UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the
Securities Exchange Act of 1934

October 25, 2019
Date of Report (Date of earliest event reported)

Windtree Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**000-26422**	**94-3171943**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification Number)

2600 Kelly Road, Suite 100
Warrington, Pennsylvania 18976
(Address of principal executive offices)

(215) 488-9300
(Registrant's telephone number, including area code)

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:
☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading symbol(s)**	**Name of each exchange on which registered**

Securities registered pursuant to Section 12(g) of the Act: Common Stock, $0.001 par value

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 or Rule 12b-2 of the Securities Exchange Act of 1934: Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02 Results of Operations and Financial Condition.

On October 25, 2019, Windtree Therapeutics, Inc. (the "Company") issued a press release which provided updates on the Company's lead development programs and business operations, including with respect to certain financial information. The press release is attached as Exhibit 99.1 hereto.

In accordance with General Instruction B.2 of Form 8-K, the information in Item 2.02 of this Current Report on Form 8-K and Exhibit 99.1 hereto relating to the Company's current financial status and all other matters except for those discussed under Item 8.01 below shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in any such filings.

Item 7.01. Regulation FD Disclosure.

In connection with ongoing business development activities, executives of Windtree Therapeutics, Inc. (the "Company") have prepared the presentation attached to this Current Report on Form 8-K as Exhibit 99.2. The information contained in the presentation is summary information that is intended to be considered in the context of more complete information included in the Company's filings with the Securities and Exchange Commission (SEC) and other public announcements that the Company has made and may make from time to time by press release or otherwise. The furnishing of the attached presentation is not an admission as to the materiality of any information contained therein.

Among other things, this presentation includes program updates for the Company's lead programs, istaroxime, AEROSURF®, and rostafuroxin; results of the istaroxime phase 2b clinical trial; information related to a planned additional study evaluating istaroxime in early cardiogenic shock; and updates to the Company's business strategy and anticipated program and corporate milestones.

Pursuant to General Instruction B.2 of Form 8-K, the information in this Item 7.01 of this Current Report on Form 8-K and Exhibit 99.2 attached hereto are being furnished and shall not be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities of that Section, nor is it to be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, regardless of any general incorporation language in such filing, except as shall be expressly set forth by specific reference in any such filing.

Item 8.01. Other Events.

The press release referred to in Item 2.02 provided updates on the Company's lead development programs and business operations. Subject to the note relating to the press release contained in Item 2.02 of this Current Report on Form 8-K, the press release is attached as Exhibit 99.1 hereto.

- Among other things, after assessing data from the istaroxime phase 2 clinical program in heart failure, the Company has added an early cardiogenic shock clinical study to the istaroxime development plan, which the Company plans to initiate in the first half of 2020 while continuing to work on a larger, acute heart failure study in a less severe population.

- In addition, the Company is actively engaged in discussions with various parties to potentially secure additional capital, through a combination of one or more of public or private equity offerings and strategic transactions, although there can be no assurance that the Company will be successful in raising sufficient amounts of capital as and when required or on terms that are favorable to the Company.

Risk Factors

As of October 25, 2019, we believe our cash resources are only sufficient to fund our business operations through November 2019. If we do not secure additional capital to support our future activities before our existing cash resources are exhausted, we likely will be unable to continue as a going concern.

As of September 30, 2019, we had cash and cash equivalents of $4.3 million. On October 24, 2019, LPH II Investments Ltd. (LPH II), an affiliate of Lee's Pharmaceutical Holdings Limited, agreed to lend the Company $1.0 million to fund the Company's operations. The Company believes that, including the LPH II loan, it currently has sufficient cash and cash equivalent resources to fund its business operations through late-November 2019. We expect to continue to incur significant losses and require significant additional capital to advance our development programs, support our operations and business development efforts, and satisfy existing obligations. These conditions raise substantial doubt about our ability to continue as a going concern.

We have not yet established an ongoing source of revenue sufficient to cover our operating costs and allow us to continue as a going concern. Our ability to continue as a going concern is dependent on our ability to raise additional capital. We plan, and are currently actively engaged in discussions with various parties, to secure the additional capital that we require potentially from a combination of public or private equity offerings and strategic transactions, including potential alliances and drug product collaborations focused on specified geographic markets; however, none of these alternatives are committed at this time and there can be no assurance that we will be successful in identifying and completing such a transaction in the future. If we are unable to identify any alternative and consummate one or more transactions on terms that are acceptable to us, or if we are unable to raise sufficient capital through such transactions, or within a time that would support our capital requirements, we likely will not have sufficient cash resources and liquidity to fund our business operations, which could significantly limit our ability to continue as a going concern. If we are unable to raise the required capital, we may be forced to curtail our activities and, ultimately, cease operations.

Our additional clinical study of istaroxime in early cardiogenic shock involves risks and uncertainties that are inherent in clinical development. Such clinical trials may be delayed, or fail, which will harm our business prospects.

Our plans include an additional clinical study of istaroxime in early cardiogenic shock, an area that we have not studied previously. To gain marketing authorization for new indications such as early cardiogenic shock, we will need to engage with the US Food and Drug Administration (FDA) and successfully complete our clinical program. We may not reach agreement with the US Food and Drug Administration (FDA) or a foreign regulator on the extent of our clinical program, the design of any one or more of the clinical trials necessary for approval. We may suffer significant delays or setbacks in any stage of our clinical trials. and if our results are inconclusive or non-compelling or otherwise insufficient to support a strategic or financing transaction, we potentially could be forced to limit or cease all development activities, which would have a material adverse effect on our business.

The timing and completion of clinical trials to study our product candidates depend on many factors, including the rate at which patients are enrolled. Delays in patient enrollment in clinical trials would likely result in increased costs, program delays, or both. Patient enrollment is a function of many factors, including potentially:

- the number of clinical sites;
- the size of the patient population;
- the perceived risks and benefits of the product candidate;
- the existence of competing clinical trials;
- the severity of the disease under investigation;
- the existence of alternative available products;
- the eligibility and enrollment criteria for the study;
- the willingness of patients (or premature infants' parents or guardians) to participate in the clinical trial;
- the trial complexity and resources required by a clinical study site to participate;
- availability of clinical supplies and materials;
- the existence of alternative available products; and
- geographical and geopolitical considerations.

In addition, additional risks and uncertainties inherent in the clinical development process include but are not limited to:

- the ability to design a clinical trial that will assure demonstration of improved efficacy over that of a comparator in the primary endpoint of a trial and demonstration of an adequate safety profile;
- the ability of third-party clinical trial consultants and third-party contract research organizations (CROs) to successfully carry out their activities or meet expected deadlines;
- our ability to adequately manage the design, execution and regulatory aspects of our complex and diverse clinical trials;
- our ability to successfully develop and manufacture our APIs, drug products and product candidates in a manner that ensures that they will perform as intended;
- the risk that our clinical trials may be interrupted, delayed or halted because of health and safety concerns (such as patient side effects) or because of matters related to the design of the study or drug availability; and
- the risk that clinical trial design and size is inadequate to assure demonstration of efficacy and meet statistical significance in outcomes, due to variation between clinicians, medical sites and countries in medical practices and procedures associated with treating our targeted diseases.

For a more detailed discussion of risks and uncertainties related to our financial and development activities, *see*, the risk factors discussed in our Annual Report on Form 10-K for the year ended December 31, 2018 that we filed with the SEC on April 16, 2019, as amended by the Form 10-K/A that we filed with the SEC on April 23, 2019, and our Quarterly Reports on Form 10-Q filed thereafter, and our other filings with the SEC, and any amendments thereto.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits:

99.1 Press Release of Windtree Therapeutics, Inc., dated October 25, 2019.
99.2 Windtree Therapeutics, Inc. Presentation dated October 2019.

Cautionary Note Regarding Forward-looking Statements:

To the extent that statements in this Current Report on Form 8-K are not strictly historical, including statements as to business strategy, outlook, objectives, future milestones, plans, intentions, goals, future financial conditions, future collaboration agreements, the success of the Company's product development, cash flows, future revenues, the timing of planned clinical trials or otherwise as to future events, such statements are forward-looking, and are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. The forward-looking statements contained in this Current Report are subject to certain risks and uncertainties that could cause actual results to differ materially from the statements made. Such risks and others are further described in the Company's filings with the Securities and Exchange Commission including the most recent reports on Forms 10-K, 10-Q and 8-K, and any amendments thereto. Any forward-looking statement made by us in this Current Report on Form 8-K is based only on information currently available to us and speaks only as of the date on which it is made. The Company undertakes no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Windtree Therapeutics, Inc.

By: /s/ Craig Fraser
Name: Craig Fraser
Title: President and Chief Executive Officer

Date: October 25, 2019

Exhibit 99.1

Windtree Therapeutics Provides Business Update

Company Has Made Substantive Progress with Lead Development Programs – istaroxime and AEROSURF®

WARRINGTON, PA – October 25, 2019 – Windtree Therapeutics, Inc. (OTCQB: WINT), a biotechnology and medical device company focused on developing drug product candidates and medical device technologies to address acute cardiovascular and pulmonary diseases, today provided updates on its lead development programs and business operations.

