UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 8-K

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

Date of Report (Date of earliest event reported): November 14, 2022

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

Delaware	**000-26422**	**94-3171943**
(State or other jurisdiction of incorporation or organization)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

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

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

Not Applicable
(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 (see General Instruction A.2. below):

☐ 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**
Common Stock, par value $0.001 per share	WINT	The Nasdaq Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

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 November 14, 2022, Windtree Therapeutics, Inc. (the "Company") issued a press release announcing its financial results for the quarter ended September 30, 2022. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

The information contained in this Item 2.02 (including Exhibit 99.1) is being furnished and 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 and shall not be deemed to be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Item 8.01 Other Events

On November 14, 2022, the Company updated information reflected in a slide presentation, which is attached as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference. Representatives of the Company will use the updated presentation in various meetings with investors from time to time.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

The following exhibits are being filed herewith:

Exhibit No.	Document
99.1	Press Release of Windtree Therapeutics, Inc., dated November 3, 2022, announcing financial results for the quarter ended September 30, 2022, furnished herewith.
99.2	Investor Presentation of Windtree Therapeutics, Inc.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

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, thereunto duly authorized.

Windtree Therapeutics, Inc.

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

Date: November 14, 2022

Windtree Therapeutics Reports Third Quarter 2022 Financial Results and Provides Key Business Updates

WARRINGTON, PA – November 14, 2022 – Windtree Therapeutics, Inc. (NasdaqCM: WINT), a biotechnology company focused on advancing multiple late-stage interventions for cardiovascular disorders, today reported financial results for the third quarter ended September 30, 2022 and provided key business updates.

"The Company had several notable deliverables this quarter and continues to focus on progressing its planned development of istaroxime. The positive results of the SEISMiC study of istaroxime in early cardiogenic shock have been well received in many scientific forums. At the same time, our team has been active in working to advance istaroxime into the next clinical trial in early cardiogenic shock. To support development and company operations, we are addressing our resources by exploring options for financing, as well as actively engaging in business development activities, both licensing and strategic," said Craig Fraser, President and Chief Executive Officer of Windtree. "Additionally, the out-licensing of our acute pulmonary KL4 surfactant platform this quarter supports our portfolio and resource prioritization strategy as we focus on istaroxime and the significant opportunity in the major markets of cardiogenic shock and heart failure. With all that we are executing, we look forward to providing our shareholders with updates on our plans and progress."

Key Business Updates

- Announced a Global License Agreement with Lee's Pharmaceutical (HK) Limited (Lee's (HK)) and its affiliate Zhaoke Pharmaceutical (Hefei) Co. Ltd. (Zhaoke), for the development and commercialization of Windtree's acute pulmonary pipeline treatments, KL4 surfactant and drug/device combination, AEROSURF®, for the treatment of preterm infants with respiratory distress syndrome and other potential applications. Under terms of the global license agreement, Lee's (HK) and Zhaoke received a global license to develop and commercialize Surfaxin®, lyophilized lucinactant, and AEROSURF for any potential indications and applications. Lee's (HK) and Zhaoke will be responsible for funding all development, intellectual property, manufacturing, and commercialization activities and provide developmental, regulatory, and eventual commercial sales milestones for Windtree of up to $78.9 million plus potential double-digit royalties. Windtree had previously granted a regional license to Lee's (HK) and Zhaoke for KL4 and AEROSURF for the territory of Greater China, for which Windtree received an upfront payment, and this new agreement expands that territory globally. With the execution of this agreement, Windtree no longer has ongoing maintenance and operating costs for the KL4 surfactant platform.

- Announced a Late Breaker presentation of the Company's positive Phase 2 SEISMiC study at the Heart Failure Society of America Annual Scientific Meeting in Washington, D.C. The presentation described dose response data from the trial, where the primary endpoint was the improvement in systolic blood pressure over the first six hours of study drug infusion. Both doses improved the blood pressure profile through 24 hours.

- Announced the publication of positive results of the Company's Phase 2 istaroxime study in early cardiogenic shock in the European Journal of Heart Failure. The study entitled, "Safety and efficacy of istaroxime in patients with acute heart failure-related pre-cardiogenic shock – a multicentre, randomized, double-blind, placebo-controlled, parallel group study (SEISMiC)" showed significant improvement in blood pressure profiles that persisted through 24 hours.

- Announced a Notice of Allowance from the U.S. Patent and Trademark office (USPTO) for a new istaroxime patent. A notice of allowance is issued by the USPTO to indicate that the application has passed its examination. The U.S. Patent, titled: "*Istaroxime-containing Intravenous Formulation for the Treatment of Acute Heart Failure (AHF)*" is a continuing patent application of the expedited U.S. Track One filing by Windtree. The claims cover longer infusion durations of istaroxime for improved outcomes in the treatment of acute heart failure. In particular, the claims are directed to an improvement in diastolic heart function following administration of istaroxime by intravenous infusion for six hours or more, which Windtree attributes to the SERCA2a mechanism of action of istaroxime and its metabolites.

- Presented at two Wall Street investor conferences, including the Ladenburg Thalmann Healthcare Conference and H.C. Wainwright's 24th Annual Global Investment Conference.

- Held an Oppenheimer virtual fireside chat on istaroxime in heart failure and cardiogenic shock. The fireside chat featured perspectives from Alexandre Mebazaa, MD, PhD, of Hôpital Lariboisière, Paris, France on the immense need for pharmacologic innovation in cardiogenic shock.

Select Financial Results for the Third Quarter ended September 30, 2022

For the third quarter ended September 30, 2022, the Company reported an operating loss of $4.7 million, compared to an operating loss of $8.1 million in the third quarter of 2021. Included in operating loss for the third quarter of 2022 is non-cash expense of $0.5 million related to the impairment of goodwill

Research and development expenses were $1.5 million for the third quarter of 2022, compared to $4.7 million for the third quarter of 2021. The decrease in research and development expenses is primarily due to (i) a decrease of $1.9 million related to the KL4 surfactant platform as we continue to focus our resources on the development of our istaroxime pipeline; (ii) a decrease of $0.5 million in non-cash stock-based compensation expense; (iii) a decrease of $0.5 million for expenditures related to the development of istaroxime for AHF; and (iv) a decrease of $0.3 million following the completion of enrollment in the SEISMiC study in March 2022.

General and administrative expenses for the third quarter of 2022 were $2.7 million, compared to $3.5 million for the third quarter of 2021. The decrease in general and administrative expenses is primarily due to (i) a decrease of $0.4 million in professional fees; and (ii) a decrease of $0.4 million in non-cash stock-based compensation expense.

The Company reported a net loss of $4.1 million ($0.13 per basic share) on 31.1 million weighted-average common shares outstanding for the quarter ended September 30, 2022, compared to a net loss of $8.2 million ($0.31 per basic share) on 26.7 million weighted average common shares outstanding for the comparable period in 2021.

As of September 30, 2022, the Company reported cash and cash equivalents of $8.4 million, which is expected to be sufficient to fund operations into the second quarter of 2023.

Readers are referred to, and encouraged to read in its entirety, the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, which will be filed with the Securities and Exchange Commission on November 14, 2022, and includes detailed discussions about the Company's business plans and operations, financial condition, and results of operations.

About Windtree Therapeutics
Windtree Therapeutics, Inc. is advancing multiple 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 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 KL4 surfactant platform, to its licensee, 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 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 and the Company's other product candidates; 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 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; 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; 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 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.

