acute heart failure. We believe istaroxime shows promise in both early cardiogenic shock and acute heart failure and could be the first drug to improve cardiac pump function without the expense of having reduced SBP or compromising renal function seen in currently available agents. We look forward to continuing our development of istaroxime and meeting with regulatory authorities and defining a potential development path to approval.”

Conference Call Details
Management will host a conference call for investors today, May 23, at 4:30 pm EDT to discuss the study results and answer questions. Conference

call, webcast and replay details are as follows:

Domestic:	+1-877-423-9813
International:	+1-201-689-8573
Conference ID:	13729315
Webcast link:	Click Here

A webcast replay will be available the investor portion of the Company website at www.windtreetx.com/events.

About Cardiogenic Shock
Cardiogenic shock is a serious condition that occurs when the heart is failing significantly and cannot pump enough blood and oxygen to the brain, kidneys, and other vital organs. Mortality rates are significant and, depending on severity, range from 7% to 40% in the U.S. There is a lack of satisfactory pharmacological intervention to reverse the condition as available therapies have unwanted side effects such as risk for arrhythmias, decreasing blood pressure, renal dysfunction and even increases in mortality that limit their usefulness and position them as “rescue medicines” for severe cases. Market research revealed 99% of 100 U.S.-based clinical cardiologists interviewed who treat cardiogenic shock patients responded that new drug innovation to treat SCAI class B cardiogenic shock patients is highly needed. The cardiogenic shock worldwide total market value is estimated to be $1.25 billion, calculated by using cardiogenic shock patient US hospital claims and worldwide prevalence data multiplied by assumed various regional prices of drug treatment.

About Istaroxime
Istaroxime is a first-in-class dual mechanism therapy designed to improve both systolic and diastolic cardiac function. Istaroxime is a positive inotropic agent that increases myocardial contractility through inhibition of Na+/K+- ATPase with a complimentary mechanism that facilitates myocardial relaxation through activation of the SERCA2a calcium pump on the sarcoplasmic reticulum enhancing calcium reuptake from the cytoplasm. Data from multiple Phase 2 studies in patients with acute heart failure (AHF) demonstrate that istaroxime infused intravenously significantly improves cardiac function and blood pressure without causing heart rate increases or rhythm disturbances.

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. 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, or 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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