"During the third quarter, we made substantive progress in two of our lead development programs – istaroxime for acute heart failure (AHF) and early cardiogenic shock, and AEROSURF® for respiratory distress syndrome (RDS) in premature infants. We have advanced our data analysis, gained increased regulatory clarity and evolved our development strategies for the next stages of program execution," commented Craig Fraser, President and Chief Executive Officer. "We are excited about the opportunities before us as a Company and believe each of our assets has the potential to find a significant place in the treatment landscape. Our late-stage, high-value programs in disease markets with significant unmet medical needs set the stage for our next phase of growth. Our experienced management team is focused on executing our strategy and leveraging potential opportunities to accelerate development of our pipeline. We are also focused on business initiatives to create value from planned milestones that have the potential to be catalysts for our Company. We look forward to keeping our stakeholders updated on our clinical execution and milestone achievements."

Recent Development and Business Highlights

Istaroxime

- **Early Cardiogenic Shock** - Based on assessment of the data from the istaroxime phase 2 program in acute heart failure and the regulatory landscape, and after discussions with advisors, the Company has added an early cardiogenic shock study to the istaroxime development plan. Cardiogenic shock is a severe presentation of heart failure characterized by very low blood pressure and hypo-perfusion to critical organs. It is associated with high mortality and morbidity and is not well treated with current therapies. The Company believes istaroxime may fulfill an unmet need in cardiogenic shock based on the profile observed in prior phase 2 clinical studies in acute heart failure, which showed that istaroxime increased systolic blood pressure by 15 mmHg (1.5 ug/kg/min dose group), suggesting that istaroxime could potentially contribute to the clinical improvement of patients in cardiogenic shock due to heart failure. Because of the unmet need, there may be opportunities for an enhanced regulatory pathway and review. According to FDA published position and actions, approval in shock potentially could be based on blood pressure changes alone (assuming comparable mortality compared to control patients at 30 days). The Company plans to execute a small study of istaroxime in early cardiogenic shock patients to evaluate the potential to improve blood pressure and organ perfusion. The study will also evaluate the safety and side effect profile of istaroxime in this patient population. The Company plans to initiate this study in the first half of 2020 while continuing to work on a larger, acute heart failure study in a less severe population.

- **Acute Heart Failure**

    - In August 2019, the FDA granted istaroxime Fast Track designation for the treatment of acute heart failure based upon the positive phase 2a and phase 2b study data and the recognized unmet medical need.

    - Based on feedback from the FDA in June 2019 and the Company's scientific advisors, the Company is focusing its next clinical trial on patients with low systolic blood pressure (SBP) and those who are diuretic resistant. These two, difficult to treat patient groups with limited treatment options could particularly benefit from istaroxime's unique profile and potential ability to increase cardiac function, increase blood pressure and improve renal function. The Company plans to initiate this next phase 2 study in the second half of 2020 and plans to extend dosing beyond what was previously studied and include clinical outcome measures that may be acceptable for registration.

AEROSURF

- Data from the AEROSURF phase 2 program continues to demonstrate the potential of AEROSURF to reduce both the rate of nasal continuous airway pressure (nCPAP) failure and the need for intubation in premature infants being treated for RDS. The phase 2 program has also produced positive initial data suggesting that AEROSURF may have the potential to lower the incidence and severity of bronchopulmonary dysplasia (BPD). The Company has completed the planned device development activities for the new Aerosol Delivery System (ADS) that is intended for use in the planned bridging study and the phase 3 clinical program and, if approved, initial commercial activity. The Company has completed design verification and conducted extensive performance testing in which this device demonstrated consistent performance under rigorous testing and design verification protocols. In addition, the new ADS has been designed for ease of use and rapid setup, both of which may lead to faster time to treatment and to potentially support better clinical outcomes. The Company is planning to execute a small (n=70) bridging study to complete the phase 2 clinical program and transition to phase 3 by demonstrating the new ADS performance in the NICU. The Company plans to advance AEROSURF at a reduced cost by leveraging development opportunities in China (the largest RDS and surfactant market) with our partner in the region. The bridging study will be conducted in China and Europe, led by the Company, and is planned to begin in Q1 2020.

Pipeline and Other Activities

- The Company continued to advance its preclinical follow-on oral and intravenous SERCA 2a heart failure compounds and continues to actively explore partnership opportunities.

- Rostafuroxin formulation work continues as the Company seeks to complete development of an improved formulation and enhanced assay (lower limit of quantification) for pharmacokinetic measurement of drug concentration as the Company prepares for an out-licensing initiative planned for 2020.

- The Company conducted an R&D Day in June 2019 that featured presentations highlighting two of the Company's lead development programs, istaroxime in acute heart failure and AEROSURF in respiratory distress syndrome in premature infants. The presentations were delivered by key thought leaders in their respective fields. A replay of this event can be found at http://windtreethe tx.investorroom.com/events.

- The Company has initiated the application process to potentially regain listing on the Nasdaq Capital Market® and is progressing toward that objective.

Financial

- As of September 30, 2019, the Company had cash and cash equivalents of $4.3 million.

- On October 24, 2019, LPH II Investments Ltd. (LPH II), an affiliate of Lee's Pharmaceutical Holdings Limited, agreed to lend the Company $1.0 million to fund the Company's operations. The Company believes that, including the LPH II loan, it currently has sufficient cash and cash equivalent resources to fund its business operations through late-November 2019.

- The Company is actively engaged in discussions with various parties to potentially secure additional capital, through a combination of one or more of public or private equity offerings and strategic transactions.

Readers are referred to the Company's October 2019 Corporate Presentation which provides additional details on the Company's development programs and plans. The October 2019 Corporate Presentation is available on the Company's website at http://windtreetx.investorroom.com/corporate_presentation.

About Windtree Therapeutics
Windtree Therapeutics, Inc. is a clinical-stage, biopharmaceutical and medical device company focused on the development of novel therapeutics intended to address significant unmet medical needs in important acute care markets. Windtree has three lead clinical development programs and multiple pre-clinical programs spanning respiratory and cardiovascular disease states, including istaroxime, a novel, dual-acting agent being developed to improve cardiac function in patients with acute heart failure with a potentially favorable safety profile; AEROSURF®, an innovative combination drug/device product candidate that is designed to deliver the Company's proprietary synthetic, peptide-containing surfactant noninvasively to premature infants with respiratory distress syndrome (RDS); and rostafuroxin, a novel precision drug product being developed to target hypertensive patients with certain genetic profiles in the important group of patients with resistant hypertension. Windtree also has multiple pre-clinical products including potential heart failure therapies delivered orally that are based on SERCA2a mechanism of action.

For more information, please visit the Company's website at www.windtreetx.com.

Forward-Looking Statements
To the extent that statements in this press release are not strictly historical, all such statements are forward-looking, and are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are subject to certain risks and uncertainties that could cause actual results, including projections of future cash balances and anticipated cash outflows, to differ materially from the statements made. Examples of such risks and uncertainties include: the risk that, as a development company with limited resources and no operating revenues, the Company's ability to continue as a going concern in the near term is highly dependent upon successful and timely advancement of its clinical development programs for istaroxime and AEROSURF®; risks that Windtree will be unable to secure significant additional capital as and when needed, or to access debt or equity financings, which could result in substantial equity dilution; risks related to Windtree's development programs, which may involve time-consuming and expensive pre-clinical studies and clinical trials and which may be subject to potentially significant delays or regulatory holds, or fail; risks related to technology transfers to contract manufacturers and manufacturing development activities, including with respect to formulation development, product and active pharmaceutical ingredient (API) release testing and related assays, and problems or delays encountered by Windtree, 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 Windtree 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 Windtree's products, and (ii) changes in the national or international political and regulatory environment may make it more difficult to gain regulatory approvals; risks related to Windtree's efforts to maintain and protect the patents and licenses related to its products; and other risks and uncertainties described in Windtree's filings with the Securities and Exchange Commission including the most recent reports on Forms 10-K, 10-Q and 8-K, and any amendments thereto.

Contact Information:
John Tattory
Senior Vice President and Chief Financial Officer
215.488.9418 or jtattory@windtreetx.com

Windtree Therapeutics, Inc.
Corporate Presentation
October 2019

OTCQB: WINT

WINDTREE THERAPEUTICS™

Forward-looking Statements

To the extent that statements in this presentation are not strictly historical, including statements about the Company's clinical development programs, business strategy, outlook, objectives, plans, intentions, goals, future financial conditions, future collaboration agreements, the success of the Company's product development activities, or otherwise as to future events, such statements are forward-looking, and are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. The forward-looking statements contained in this presentation are subject to certain risks and uncertainties that could cause actual results to differ materially from the statements made, including risks relating to the Company's recent merger with CVie Therapeutics. These risks are further described in the Company's periodic filings with the Securities and Exchange Commission (SEC), including the most recent reports on Forms 10-K, 8-K and 10-Q, and any amendments thereto ("Company Filings")

Under no circumstances shall this presentation be construed as an offer to sell or as a solicitation of an offer to buy any of the Company's securities. In addition, the information presented in this deck is qualified in its entirety by the Company Filings. The reader should refer to the Company Filings for a fuller discussion of the matters presented here.