Contact Information:
Monique Kosse
LifeSci Advisors
212.915.3820 or monique@lifesciadvisors.com

+++++ Tables to Follow +++++

WINDTREE THERAPEUTICS, INC. AND SUBSIDIARIES
Consolidated Balance Sheets

(in thousands, except share and per share data)

	September 30, 2022	December 31, 2021
	Unaudited	
ASSETS		
Current Assets:		
Cash and cash equivalents	$ 8,436	$ 22,348
Prepaid expenses and other current assets	1,596	1,143
Total current assets	10,032	23,491
Property and equipment, net	286	1,011
Restricted cash	154	154
Operating lease right-of-use assets	1,964	2,381
Intangible assets	32,070	32,070
Goodwill	3,592	15,682
Total assets	$ 48,098	$ 74,789
LIABILITIES & STOCKHOLDERS' EQUITY		
Current Liabilities:		
Accounts payable	$ 410	$ 693
Accrued expenses	2,496	3,408
Operating lease liabilities - current portion	416	528
Loans payable - current portion	629	294
Total current liabilities	3,951	4,923
Operating lease liabilities - non-current portion	1,732	2,071
Restructured debt liability - contingent milestone payments	15,000	15,000
Other liabilities	3,800	3,800
Deferred tax liabilities	6,195	7,114
Total liabilities	30,678	32,908
Stockholders' Equity:		
Preferred stock, $0.001 par value; 5,000,000 shares authorized; 0 shares issued and outstanding	-	-
Common stock, $0.001 par value; 120,000,000 shares authorized at September 30, 2022 and December 31, 2021; 32,646,735 and 28,268,950 shares issued at September 30, 2022 and December 31, 2021, respectively; 32,646,711 and 28,268,926 shares outstanding at September 30, 2022 and December 31, 2021, respectively	33	28
Additional paid-in capital	835,281	830,231
Accumulated deficit	(814,840)	(785,324)
Treasury stock (at cost); 24 shares	(3,054)	(3,054)
Total stockholders' equity	17,420	41,881
Total liabilities & stockholders' equity	$ 48,098	$ 74,789

WINDTREE THERAPEUTICS, INC. AND SUBSIDIARIES
Consolidated Statements of Operations

(in thousands, except per share data)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	**2021**	**2022**	**2021**
Expenses:				
Research and development	$ 1,543	$ 4,680	$ 9,883	$ 13,311
General and administrative	2,653	3,467	8,548	11,507
Loss on impairment of goodwill	454	-	12,090	-
Loss on impairment of intangible assets	-	-	-	37,770
Total operating expenses	4,650	8,147	30,521	62,588
Operating loss	(4,650)	(8,147)	(30,521)	(62,588)
Other income (expense):				
Interest income	39	1	57	90
Interest expense	(14)	(14)	(40)	(101)
Other income (expense), net	569	(53)	988	(296)
Total other income (expense), net	594	(66)	1,005	(307)
Loss before income taxes	(4,056)	(8,213)	(29,516)	(62,895)
Deferred income tax benefit	-	-	-	8,332
Net loss	$ (4,056)	$ (8,213)	$ (29,516)	$ (54,563)
Net loss per common share				
Basic and diluted	$ (0.13)	$ (0.31)	$ (1.00)	$ (2.31)
Weighted average number of common shares outstanding				
Basic and diluted	31,135	26,704	29,554	23,616


Windtree Therapeutics
Company Overview
November 14, 2022
WINDTREE
THERAPEUTICS™
(NASDAQ: WINT)

Forward-Looking Statements

This presentation includes forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These statements, among other things, include 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. The forward-looking statements provide our current expectations or forecasts of future events and financial performance and may be identified by the use of forward-looking terminology, including such terms as "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "will," "should," "could," "targets," "projects," "contemplates," "predicts," "potential" or "continues" or, in each case, their negative, or other variations or comparable terminology, though the absence of these words does not necessarily mean that a statement is not forward-looking. We intend that all forward-looking statements be subject to the safe-harbor provisions of the Private Securities Litigation Reform Act of 1995. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. These risks and uncertainties are further described in the Company's periodic filings with the Securities and Exchange Commission ("SEC"), including the most recent reports on Form 10-K, Form 10-Q and Form 8-K, and any amendments thereto ("Company Filings"). Moreover, we operate in an evolving environment. New risks and uncertainties may emerge from time to time, and it is not possible for management to predict all risks and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

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 Therapeutics and Istaroxime Highlights

- **Biopharmaceutical company with advanced clinical focused on significant acute CV markets with high unmet needs and with supportive regulatory paths and designations** (NASDAQ: WINT)
- **Through three Phase 2 global studies, lead asset istaroxime has consistently demonstrated a highly unique and attractive profile**
  - It is the only acute heart failure or shock drug that has demonstrated both significant improvement in cardiac function of a failing heart, as well as rapid and significant improvement in blood pressure, with what so far has been a differentiating safety profile (avoiding many of the use-limiting side effects of existing therapies)
- **Recent positive Phase 2 study with istaroxime in early cardiogenic shock (ECS) paves the way for what we believe is a relatively fast and less expensive developmental and regulatory pathway**
  - Precedent shows blood pressure response can be acceptable as the primary endpoint in a pivotal shock study. Additionally, istaroxime is demonstrating significant other benefits that we plan to build upon in the larger phase 3 to create a strong, evidence-based clinical and pharmacoeconomic positioning
  - Given what we believe to be an attractive opportunity that may be pursued with less spend and have faster time to market, cardiogenic shock has become the organization's priority and focus
- **Highly experienced management team and company leadership**

Pipeline

Lead Products	Indication	Phase	Development Status	Regulatory Status
Istaroxime	Early Cardiogenic Shock	Phase 2	• Positive Phase 2 study • Planning the execution of the next study and plans to meet with regulatory agencies regarding development path	*Potential for Breakthrough Designation*
Istaroxime	Acute Heart Failure	Phase 2b	• Plan a second Phase 2b clinical trial in ~300 patients targeted to start once clinical trial operations are fully funded	*FDA Fast Track Designation*
Oral SERCA2a Activators	Chronic Heart Failure, including potentially HFpEF	Preclinical	• Chronic and Acute Heart Failure • Target for collaboration/partnership	
Rostafuroxin	Genetically Associated Hypertension	Phase 2b	• Out-licensing opportunity	
KL4 Surfactant and AEROSURF	KL4 surfactant Drug/Device Tx for RDS and potential other applications	Phase 2b	• Global out-license to Lee's Pharmaceutical and Zhaoke Pharmaceutical	*FDA Fast Track Designation, Orphan Drug*

Istaroxime

Early Cardiogenic Shock

Potential indication in active clinical development

WINDTREE THERAPEUTICS

Cardiogenic Shock

A severe presentation of heart failure characterized by **very low blood pressure and hypoperfusion** accompanied by high filling pressures of the heart and decreased urine output. It is a **treatment emergency**

- Caused by severe impairment of cardiac function that results in diminished cardiac output, end-organ hypoperfusion and hypoxemia
- Commonly requires pharmacological or mechanical intervention to increase SBP to >90mmHg and improve tissue perfusion
- High in-hospital mortality (~30-40%) and substantial morbidity in survivors[1]
- Represents an approximate $1.25B total market potential[2]

