Windtree Therapeutics Initiates SEISMiC C Study of Istaroxime in SCAI Stage C Cardiogenic Shock for Planned Completion of Phase 2b and Transition to Phase 3

October 30, 2024

After successful SEISMiC A and B studies in Early Cardiogenic Shock, SEISMiC C will treat more severe SCAI Stage C cardiogenic shock to complete the assessment of the intended Phase 3 patient population

Windtree plans to engage with regulatory authorities in 2025 for Transition to Phase 3 clinical trial

WARRINGTON, Pa., Oct. 30, 2024 (GLOBE NEWSWIRE) -- Windtree Therapeutics, Inc. ("Windtree" or the "Company") (NasdaqCM: WINT), a biotechnology company focused on advancing early and late-stage innovative therapies for critical conditions and diseases, today announced the initiation of enrollment in the SEISMiC C trial in SCAI Stage C cardiogenic shock. This study follows the positive results in both SEISMiC A and B in SCAI Stage B cardiogenic shock trials. In these trials, istaroxime improved systolic blood pressure, cardiac function and renal function without an increased risk for cardiac arrhythmias, a profile that differentiates istaroxime from currently used medications to treat shock. SCAI Stage C cardiogenic shock is a more severely ill population than was previously studied with istaroxime. SCAI Stage C patients have progressed in their cardiogenic shock and heart failure to the point of tissue and vital organ hypoperfusion (lack of blood flow and oxygen) and typically require inotropic or vasopressor drugs for support. These drugs are used with caution due to deleterious side effects – many of which we believe istaroxime may potentially avoid based on results to date from four previous studies in acute heart failure and early cardiogenic shock. The Company intends to include SCAI Stage C patients as part of the Phase 3 patient population for cardiogenic shock.

The SEISMiC C study is a global trial including sites in the U.S,. Europe and Latin America. It is a placebo-controlled, double-blinded study with istaroxime being added to current standard of care, inotropes or vasopressors. The effect of istaroxime in addition to these therapies will be assessed for 6 hours and based on the patient's condition, a withdrawal of the other therapies. The primary endpoint of the study is assessment of systolic blood pressure (SBP) profile over the first 6 hours of treatment. Other key study measurements include various measures of cardiac function, SBP changes at specified timepoints, the vasopressor-inotrope score, avoidance of progression to SCAI Stage D or E cardiogenic shock and need for mechanical cardiac support, time to treatment failure, arrhythmia assessments, days alive and out of the hospital through day 30, physiologic measures (e.g., cardiac index) and length of stay in the intensive care unit and hospital. There will be a planned data review after enrollment of approximately 20 subjects with SCAI Stage C cardiogenic shock due to acute decompensated heart failure planned for late Q1 / early Q2 2025 followed by guidance from the Company on the number of additional patients and timing to complete the study and planned Phase 2 completion.

The Company believes that the data from SEISMiC C trial will help characterize the potential advantages of istaroxime compared to current standard of care therapies and that this SCAI Stage C trial is important for Phase 3 readiness of istaroxime in cardiogenic shock because these patients are intended to be part of the target patient population. The Company expects these data to also be useful for discussions with regulatory agencies to finalize plans for the Phase 3 program design.

"We are pleased to have this study underway and enrolling patients. The study is intended to build on the positive results to date and moves us forward into this important SCAI Stage C patient population for the development program," said Steve Simonson, CMO and SVP of Windtree Therapeutics. "With SCAI Stage C acceptable results, we expect to move steadily toward Phase 3 in cardiogenic shock."

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 early cardiogenic shock or acute decompensated heart failure demonstrate that istaroxime infused intravenously significantly improves cardiac function and blood pressure without increasing heart rate or the incidence of cardiac rhythm disturbances.

About Windtree Therapeutics, Inc.
Windtree Therapeutics, Inc. is a biotechnology company focused on advancing early and late-stage innovative therapies for critical conditions and diseases. Windtree's portfolio of product candidates includes istaroxime, a Phase II candidate with SERCA2a activating properties for acute heart failure and associated cardiogenic shock, preclinical SERCA2a activators for heart failure and preclinical precision aPKCi inhibitors that are being developed for potential in rare and broad oncology applications. Windtree also has a licensing business model with partnership out-licenses currently in place.

Forward Looking Statements
This press release contains statements related to the potential clinical effects of istaroxime; the potential benefits and safety of istaroxime; the clinical development of istaroxime; and our research and development program for treating patients in early cardiogenic shock due to heart failure. Such statements constitute 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, among other things: the Company's ability to secure significant additional capital as and when needed; the Company's ability to achieve the intended benefits of the aPKCi asset acquisition with Varian Biopharmaceuticals, Inc.; the Company's risks and uncertainties associated with the success and advancement of the clinical development programs for istaroxime and the Company's other product candidates, including preclinical oncology candidates; 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, and other materials on a timely basis and in sufficient amounts; risks relating to rigorous regulatory requirements, including that: (i) the U.S. Food and Drug Administration 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; the rate and degree of market acceptance of the Company's product candidates, if approved; the economic and social consequences of the COVID-19 pandemic and the impacts of political unrest, including as a result of geopolitical tension, including the conflict between Russia and Ukraine, the People's Republic of China and the Republic of China (Taiwan), and the evolving events in the Middle East, and any 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. These and other risks are described in the Company's periodic reports, including its 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