Windtree Investment Highlights

- Late-stage pipeline of novel cardiovascular and pulmonary programs
  - Three phase 2 clinical programs and additional pre-clinical pipeline candidates in both cardiovascular and pulmonary indications
- Lead cardiovascular program, istaroxime (ista), is a first-in-class SERCA2a activator being developed for acute heart failure (AHF)
  - Phase 2 clinical trials demonstrated significant improvement in diastolic and systolic function
  - FDA Fast-Track designation granted in July 2019
  - New planned clinical study in early cardiogenic shock may provide a pathway to an accelerated review of this indication
- Lead pulmonary program, AEROSURF®, is being developed to provide noninvasive delivery of aerosolized KL4 surfactant to improve the management of respiratory distress syndrome (RDS) in premature infants
  - Completed phase 2 clinical trials show the potential to reduce nCPAP failure and need for intubation
  - Planned bridging study to support transition to phase 3 expected to leverage partner resources
  - FDA Fast-Track designation granted in September 2016
- Strong news flow with data readouts for both ista and AEROSURF as well as potential business development activities in next 12–18 months
- Public biopharma company (OTCQB:WINT) with market cap ~$113 million

Windtree Therapeutics Portfolio
Late Stage Programs in Cardiovascular and Acute Pulmonary

Cardiovascular

Istaroxime
for the Treatment of Acute Heart Failure

+ Pre-Clinical Oral, Heart Failure Candidates and Programs:

CV-IST2 (Next Generation Dual Action SERCA2a)
Oral & i.v. for chronic and acute heart failure

SERCA2a (Selective Action)
Oral & i.v. for chronic and acute heart failure

Rostafuroxin
for genetically targeted resistant hypertension and renal impairment

Acute Pulmonary

AEROSURF®
for noninvasive treatment of RDS

Lyophilized KL4 Surfactant (LS)
for RDS

+ Pre-Clinical Programs:

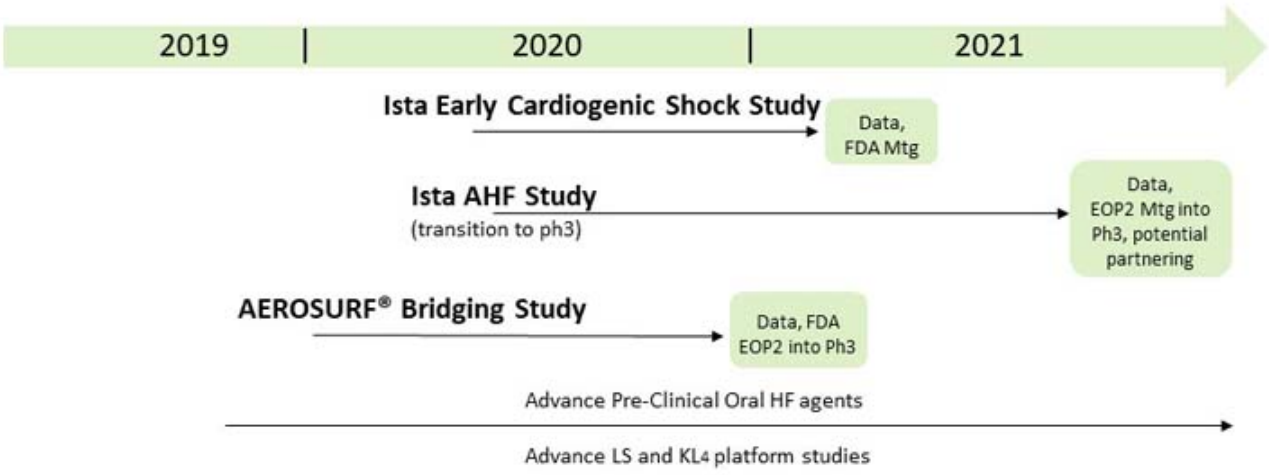
Eleison
aerosol oncology collaboration

KL4 Platform
for lung protection and drug delivery

Strategy for Value Creation

Planned Milestones

- **Three late-stage programs** focused on significant markets with unmet needs
- **Multiple clinical and business milestones which have the potential to be catalysts**
- Highly-experienced management team conducting **smart, rigorous execution** and leveraging opportunities for **acceleration and non-dilutive funding** of development
- **Business development initiatives for the realization of value**



Corporate Milestones:

Nasdaq Listing Application

Rosta deal process
(potential out-license)

WINDTREE THERAPEUTICS

Istaroxime

Dual Mechanism, SERCA2a Activator for the
Treatment of Acute Heart Failure
and Early Cardiogenic Shock

WINDTREE THERAPEUTICS

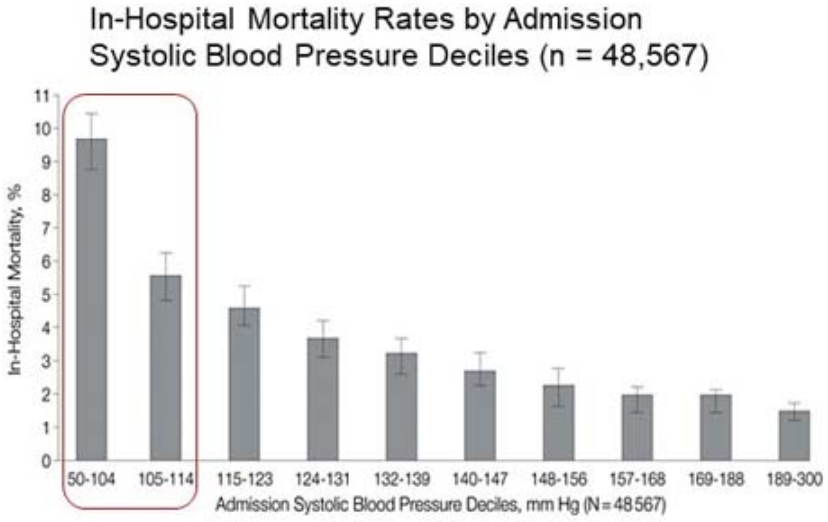
Heart Failure -
Significant Healthcare Issue with Significant Unmet Clinical Need

- 6 million patients in the U.S. and over 18 million worldwide. The prevalence of HF is on the rise as is mortality
- **#1 cause of hospitalizations in** patients over 65 years old **in the United States** and Western Europe with **greater than 1.3 million admissions annually in US and ~1.5 million in the EU**
- **Inpatient mortality** as high as 7 percent and 30-day mortality can exceed 10 percent
- **HF has a significant cost**. Estimates place direct hospital costs at >$18B annually in the U.S. alone. Heart failure is the most expensive of the Medicare diagnoses in the U.S.
- Due to the unmet need and lack of therapeutic advances, the **FDA issued new Heart Failure Guidance** in July 2019 reflecting greater flexibility in order to support development

Acute Heart Failure -
Significant Healthcare Issue with Significant Unmet Clinical Need

- Despite the need, there have not been meaningful new therapeutic advancements in acute heart failure for decades
- Current approaches to improve acute cardiac dysfunction are associated with unwanted effects:
  - Heart rhythm disturbances
  - Increased heart rate and myocardial oxygen demand
  - Decreased blood pressure
  - Potential damage to the heart muscle (increased troponin)
  - Worsening renal function
  - Mortality
- Patients with low blood pressure and peripheral hypoperfusion are at high risk for poor outcomes and are difficult to manage. They also are generally resistant to diuretic therapy and often discharged in a sub-optimal state

Cardiac Output, Blood Pressure and Renal Function are Critical Factors in Managing AHF Patients and Their Outcomes

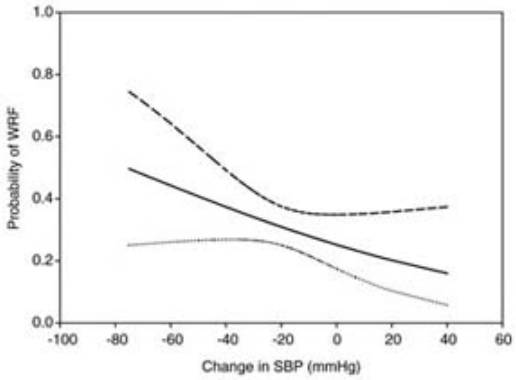


Gheorghiade, M. et al. JAMA 2006;296:2217-2226.