WINDTREE THERAPEUTICS

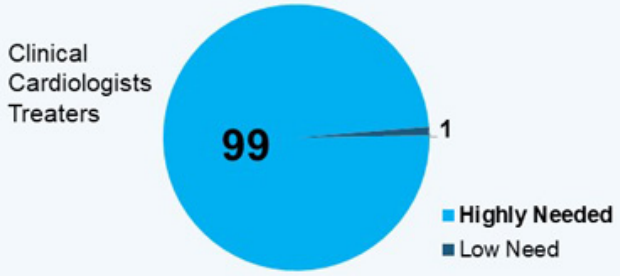
1) Kolte D, American Heart Association; 2014 Jan 13
2) Estimates from claims data and epi data September 2021, multiplied by assumed various regional prices

Early Cardiogenic Shock Treatment

Istaroxime Potential Opportunity to Address Significant Unmet Need

- No satisfactory pharmacological intervention to reverse the conditions
  - 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
- A therapy that can be used **earlier** to rapidly **improve blood pressure and cardiac function without unwanted side effects** is needed

100 U.S. Cardiologists *questioned on degree of* ***unmet need for new innovative pharmacologic treatments for ECS***



- ✓ **84%** of the cardiologists responded they would be **likely to extremely likely to use** istaroxime for early cardiogenic shock patients
- ✓ Majority responded they would position utilization before use of other existing classes of therapies such as inotropes and vasopressors

WINDTREE THERAPEUTICS

Market research conducted by Sermo, a leading provider of real time physician insights

Istaroxime – Novel First-in-Class Therapy

Novel intravenous agent designed to **improve systolic contraction *and* diastolic relaxation of the heart**

Dual Mechanism of Action

1 **Inhibition of the sodium-potassium pump and effects on the sodium-calcium exchanger results in increased contraction**

Istaroxime

2 **Stimulation of SERCA2a activity enhances calcium reuptake resulting in improvement of the diastolic relaxation and subsequent contraction cycle**

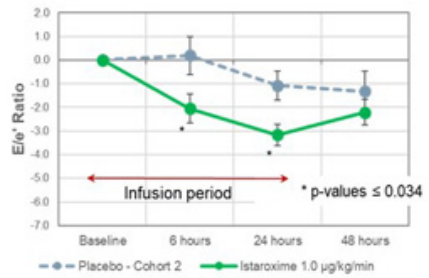
Impact on both systolic and diastolic dysfunction

WINDTREE THERAPEUTICS

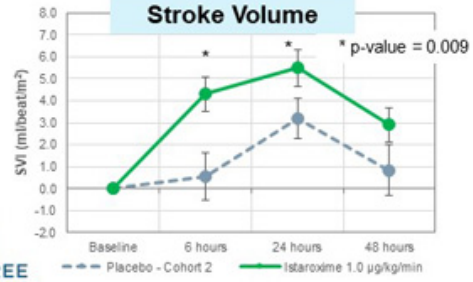
Rationale for Istaroxime in Cardiogenic Shock Came from AHF Phase 2 Trials

E/e' (cardiac filling pressure)

Istaroxime 1.0 µg/kg/min vs. placebo



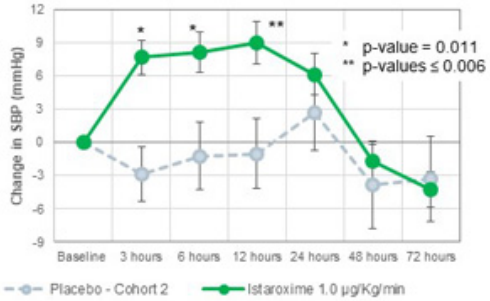
Stroke Volume



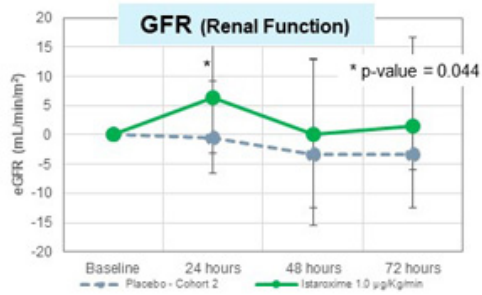
Improved cardiac function ***and*** SBP along with a favorable renal profile

Systolic Blood Pressure (SBP)

Istaroxime 1.0 µg/kg/min vs. placebo



GFR (Renal Function)



WINDTREE THERAPEUTICS

Early Cardiogenic Shock Treatment
Istaroxime Potential Opportunity for Accelerated Pathway

Potential for a relatively fast and less expensive developmental and regulatory pathway

FDA Regulatory Commentary with Break-Through Therapy Designation Potential

Sponsors are potentially **not required to show benefit other than an increase in blood pressure to support approval of drugs to treat hypotension in the setting of shock**[1]

Precedent NDA: Giapreza® (IV Angiotensin II), approved in 2017 for increasing MAP in distributive shock – a different type of shock, not a competitor to istaroxime in early cardiogenic shock)[2] Precedent also indicates potential accelerated regulatory pathway and review opportunities

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

SEISMiC Early Cardiogenic Shock Study

Clinical strategy: Start development with patients in early cardiogenic shock caused by severe heart failure

60 patients in early cardiogenic shock (SBP 75-90mmHg) with AHF

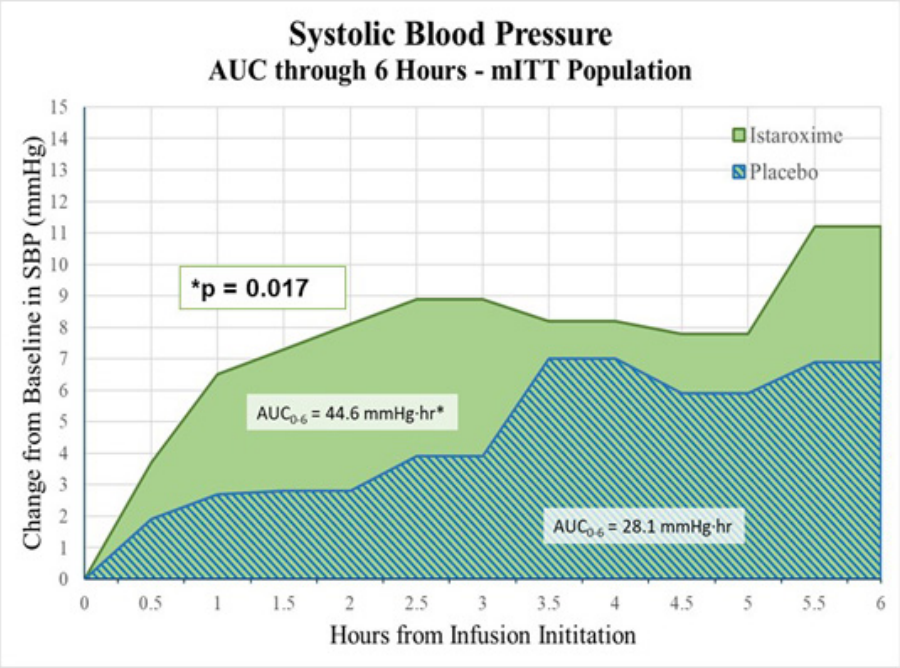
Study drug was infused for 24 hours in a 1:1 randomization to placebo or istaroxime. Two istaroxime target doses were evaluated, 1.5µg/kg/min in the first group and 1.0 µg/kg/min in the next group.

