Windtree Therapeutics Announces Reduction In Arrythmias In A New Study With Istaroxime And A Pure SERCA2a Activator

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The new preclinical data further supports istaroxime clinical data from three Phase 2 studies

Arrythmias can be a serious complication of current rescue therapies for treatment of patients with acute heart failure

WARRINGTON, Pa., Jan. 02, 2024 (GLOBE NEWSWIRE) -- Windtree Therapeutics, Inc. ("Windtree" or the "Company") (NasdaqCM: WINT), a biotechnology company focused on advancing late-stage interventions for critical cardiovascular disorders, today announced new preclinical data on the Company's lead product candidate, istaroxime, and another preclinical pipeline drug candidate, CVie-216, showing reductions in ventricular arrythmias in a rat heart model of diabetes with restricted and restored coronary blood flow induced injury. Istaroxime and CVie-216 are each designed to act on pumps in the cardiac cells that are important in calcium handling. Istaroxime is a dual mechanism of action compound that has been shown to inhibit the sodium potassium ATPase and activates SERCA2a. CVie-216 is designed to selectively activate SERCA2a.

Nearly 300 patients with acute decompensated heart failure were treated with istaroxime in three Phase 2 studies, including a study that evaluated patients with early cardiogenic shock. In these studies, istaroxime has not been associated with an increase in clinically significant arrythmias, raising the potential for a new therapy with substantial advantages over current rescue drug therapies used to treat acute heart failure and cardiogenic shock. Windtree is continuing to obtain data to evaluate the potential benefits of SERCA2a activation on arrythmia risk in all ongoing clinical trials. To further explore this potential benefit associated with SERCA2a activation, Windtree conducted a study of restricted and restored coronary blood flow induced injury in the hearts of rats with diabetes that were infused with either istaroxime, pure SERCA2a activator CVie-216 or placebo (control). The rat model generated a reproducible incidence of ventricular arrythmias. This study demonstrated a reduction in arrythmias in the istaroxime and CVie-216 pretreated groups compared to the control group. The Company plans to publish the results and is in the process of pursuing additional intellectual property protection based on these findings.

"This new data suggests that improving SERCA2a activity has the potential to improve arrythmia risk as well as improve overall cardiac function," said Craig Fraser, CEO of Windtree Therapeutics. "We expect to continue to obtain additional data in our ongoing clinical trial to characterize the impact of our SERCA2a activation with istaroxime on clinically significant arrythmias and we expect to extend these observations with additional preclinical work with the oral SERCA2a Activators."

Arrythmias are irregular heartbeats that can impact the pumping function of the heart. Patients with heart failure and cardiomyopathy are at risk for arrythmias. Arrythmias in these patients can be caused by their underlying cardiac disease or by drugs used to treat the heart failure such as catecholamines. Arrythmias can impair proper filling of the heart with blood and, importantly, cardiac output to the body. Ventricular arrythmias are particularly dangerous and can be fatal.

Innovative drugs have the potential to treat acute heart failure and cardiogenic shock to improve cardiac function without increasing the risk for arrythmias. Acute decompensation of heart failure is responsible for approximately 1.3 million hospital admissions in the U.S. and approximately 1.5 million in the EU. It is the #1 cause of U.S. hospitalizations in patients >65 years of age and is the most expensive Medicare diagnosis to treat. Cardiogenic shock can be a severe presentation of heart failure characterized by low blood pressure and inadequate blood flow to vital organs. It has a mortality rate as high as 30-40% and substantial morbidity in survivors. Istaroxime is administered intravenously in the hospital where acute heart failure and cardiogenic shock patients are treated. CVie-216 is in the preclinical stage of development and has potential for intravenous administration or oral (tablet) use in the out-patient setting in chronic heart failure. Chronic heart failure affects approximately 6 million people (nearly 2% of the adult population) in the U.S. The combined U.S., EU and Japan market has more than 18 million patients with chronic heart failure.

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 Pure SERCA2a Activators
These compounds activate SERCA2a and Windtree Therapeutic's research and development program is evaluating these preclinical product candidates, including oral and intravenous SERCA2a activator heart failure compounds.

About Windtree Therapeutics, Inc.
Windtree Therapeutics, Inc. is advancing late-stage interventions for cardiovascular 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 cardiogenic shock and acute decompensated heart failure. Windtree's heart failure platform includes follow-on pre-clinical SERCA2a activator assets as well. In pulmonary care, Windtree has focused on facilitating the transfer of the KL4 surfactant platform, to its licensee, Lee's Pharmaceutical (HK) Ltd. and Zhaoke Pharmaceutical (Hefei) Co. Ltd. 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 success and advancement of the clinical development programs for istaroxime and the Company's other product candidates; 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, 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 Israel and Gaza, 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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