European Journal of Heart Failure (2011) 13, 961–967
doi:10.1093/eurjhf/hfr060

Early drop in systolic blood pressure and worsening renal function in acute heart failure: renal results of Pre-RELAX-AHF

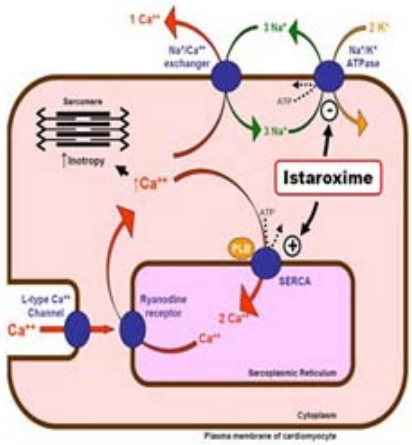
Adriaan A. Voors[1*], Beth A. Davison[2], G. Michael Felker[3], Piotr Ponikowski[4], Elaine Unemori[5], Gadi Cotter[2], John R. Teerlink[6], Barry H. Greenberg[7], Gerasimos Filippatos[8], Sam L. Teichman[5], and Marco Metra[9] on behalf of the Pre-RELAX-AHF study group



WINDTREE THERAPEUTICS

Istaroxime – Novel First-in-Class Therapy

- Novel intravenous agent designed to improve systolic contraction and diastolic relaxation and fill function of the heart
- Unique, ***dual*** **mechanism of effect that has been shown to impact *both* systolic and diastolic dysfunction**
  - Inhibition of the sodium-potassium pump and effects on the sodium-calcium exchanger results in more calcium available for contraction (systolic effect)
  - Stimulation of SERCA2a activity **enhances calcium reuptake** improving the relaxation-contraction cycle resulting in improved diastolic ventricular function

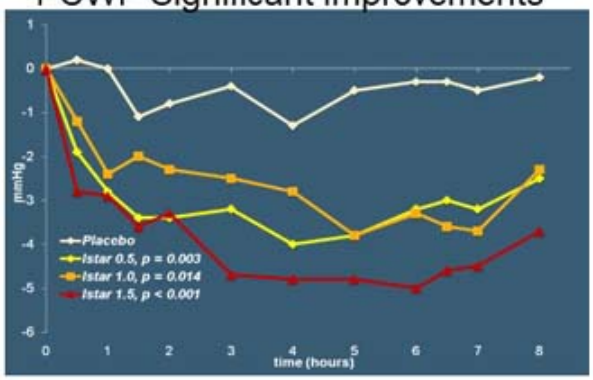


Istaroxime Phase 2a (HORIZON-HF) Study

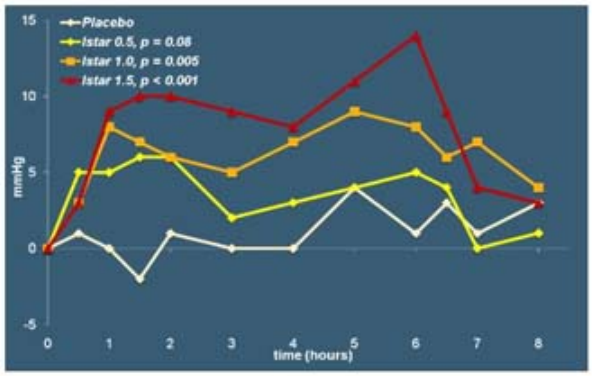
- Multicenter, double blind, placebo-controlled, doses 6-hour infusion of istaroxime 0.5, 1.0, 1.5 ug/kg/min, conducted in the EU
- Hospitalized with AHF, with criteria including:
  - LVEF ≤ 35%
  - SBP 90-150 mmHg
- N=120 (30/group)
- Significant improvement in PCWP, SBP, heart rate was lower. Istaroxime was generally well tolerated with no unexpected adverse events

Primary Endpoint:

PCWP Significant Improvements



Dose-dependent Increase in SBP



Istaroxime Phase 2b Study Design and Measures

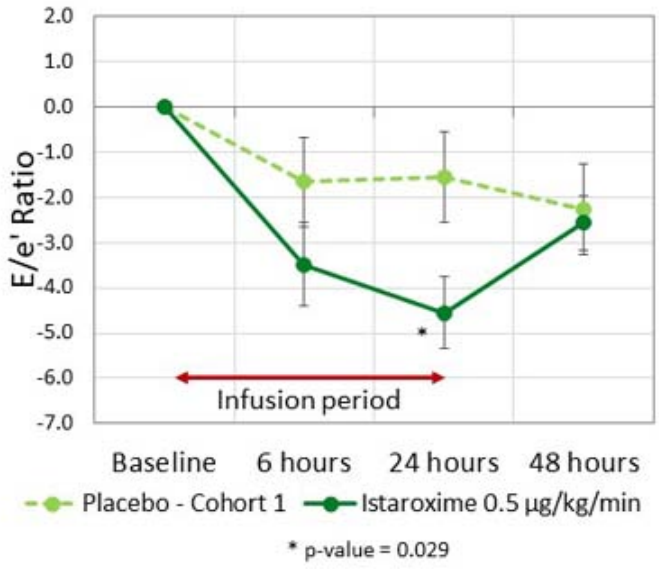
- After a positive phase 2a trial, the predecessor company conducted a phase 2b trial that was multicenter, double blind, placebo-controlled, parallel group
- Hospitalized for recurrent AHF (dyspnea plus need for IV furosemide ≥40 mg); adult population
  - Left Ventricle Ejection Fraction (LVEF) ≤ 40%, E/e' ratio >10
  - BNP ≥ 350 or NT-pro-BNP ≥1400 pg/mL
  - Systolic Blood Pressure (SBP) 90-125 mmHg
- N=120 (24 Italy, 96 China)
  3 arms (1:1:1): 0.5 or 1.0 µg/kg/min, or placebo dosed for 24 hours
- Outcome measures
  - Echo - primary endpoint: Change in E/e' at 24 hrs
  - BNP, cTnT, ventricular ectopy
  - Dyspnea measured by VAS

WINDTREE THERAPEUTICS

Primary Endpoint –

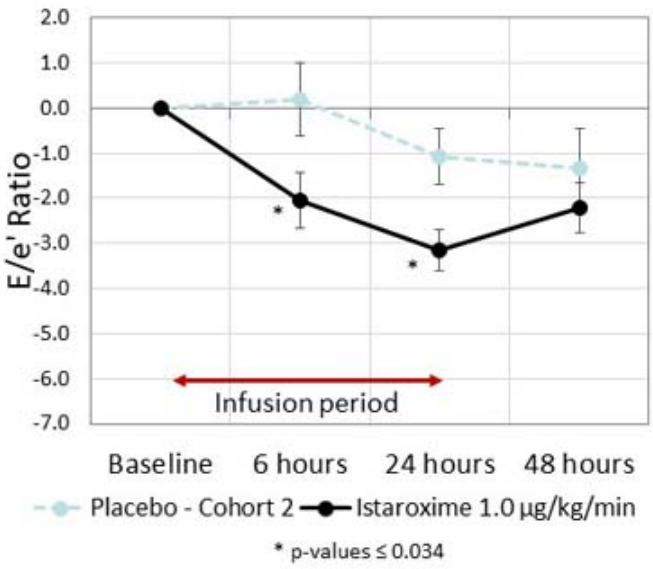
Significant Changes in E/e' Ratio

istaroxime 0.5 µg/kg/min vs. placebo



* p-value = 0.029

istaroxime 1.0 µg/kg/min vs. placebo



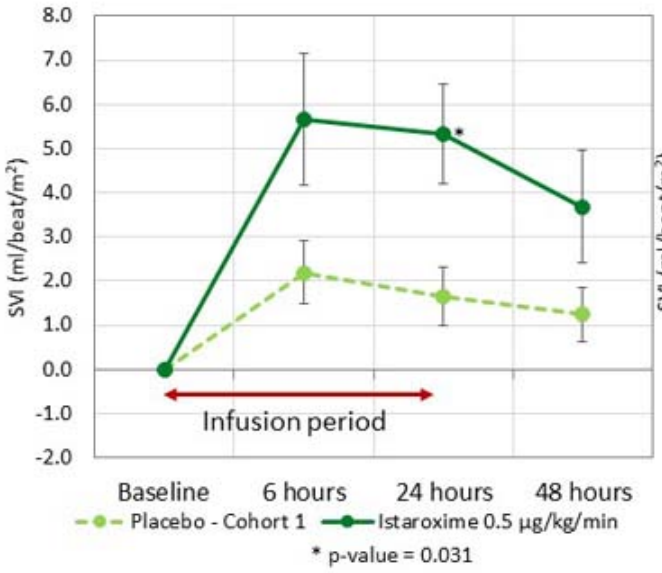
* p-values ≤ 0.034

Data shown as means and standard errors

WINDTREE THERAPEUTICS

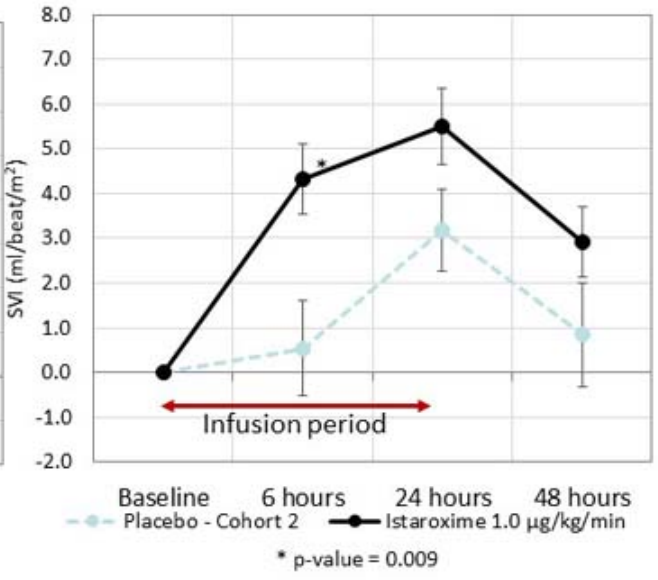
Substantial Change in Stroke Volume Index