Primary endpoint was SBP AUC at 6 hours comparing istaroxime to placebo

Secondary measures included: SBP profile at 24 hours, echocardiology measures associated systolic and diastolic cardiac function, renal function, various safety and tolerability measures

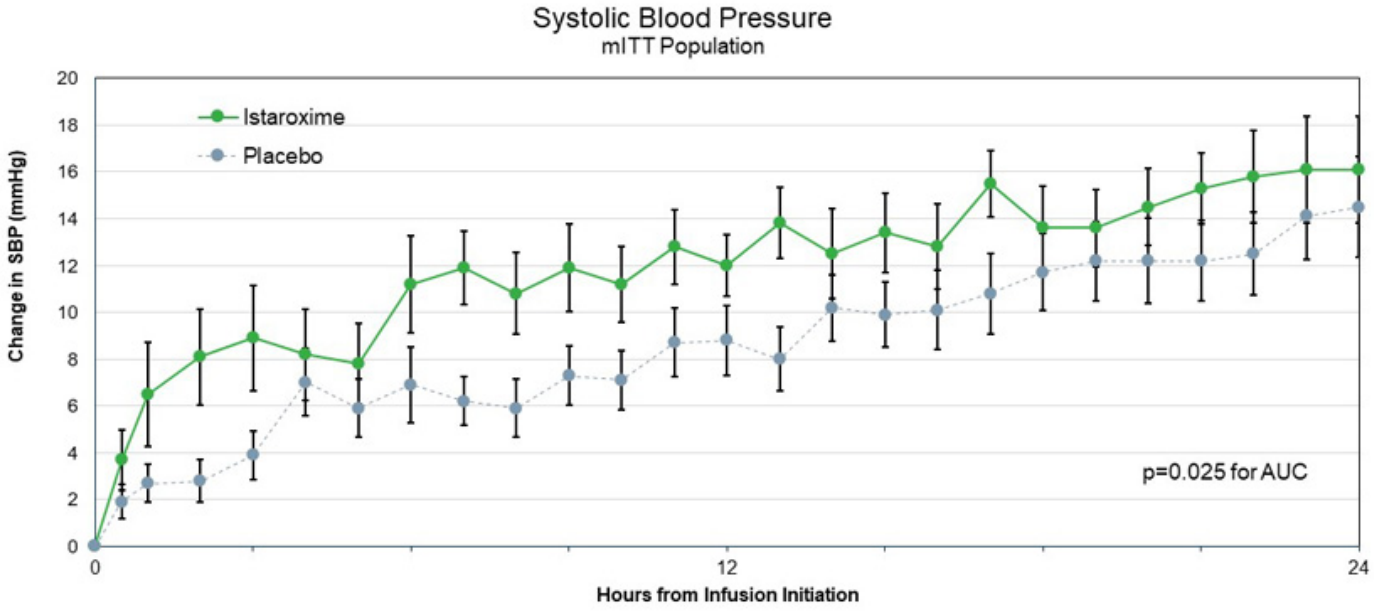
WINDTREE THERAPEUTICS

Difference in SBP Profile



WINDTREE THERAPEUTICS

Systolic BP Improvements Persisted over 24 Hours



WINDTREE THERAPEUTICS

Cardiac Function Improvement

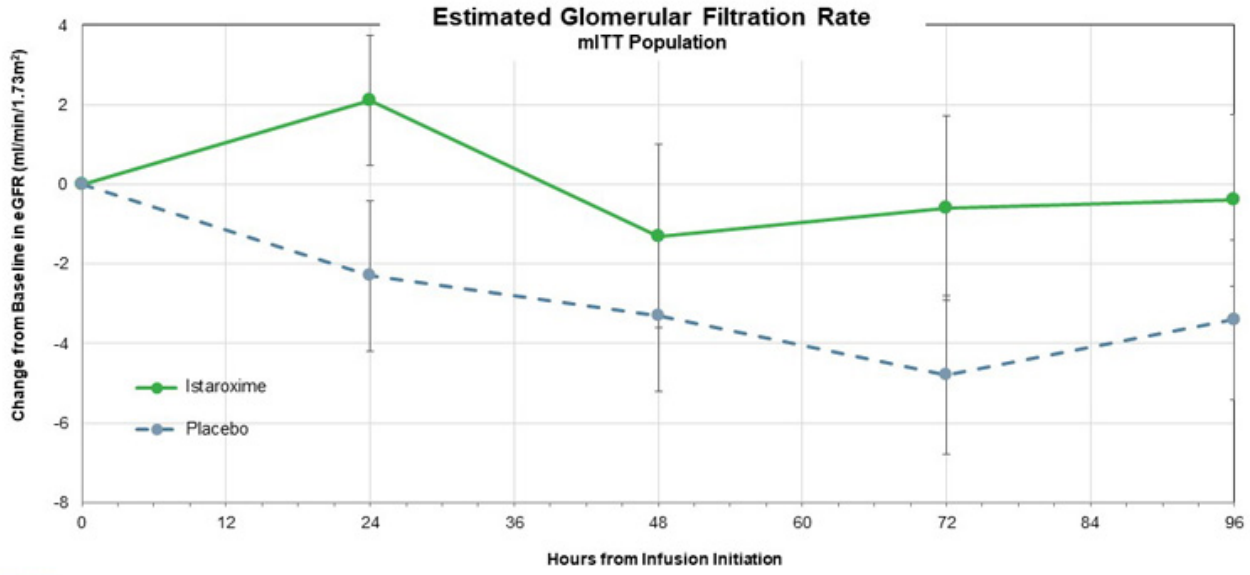
Echocardiography demonstrated improvements in key systolic and diastolic cardiac function measures including:

- **Cardiac index significantly increased**
- **Stroke volume index substantially increased** (4 mL/m^2) approaching statistical significance
- Other echocardiographic measurements improved:
  - **Left atrial area was reduced**
  - **Left ventricular end systolic volume was reduced**
  - **Left ventricular end diastolic volume was reduced**

WINDTREE THERAPEUTICS

Treatment was Associated with a Favorable Renal Profile

Renal function was not decreased in istaroxime treated patients



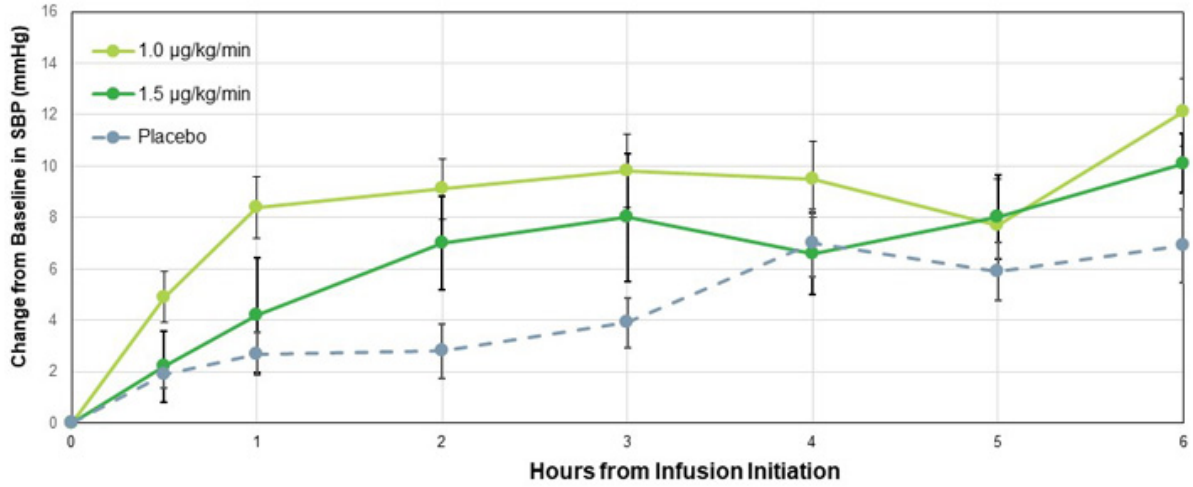
WINDTREE THERAPEUTICS

Data shown as means and standard errors

1.0 µg/kg/min Produced a Favorable Effect on SBP

1.0 µg/kg/min dosing was associated with:

- Early, rapid SBP increase and improvement in more echocardiographic assessments of cardiac function
- More favorable adverse event, serious adverse event and clinical event profile



WINDTREE THERAPEUTICS

All Subjects (n=60)

SEISMiC Results Summary

SEISMiC was a positive study in early cardiogenic shock patients

- ✓ Systolic blood pressure significantly increased within the first 6 hours of initiating the infusion (p=0.017) and the increase was maintained throughout the 24-hour infusion (p=0.025)
  - SBP increases were rapid within the first hour and sustained through the 96-hour post-infusion measure
- ✓ Key secondary endpoints of systolic and diastolic cardiac function and performance were improved
- ✓ Renal function was maintained
- ✓ SEISMiC provided valuable information for optimizing our dose moving forward
- ✓ These data substantiate and advance the rationale for istaroxime as a potential treatment for cardiogenic shock and support the existing data from the program in AHF

WINDTREE THERAPEUTICS

Cardiogenic Shock Opportunity

INTENDED TARGET THERAPEUTIC PROFILE

"For patients in cardiogenic shock due to heart failure, Istaroxime will be a unique, first-in-class dual action agent and the only treatment for cardiogenic shock that rapidly and significantly improves blood pressure *and* cardiac output performance and does so while maintaining a favorable renal and overall safety profile - unlike other available agents. Istaroxime will be associated with an improved clinical course that has less resource utilization and cost reductions for positive Pharmacoeconomics for the hospital and health system".

INTENDED POSITIONING:

1. ***Expand the Market due to Profile:***
   Used in SCAI Stage B / Early Cardiogenic Shock (where vasopressors are reserved) to help stabilize the patient and prevent deterioration

+

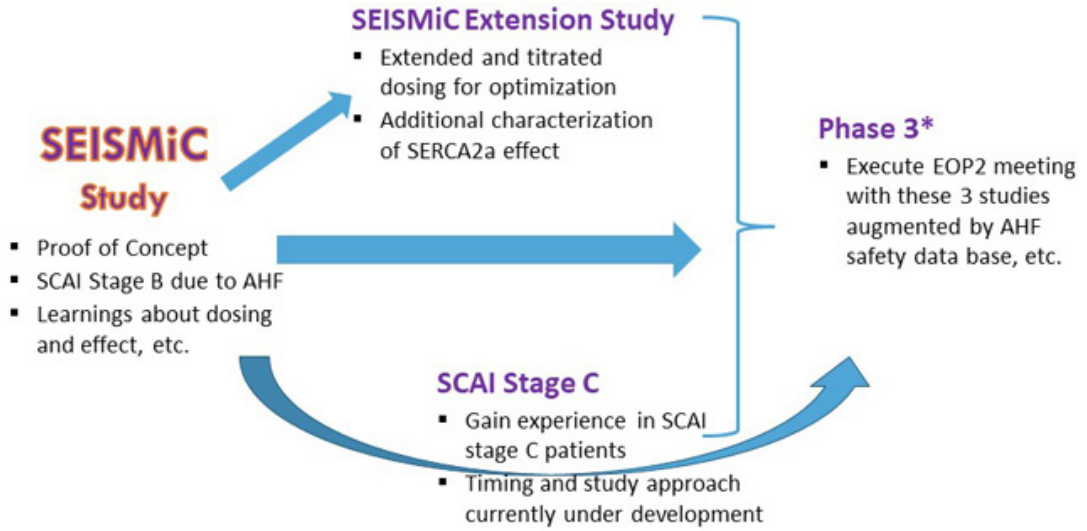
2. ***Become the Preferred Agent:***
   Preferred agent with first line use in SCAI Stage C / Classic Cardiogenic Shock due to differentiation

OPPORTUNITY DRIVERS

- ✓ Currently available pharmacologic treatments have undesirable side effects and poor outcomes
- ✓ Very high cost of cardiogenic shock treatment create opportunity for Istaroxime pharmacoeconomic benefits
- ✓ Lack of active competition in development or the market
- ✓ Attractive commercial market potential (as well as time and cost of development)

WINDTREE THERAPEUTICS

Cardiogenic Shock Development Strategy



WINDTREE THERAPEUTICS

** Study plans and progression to Phase 3 dependent upon regulatory alignment and resourcing*

Plan for Dose Optimization – Extension Study

Following the positive results in the early cardiogenic shock study, an extension study is planned to support ongoing development in early cardiogenic shock and acute heart failure

Study objectives:

- ✓ Advance the characterization of the physiology associated with longer istaroxime dosing as well as evaluate a dose titration
- ✓ More fully illuminate the effects and potential benefits associated with SERCA2a activation
- ✓ Support our regulatory strategy for istaroxime

Current study plan design:

Double-blind, placebo controlled in up to 30 patients (2:1 randomization) with SBP between 70-100mmHg conducted in sites in the US, EU and LATAM

Two treatment arms of 60-hour infusions, titrating down from 1.0 starting dose
Placebo controlled arm

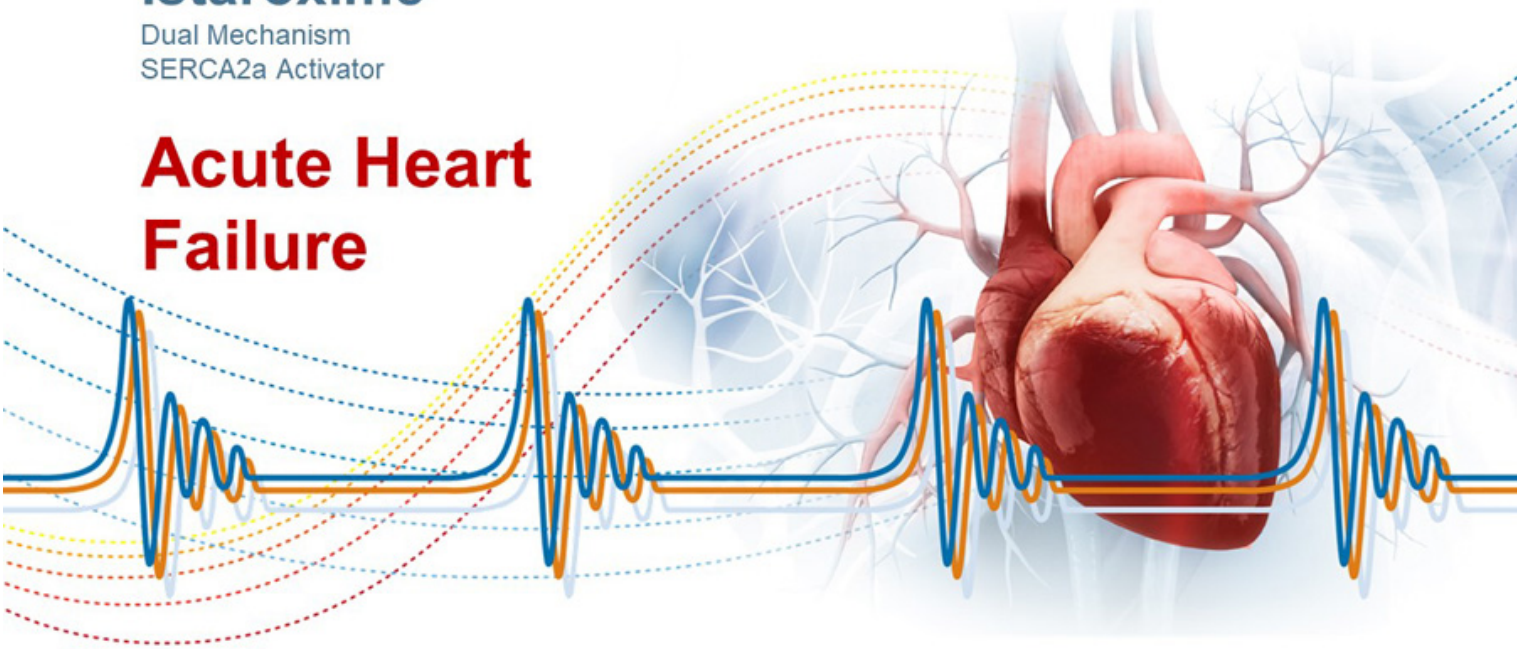
Multiple physiologic measures associated with cardiac function, blood pressure and safety