istaroxime 0.5 µg/kg/min vs. placebo



* p-value = 0.031

istaroxime 1.0 µg/kg/min vs. placebo



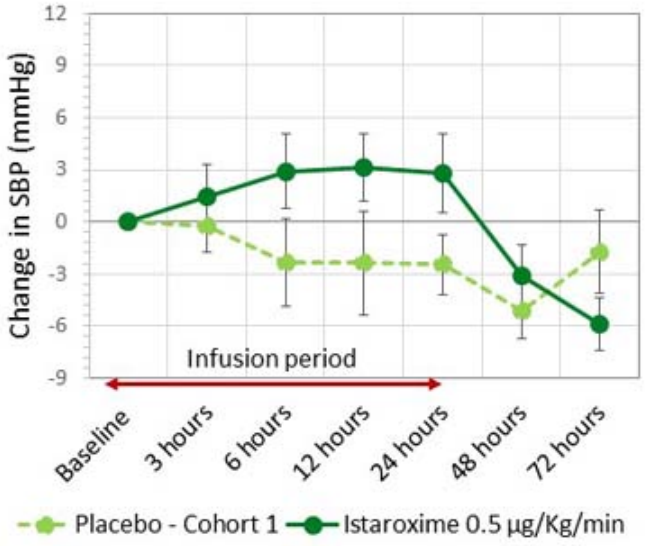
* p-value = 0.009

Data shown as means and standard errors

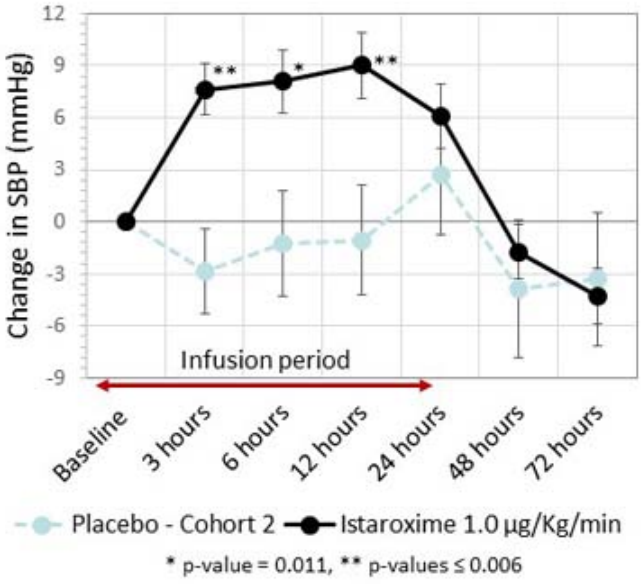
WINDTREE THERAPEUTICS

Systolic Blood Pressure Maintained or Increased During Treatment

istaroxime 0.5 µg/kg/min vs. placebo



istaroxime 1.0 µg/kg/min vs. placebo



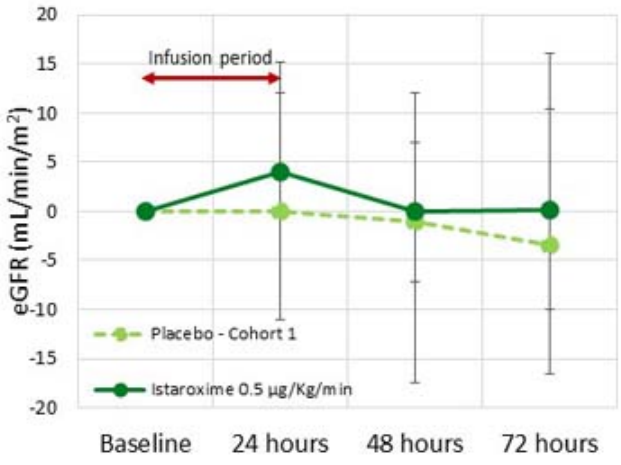
* p-value = 0.011, ** p-values ≤ 0.006

Data shown as means and standard errors

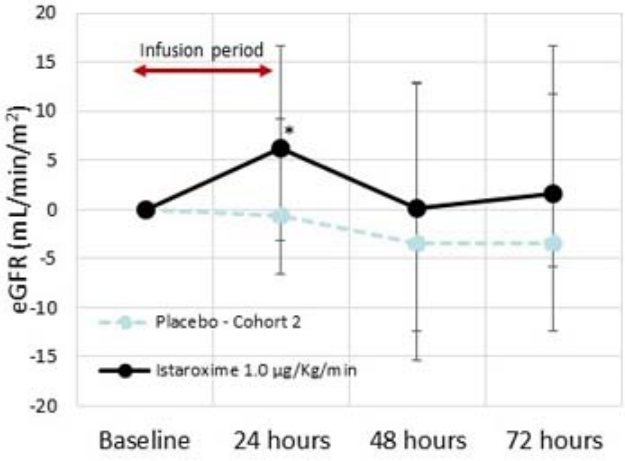
WINDTREE THERAPEUTICS

eGFR Maintained or Improved with Istaroxime

istaroxime 0.5 µg/kg/min vs. placebo



istaroxime 1.0 µg/kg/min vs. placebo

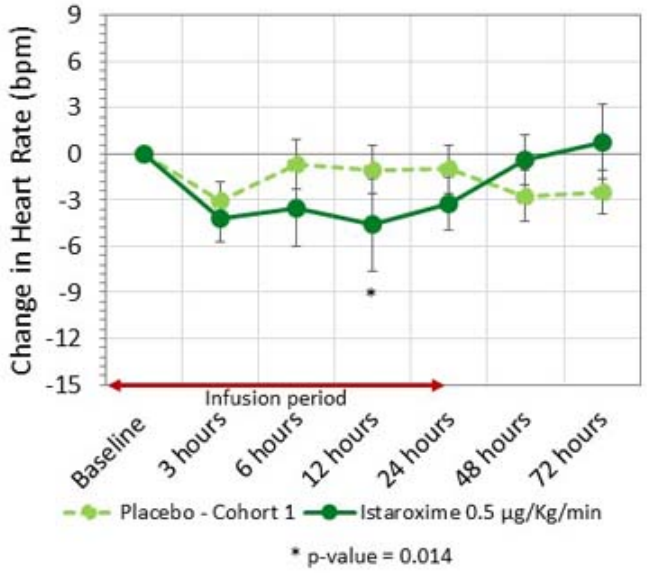


* p-value = 0.044

Data shown as median (IQR)

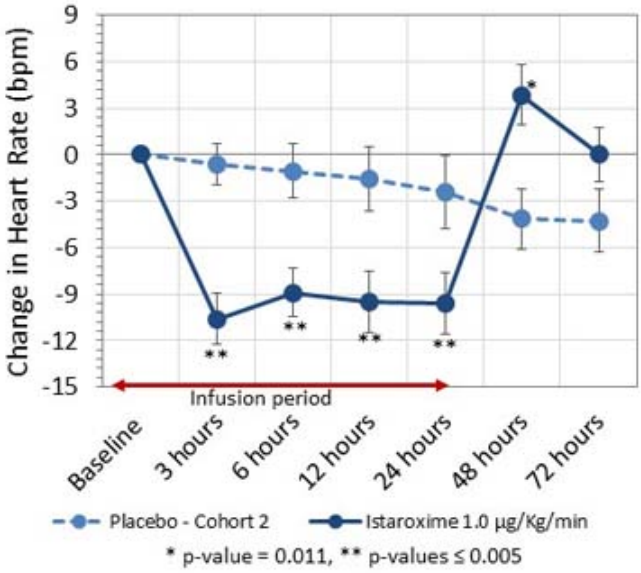
Heart Rate was Lowered During Treatment

istaroxime 0.5 µg/kg/min vs. placebo



* p-value = 0.014

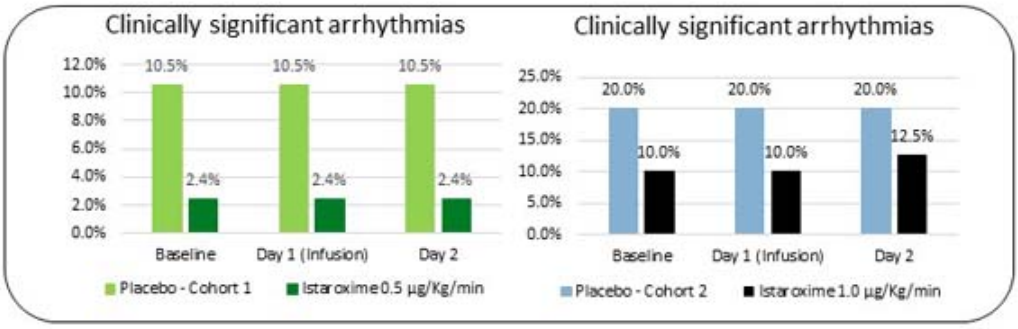
istaroxime 1.0 µg/kg/min vs. placebo

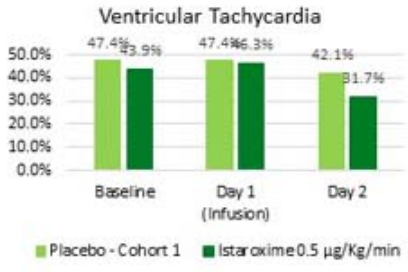


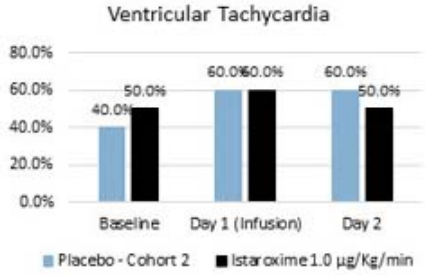
* p-value = 0.011, ** p-values ≤ 0.005

Data shown as means and standard errors

Favorable Profile Observed with 24-hour Holter Monitoring

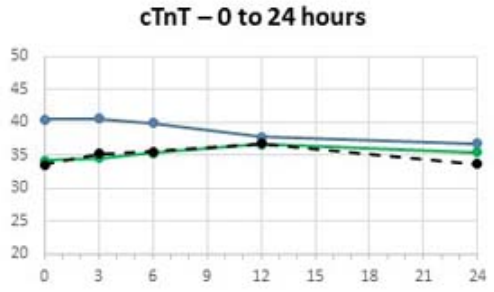


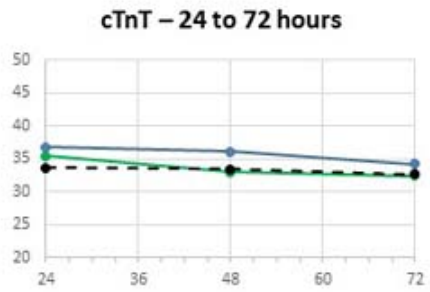


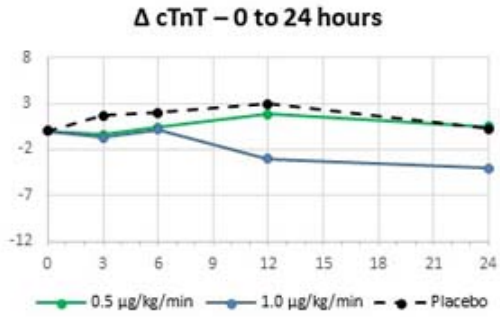


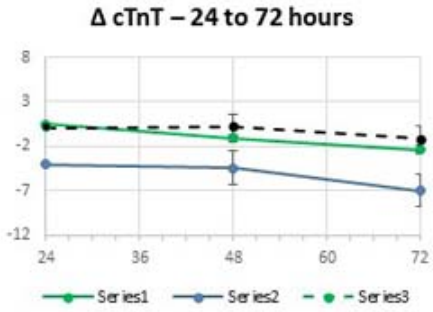
PVCs (n°/24 hours) shown as median, ventricular tachycardia and clinically significant arrhythmias shown as percentage of patients

No Meaningful Increases in Troponin (cTnT) During Treatment









Adverse Events

Event	Pooled placebo (n=39)	istaroxime 0.5 mg/Kg/min (n=41)	istaroxime 1.0 mg/Kg/min (n=40)
All adverse events	23 (59.0%)	31 (75.6%)	33 (82.5%)
Adverse events leading to discontinuation	1 (2.6%)	-	4 (10.0%)
Serious adverse events	2 (5.1%)	2 (4.9%)	6 (15.0%)
Cardiac death	-	-	1 (2.5%)
Cardiogenic shock	-	-	1 (2.5%)*
Cardiac failure	1 (2.6%)	2 (4.9%)	3 (7.5%)
Renal embolism	-	-	1 (2.5%)
Transient ischemic attack	1 (2.6%)	-	-
Hyperventilation	1 (2.6%)	-	-
Hypotension	1 (2.6%)	-	-
Adverse Drug Reactions†	10 (25.6%)	23 (56.1%)	25 (62.5%)
Cardiovascular††	**9 (23.1%)**	**4 (9.8%)**	**7 (17.5%)**
Gastrointestinal‡	2 (5.1%)	4 (9.8%)	14 (35.0%)
Infusion site pain/inflammation	-	20 (48.8%)	13 (32.5%)

Note: data shown as n° patients (%) - patients can have more than one event during the 30-day follow up period
* Same patient who then died, and 1 additional death occurred at Day 31 (cardiac death) outside the 30 day window
† Adverse Drug Reactions are AEs related to study drug
††Most common - arrhythmia, atrial fibrillation, cardiac failure, ventricular tachycardia
‡ Most common - abdominal pain, nausea, vomiting, diarrhoea

Istaroxime Phase 2b Study - Summary

- A 24-hour infusion of istaroxime at doses of 0.5 and 1.0 mg/kg/min was associated with significant improvements in diastolic and systolic cardiac function at 24 hours.
  - The primary endpoint, E/e' at 24 hours, was significantly ($p<0.05$) improved by both doses of istaroxime
  - Stroke volume was substantially increased at 24 hours
- Istaroxime maintained / increased systolic blood pressure; renal function also tended to improve. Additionally, heart rate decreased.
- Istaroxime was generally well tolerated with no unexpected adverse events; there were no major concerns related to arrhythmias and cTnT; pain at infusion site was reported primarily with short catheters and GI symptoms primarily with high dose.
- Results reproduced the favorable effects and safety profile seen in the phase 2a clinical trial. This study also supports SERCA2a stimulation as a novel and valid therapeutic target for AHF

Istaroxime – Acute Heart Failure – Program Status

1. The Company has worked with top Heart Failure advisors and has had positive engagement and guidance from the FDA
   - ✓ The FDA granted Fast Track designation to the program in July 2019
2. The Company plans to transition istaroxime to phase 3-ready and partnership position by executing an additional study that is expected to complete phase 2 and inform phase 3 to:
   - ✓ leverage the characteristics of istaroxime in a target population that most particularly may benefit from the unique attributes of the drug – patients with low blood pressure and/or diuretic resistant
   - ✓ increase infusion time to greater than 24 hours (ideally 48 – 72 hours)
   - ✓ include endpoints acceptable to the agencies for approval (and that support commercial / payer messaging)
3. The study is expected to commence in the second half 2020 and has the potential to be a major catalyst to the program and for the Company

Early Cardiogenic Shock Treatment

Istaroxime Potential Opportunity for Accelerated Approval Pathway

- Cardiogenic shock is a severe presentation of heart failure characterized by very low blood pressure and hypoperfusion accompanied by high PCWP and decreased urine output
  - Approximately 110,000 patients per year in the US/EU[1]
  - Early cardiogenic shock patients have SBP ~90-75mmHg
- Cardiogenic shock is an area of extreme unmet need with no satisfactory pharmacologic interventions to reverse the condition, thus it has a high associated mortality and morbidity
- Because of the unmet need, there are potential opportunities for an accelerated regulatory pathway and review. According to FDA published position and actions, approval in shock potentially could be based on blood pressure changes (assuming comparable mortality compared to control patients at 30 days)

1) Kosaraju A, Hai O. Cardiogenic Shock. [Updated 2019 Jan 25]. In: https://www.ncbi.nlm.nih.gov/books/NBK482255/