~6 months to execute and $3.5MM
Study plans and progression dependent upon regulatory alignment and resourcing

Istaroxime

Dual Mechanism
SERCA2a Activator

Acute Heart Failure



WINDTREE THERAPEUTICS

Heart Failure – Large, Growing Market But Underserved

The prevalence and mortality of heart failure is high and increasing

#1 cause of U.S. hospitalization in patients > 65 years old

Annual Admissions

~1.3M U.S.

~1.5M E.U.

Patients

7M U.S.,

25M+ worldwide

~7%

In-patient mortality

30-day mortality can exceed 10%

>$18B

annual U.S. hospital costs

Most expensive of the Medicare diagnoses

0

New pharmacologic advancements in acute heart failure for decades

Lack of therapeutic advances led the FDA to issue new Heart Failure Guidance in July 2019 for greater development flexibility in acceptable endpoints, specifically acknowledging mortality is not required

WINDTREE THERAPEUTICS

Sources: American Heart Association; DRG Data

Acute Heart Failure – Significant Unmet Clinical Need

Patient Management Goals

- **Clinical objectives** for AHF patient management include:
  - **Relieve pulmonary congestion** and general edema (e.g., "dry out") with IV diuretics
  - **Improve cardiac function** and peripheral/organ perfusion
  - **Achieve stable, fully compensated** clinical state
  - Transition to oral, outpatient medicines (for chronic management of heart failure)

Current Treatment Options

- **Current approaches to acutely improve cardiac function are associated with unwanted effects**:
  - Heart rhythm disturbances
  - Increased heart rate and myocardial oxygen demand
  - Decreased blood pressure
  - Potential damage to the heart muscle
  - Worsening renal function
  - Mortality
- **Patients with low blood pressure (SBP) and peripheral hypoperfusion are high risk, challenging patients who are also generally resistant to diuretic therapy and often discharged in a sub-optimal state**

WINDTREE THERAPEUTICS

1) ADHERE Registry, n=48,567; JAMA 2006
2) European Journal of Heart Failure; Voors, PRE-RELAX AHF Study; 2011; 13

Istaroxime AHF Phase 2a & 2b Studies

Phase 2a

n=**120**
ADHF Patients

Dosing=
0.5, 1, 1.5 µg/kg/min

6 hour
Infusion

- Primary: PCWP significantly improved
- Stroke Vol & SBP – significant increase
- Heart Rate (HR) - lowered

Phase 2b

n=**120**
ADHF Patients
(dyspnea plus need for IV furosemide ≥ 40mg)

Dosing=
0.5, 1.0 µg/kg/min

24 hour
Infusion

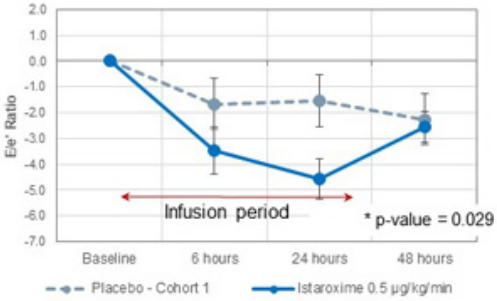
Results

Positive Phase 2 trial results demonstrated improved cardiac function **without unwanted side effects of existing rescue therapies**

WINDTREE THERAPEUTICS

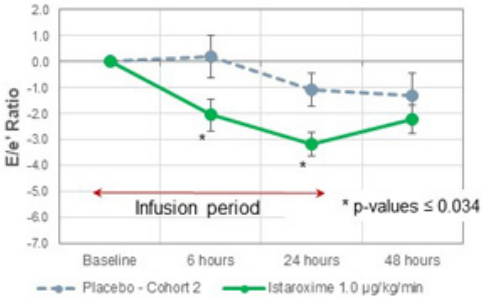
Primary Endpoint Achieved
Significant Changes in E/e' Ratio[1] and Stroke Volume

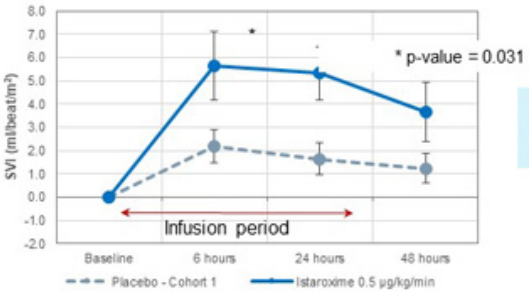
Istaroxime 0.5 µg/kg/min vs. placebo



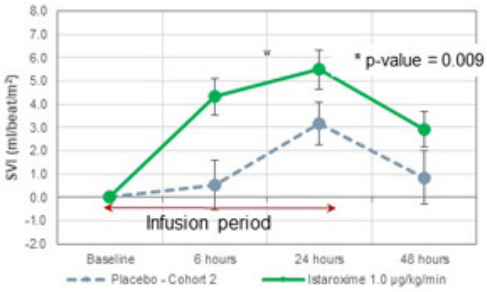
E/e'

Istaroxime 1.0 µg/kg/min vs. placebo





Stroke Volume

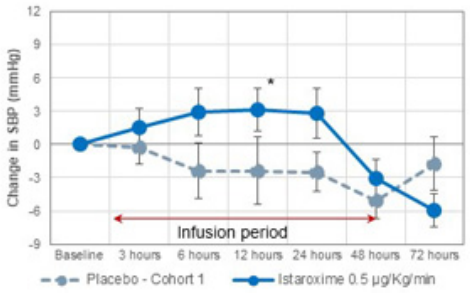


WINDTREE THERAPEUTICS

1) E/e' echocardiographic assessment of PCWP; Note: Data shown as means and standard errors

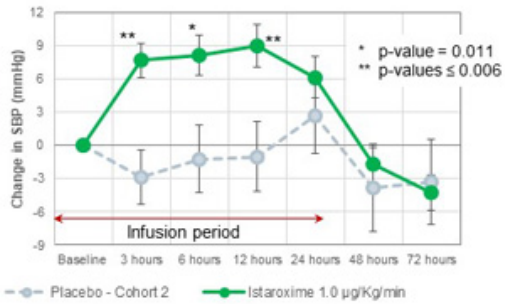
Systolic Blood Pressure Increased During Treatment and Renal Function Tended to Improve