WINDTREE THERAPEUTICS

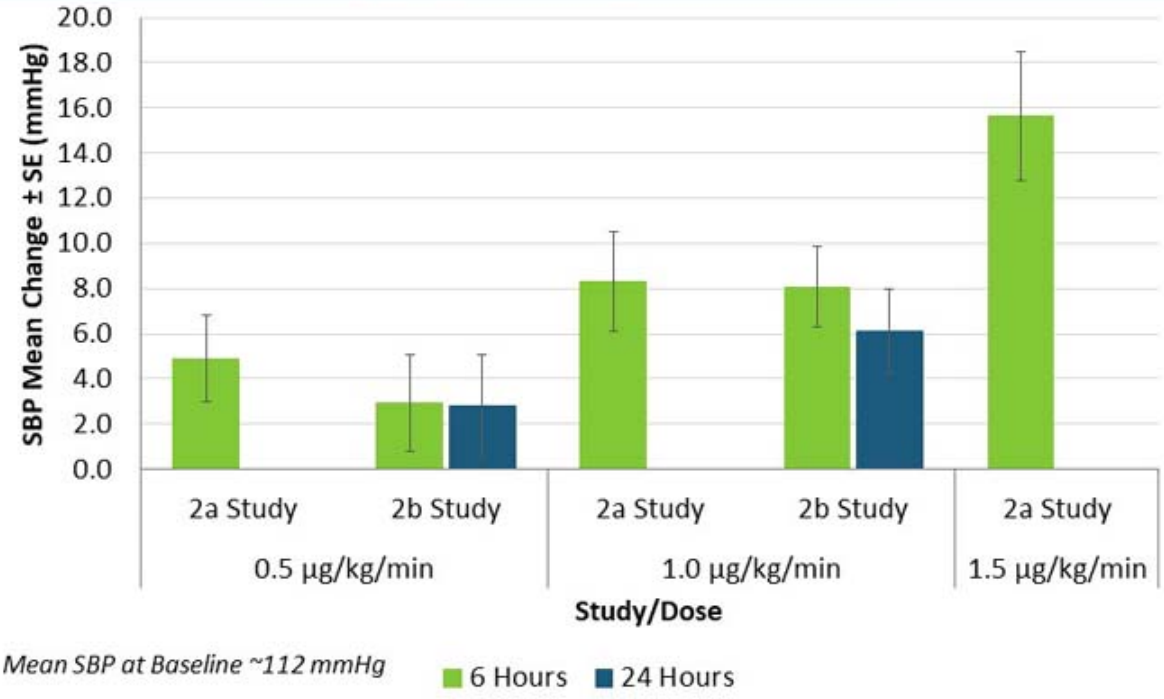
Istaroxime – Early Cardiogenic Shock

- FDA continues to recognize cardiogenic shock as an unmet medical need[1]
- FDA has outlined their current regulatory position regarding approval of drugs for shock
  - Sponsors are not required to show a benefit other than an increase in blood pressure to support approval of drugs to treat hypotension in the setting of shock
  - Precedent: NDA for Giapreza® (IV Angiotensin II), approved in 2017 for increasing MAP in distributive shock[2]

[1] CSRC Think Tank - July 24, 2019
[2] Senatore et al., Am J Cardiovasc Drugs, February 2019, Volume 19, Issue 1, pp 11–20 (https://doi.org/10.1007/s40256-018-0297-9)

Istaroxime SBP Change from Baseline to 6 or 24 Hours from the Phase 2a and 2b Dose Groups

Istaroxime has the potential to improve blood pressure and organ perfusion in patients with AHF



Mean SBP at Baseline ~112 mmHg

6 Hours 24 Hours

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Rationale for Istaroxime in Early Cardiogenic Shock

- Dose related changes in systolic blood pressure in the phase 2 clinical program suggest a meaningful increase in blood pressure may be achieved in early cardiogenic shock by istaroxime
- Improving systolic and diastolic cardiac function without increasing heart rate, risk for arrythmias, or myocardial oxygen demand (based on preclinical studies) would be beneficial in these patients
- The Company plans to execute a study in early cardiogenic shock while preparing to start the larger phase 2b acute heart failure study

Novel Heart Failure Portfolio-

Oral and IV SERCA2a Activators for Chronic & Acute Heart Failure

Dual Mechanism SERCA2a Activators

- SERCA2a activators with Na^+/K^+ pump inhibitory activities
- As oral and i.v. therapies for AHF and/or chronic heart failure (CHF)

Selective SERCA2a Activators

- Selective SERCA2a Activators devoid of any Na^+/K^+ pump inhibitory activities
- As oral and i.v. therapies for AHF and/or CHF
- Select SERCA2a is an attractive approach for heart failure with preserved ejection fraction (HFpEF)

These next generation agents and platform are to be part of a complete chronic and acute portfolio opportunity for licensing / partnership

Heart Failure is a therapeutic area of focus for many large pharmaceutical companies and SERCA2a is of particular interest

WINDTREE THERAPEUTICS

AEROSURF®

Synthetic KL4 Surfactant with
Proprietary Aerosol Delivery System
for the Treatment of RDS

Respiratory Distress Syndrome (RDS)
Current Treatment Pathways

Premature infants experience RDS due to underdeveloped lungs lacking endogenous surfactant. Surfactant helps keep lungs open between breaths and proper gas exchange

Initial treatment options include invasive and noninvasive methods:

Surfactant therapy + Invasive mechanical ventilation (IMV)	VS.	**nCPAP support until endogenous surfactant production**
• Animal-derived surfactant • Delivered via intubation, usually in combination with mechanical ventilation		• Noninvasive nasal delivery of continuous positive airway pressure (nCPAP) • Supports breathing

TRADE-OFFS

Timely therapy delivery vs. Exposure to known significant complications

Avoid exposure to significant complications vs. Foregoing surfactant treatment results in notable nCPAP failure rate

Ultimately, more than 50% of RDS infants are intubated and ventilated

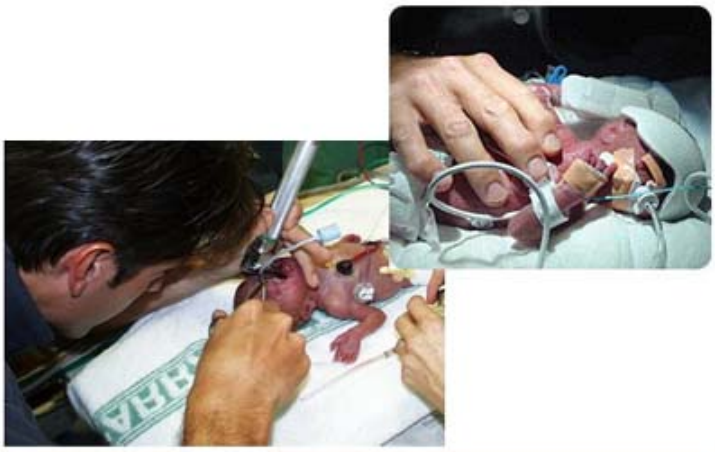
WINDTREE THERAPEUTICS

Source: Windtree and third-party market research

Clinicians Seeking a Noninvasive Way to Deliver Surfactant

What is wanted[1]:

- ✓ **Avoid the risks, complications and clinical instability** associated with delivery of surfactant therapy via intubation and mechanical ventilation
- ✓ Possibility of **repeat doses**
- ✓ Enable **administration by non-specialist staff**
- ✓ **Reduce costs of treatment**
- ✓ **Better long-term outcomes**



Reported Potential Value Drivers[2]:

- **#1 stated need for RDS management**
- **Reduction in bronchopulmonary dysplasia (BPD) would make standard of care**
- **Sell drug *and* device-related supplies; reduce hospital costs by avoiding intubation and mechanical ventilation**
- **Market expansion to areas not qualified to invasively deliver surfactants**

1. Pillow & Minocchieri: Neonatology, 2012
2. N=278 Neonatologists, US & EU; WINT primary market research (2014)

WINDTREE THERAPEUTICS

Windtree Technology Platform - AEROSURF®

Proprietary Synthetic KL4 Surfactant + **Proprietary Innovative Aerosol Delivery System (ADS)**

Structurally similar to human lung surfactant

Liquid KL4 surfactant (intratracheal instillate) for RDS **approved by the FDA**

Lyophilized KL4 surfactant currently being developed for **AEROSURF**

Utilizing pressure and heated capillary has demonstrated ability to **aerosolize KL4 surfactant**