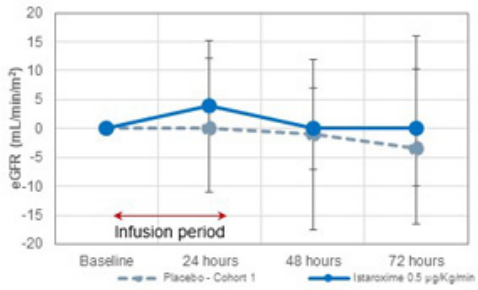
Istaroxime 0.5 µg/kg/min vs. placebo



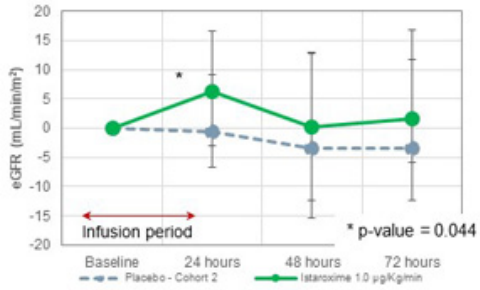
Systolic Blood Pressure (SBP)

Istaroxime 1.0 µg/kg/min vs. placebo





GFR (Renal Function)

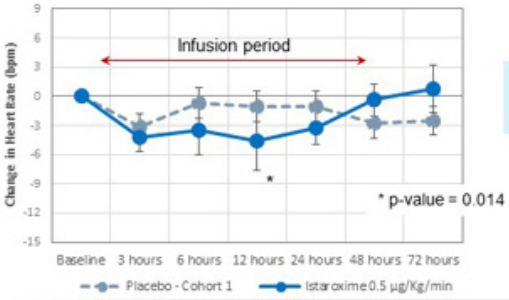


WINDTREE THERAPEUTICS

Data shown as means and standard errors

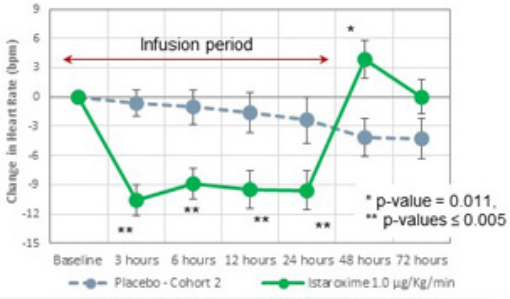
Heart Rate Decreased and No Increases in Cardiac Troponins

Istaroxime 0.5 µg/kg/min vs. placebo

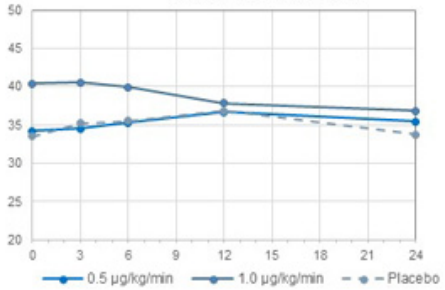


Heart Rate

Istaroxime 1.0 µg/kg/min vs. placebo

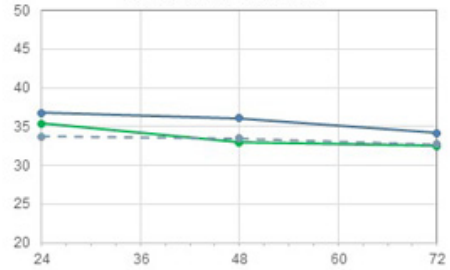


cTnT – 0 to 24 hours



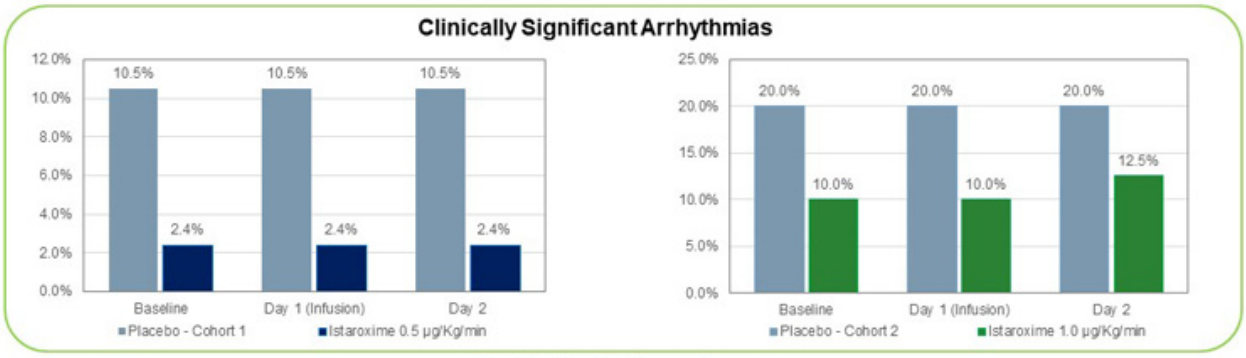
Cardiac TnT (Myocardial Damage)

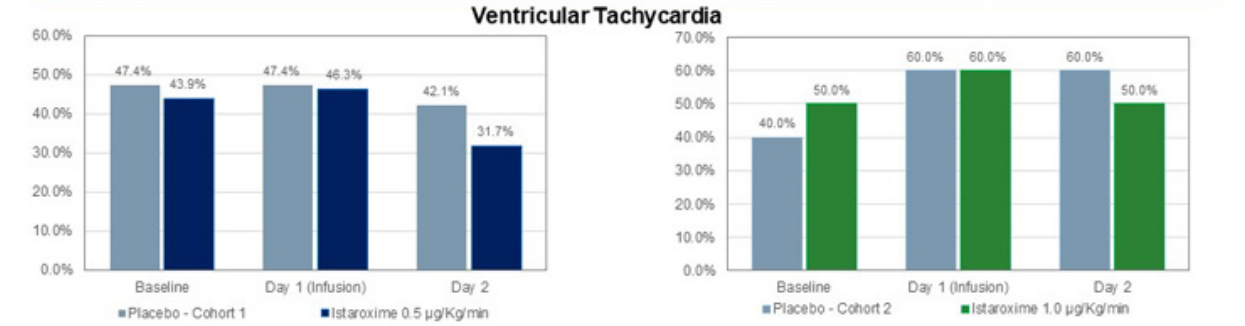
cTnT – 24 to 72 hours



WINDTREE THERAPEUTICS

Favorable Profile Observed with 24-hour Holter Monitoring





WINDTREE THERAPEUTICS

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

Istaroxime – Acute Heart Failure

Objective: Optimize therapy and employ study enrichment strategies to create strong Phase 3 and partnership position

Execute an additional study designed to complete Phase 2 and inform Phase 3 - 300 patients, 60 centers globally*

Enrich therapeutic impact by leveraging characteristics in target population whose needs match the unique attributes of istaroxime: patients with low blood pressure and/or diuretic resistance

Increase infusion time to >24 hours in pursuit of dose optimization

Primary endpoint will again be E/e', but also obtain data on measures that will inform Phase 3 design and pivotal endpoint

Pending adequate funding; ~18 months to execute

WINDTREE THERAPEUTICS

* Estimates

Next Generation, Oral SERCA2a Activators Acute and Chronic Heart Failure Platform

The Company also has pre-clinical programs on product candidates including:

Selective SERCA2a Activators

- **Oral & i.v.** therapies for chronic heart failure (CHF) and AHF
- Attractive approach for **heart failure with preserved ejection fraction (HFpEF)**

Dual Mechanism, (SERCA2a & Na+/K+) Compounds

"Next generation istaroxime" as oral/i.v. for **in-patient acute and out-patient chronic use**

These next generation agents help form complete chronic and acute heart failure treatment portfolio for both licensing/partnership and potential commercialization