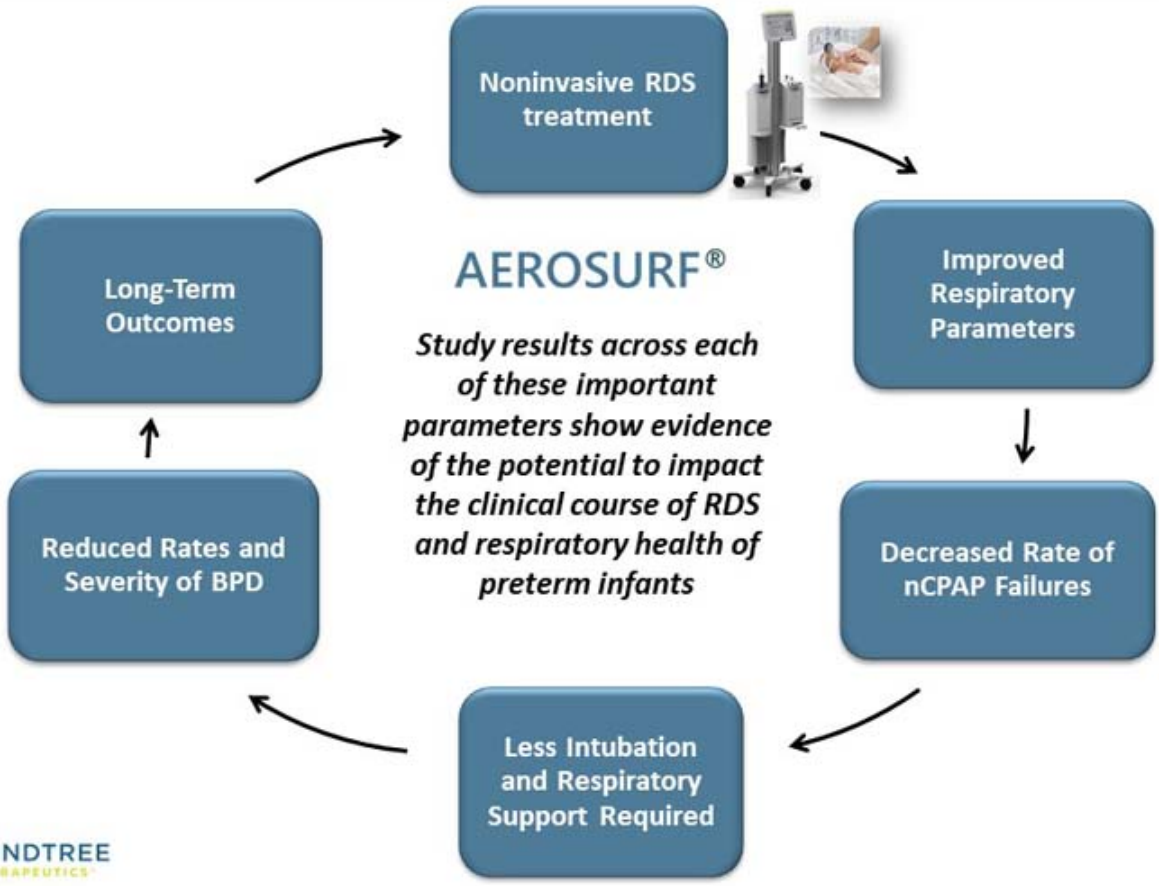
Controlled, effective and reproducible performance validated in studies

- KL4 surfactant has been shown to improve lung function in premature infants, resulting in decreased nCPAP failures and need for invasive intubation
- KL4 surfactant also has anti-inflammatory and other potentially positive attributes

WINDTREE THERAPEUTICS

AEROSURF® - Potential to Impact on the Clinical Course of RDS

Building Evidence From Nearly 400 Patients Studied



WINDTREE THERAPEUTICS

AEROSURF® Program Evolution and Strategy

Mitigating Risks and Strengthening Our Approach

Program Evolution

- The four phase 2a and 2b clinical trials have **reproduced efficacy in reducing nCPAP failure and the need for intubation** and observed **important positive BPD data.**
  - AEROSURF has received Fast Track and Orphan designations
- The Company has transitioned to the **newly-developed ADS**, which is designed for consistent performance, faster time to treatment and improved ease of use, potentially enabling better clinical outcomes
- The AEROSURF safety profile supports **employing a dosing regimen to deliver more surfactant in a shorter period of time**

Program Strategy

- **Execute a small (n=70) Bridging Study to transition to EOP2 / phase 3,** demonstrate that the new ADS works, and supplement phase 2 data
- **Leverage China** - the largest market for RDS and surfactants - and use the partnership with Lee's to gather data in China pre-phase 3 (after site vetting and profiling). The Company expects that development in China will be funded under Lee's license agreement
- **The Company plans to continue ongoing Business Development activities and potentially identify and enter into one or more non-dilutive transactions**

Rostafuroxin

for genetically targeted resistant hypertension and renal impairment

WINDTREE THERAPEUTICS

Hypertension Market –
A Unique, Genetically-Targeted Approach

- **Hypertension is a very large market with high unmet need**
  - Over 1/3 of the adult population in the U.S. has hypertension and the majority of treated patients (50-85% globally) do not reach target for control. Well known that ethnicity can impact response to different classes of agents
- **Uncontrolled/resistant hypertension has been associated with certain genetic subsets of the population**
  - Adducin polymorphisms and endogenous ouabain can trigger hypertension by enhancing renal tubular sodium reabsorption and increasing vascular tone
- **Rostafuroxin is designed to be a potent and selective antagonist of ouabain and of the mutant adducin molecule and the functional effects**
  - Phase 2a and 2b demonstrated the possibility to reduce blood pressure in a ***genetically identified subset of patients representing approximately 28%*** *of hypertensives*
  - While the blood pressure reduction in Caucasians was notable in the phase 2a and 2b trials, blood pressure response in Chinese patients was dose ordered but significantly less pronounced at the same doses. The Company is exploring the reasons for the differential response in populations.

Rostafuroxin Next Steps

1. Complete pharmaceutical development work for final formulation

2. Continue ongoing work to explain the ethnic differences seen in the Phase 2b clinical trial, including a more sensitive assay to measure drug concentration

3. Seek to develop rostafuroxin into an asset that is attractive for partnering and conduct business development to identify a transaction - including with companies that have previously expressed and interest.

Financial Update

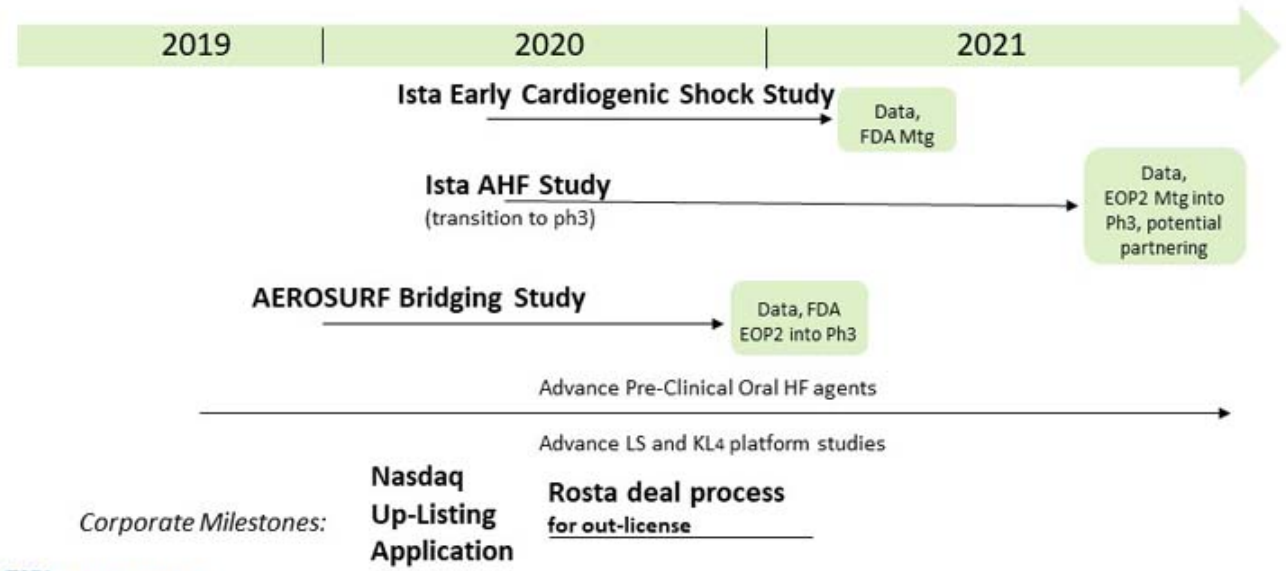
As of June 30, 2019

- Cash and marketable securities of $6.1 million as of June 30, 2019
  - Supports development activities, operations and debt service through October 2019
  - The Company is actively engaged in discussions with a number of potential counterparties to secure additional required capital
- Debt of $7.5 million
  - $4.5 million in a bank credit facility currently due in March 2020 (under discussion with bank to extend to 2H 2021)
  - $3.0 million due to Lee's Pharmaceuticals
- Fully diluted outstanding shares of 46.4 million and 72.0 million available for future issuance
  - Market cap ~$113 million (10/11/19)

Strategy for Value Creation

Planned Milestones

- ✓ **Ista:** conduct clinical study of early cardiogenic shock to explore potential accelerated pathway for approval of this indication. Complete ista phase 2 clinical program and develop strong phase 3 and partnership position; to create added value, advance oral product candidates through proof of concept.
- ✓ **AEROSURF®:** transition to Phase 3 with bridging study; leverage partnerships and non-dilutive funding.
- ✓ **Rosta:** out-license and use proceeds to provide non-dilutive funding of other, core programs.
- ✓ **Investment Activities:** Nasdaq listing application; seek additional clinical and BD activities.



Windtree Therapeutics

"Striving to deliver Hope for a Lifetime!"

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