Summary

- Istaroxime has produced positive, differentiating data in three Phase 2 studies for two separate and complementary indications. These markets have significant unmet needs, and no known other late-stage programs in development to address the acute decompensated patient
  - The data is consistent, across all regions/populations and across many endpoints (including many in early cardiogenic shock despite small trial)
- Istaroxime has demonstrated a highly unique and desirable profile as compared to existing therapies:
  - Improved cardiac function **and** SBP while maintaining renal function and overall safety profile
- Recent positive Phase 2 study with istaroxime in early cardiogenic shock (ECS) paves the way for what we believe is a relatively fast and less expensive developmental and regulatory pathway
- The AHF program will proceed with business development (which remains a pre-Phase 3 strategy for istaroxime) and/or additional resourcing while also advancing the next generation, oral SERCA2a activators for chronic and acute HF including HFpEF

WINDTREE THERAPEUTICS

Funding Development-
Actively Engaged to Address Resources and Create Opportunity

Windtree is actively engaged and assessing various options to fund development and operations including:

Strategic Transaction

- Mergers & Acquisitions
- Management Buyout

Business Development – Licensing

- Global or regional out-licensing

Capital Markets

- Public or Private
- Possible role for debt

WINDTREE THERAPEUTICS

Financial Summary & Capitalization

Cash & Equivalents of ~$8.4 million as of September 30, 2022

Securities	Common Equivalents as of November 14, 2022
Common Stock	38,610,119
Options (WAEP $7.64)	3,883,169
Restricted Stock Units	558,100
Warrants (WAEP $6.64)	16,546,336
Fully Diluted Equivalents	59,597,724

WINDTREE THERAPEUTICS

Strategy for Value Generation

www.windtreetx.com

WINDTREE THERAPEUTICS


WINDTREE
THERAPEUTICS

Appendix

Istaroxime Unique Opportunity With Attractive Risk / Return Profile

1. Highly consistent results across 3 controlled Phase 2 studies (and 300 patients dosed thus far), in a spectrum of severity and executed in all regions of the world

2. Attractive profile as the only acute heart failure or shock drug that has been shown to significantly improve cardiac function of a failing heart, while rapidly and significantly improving blood pressure, with what so far has been a differentiating safety profile (avoiding many of the use-limiting side effects of existing therapies such renal, arrhythmias, etc.)

Istaroxime: Attractive Risk, Time, Cost and Return Profile

3. Complementary acute CV programs with high unmet need and no active or developing competition

5. Long, successful history of CMC

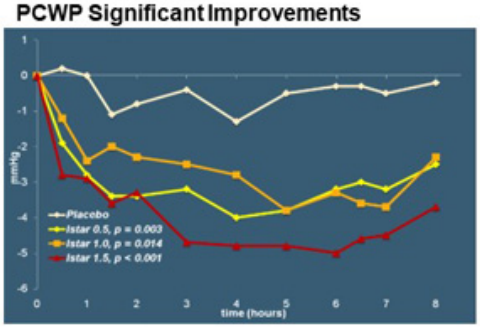
4. Faster and less expensive developmental and regulatory pathway possible
   - Attractive pivotal endpoint of blood pressure response is expected to be more straight-forward and better align with a smaller study than one requiring clinical outcome measures.
   - Additionally, istaroxime demonstrated significance in many other benefits that we expect will continue to help us build a strong evidence-based position with dose-optimization and the larger Phase 3 planned for 2023.

WINDTREE THERAPEUTICS

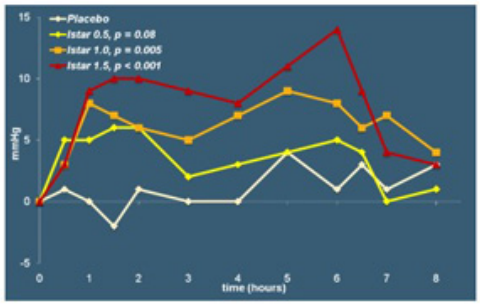
Istaroxime Phase 2a (HORIZON-HF) Study

- 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



WINDTREE THERAPEUTICS

Istaroxime AHF Phase 2b 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

WINDTREE THERAPEUTICS

SEISMiC: Serious Adverse Events and Adverse Drug Reactions

Event	Istaroxime (N=29)	Placebo (N=31)
All adverse events	27 (93%)	25 (81%)
Serious adverse events	6 (21%)	6 (19%)
Cardiac arrest	1 (3%)	0
Cardiac failure	2 (7%)	2 (6%)
Cardiac failure acute	0	1 (3%)
Cardiac ventricular thrombosis	0	1 (3%)
Cardiac artery stenosis	0	1 (3%)
Ventricular fibrillation	1 (3%)	0
Ventricular tachycardia	1 (3%)	0
Coronavirus infection	0	1 (3%)
Pneumonia	1 (3%)	0
Acute kidney injury	1 (3%)	0
Adverse drug reactions†	15 (52%)	3 (10%)
Gastrointestinal‡	9 (31%)	2 (6%)
Infusion site pain/inflammation	4 (14%)	1 (3%)

WINDTREE THERAPEUTICS

Note: data shown as n (%); patients can have more than one event during the 30-day follow up period
† Adverse drug reactions are AEs possibly related or related to study drug
‡ Most common - nausea, vomiting

SEISMiC: Safety and Efficacy Appeared More Favorable with the 1.0 vs 1.5 µg/kg/min and Placebo

1.0 µg/kg/min dosing was associated with:

- **Early SBP increase and improvement in more echocardiographic parameters of cardiac function**
- **More favorable adverse event, serious adverse event and clinical event profile**

Clinical Events by Dose	Statistic	Placebo (N=31)	Istaroxime 1.0 µg/kg/min (N=16)	Istaroxime 1.5 µg/kg/min (N=13)
SBP AUC 0-24hrs	LS-Means (SE)*	209.9 (27.38)	282.7 (35.79)	304.1 (44.11)
Worsening HF through 96-hours	No. events	1 (3%)	0 (0%)	5 (38%)
Heart Failure Readmissions through 30-days	No. events	3 (12.9%)	0 (0%)	0 (0%)
Length in ICCU/CCU, days [c]	Mean (SD)	4.55 (2.23)	3.50 (1.41)	6.38 (4.46)
All-Cause Mortality through 30-Days	No. events (%)	1 (3%)	1 (6%)	3 (23%)
All-Cause mortality or HF readmission through 30-days	No. events (%)	4 (12%)	1 (6%)	3 (23%)

WINDTREE THERAPEUTICS

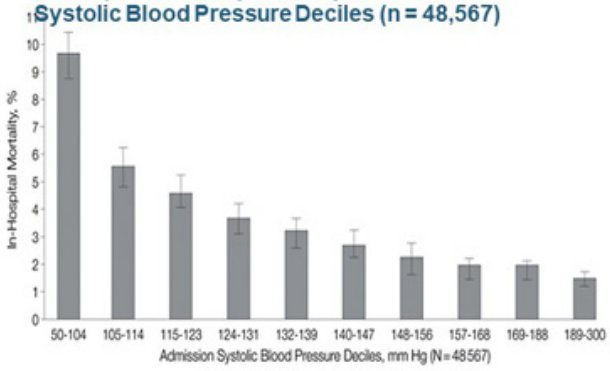
* LS-Means and associated p-values from ANCOVA model adjusted for pooled site, treatment, and baseline systolic BP.

Acute Heart Failure

Significant Healthcare Issue with Significant Unmet Clinical Need

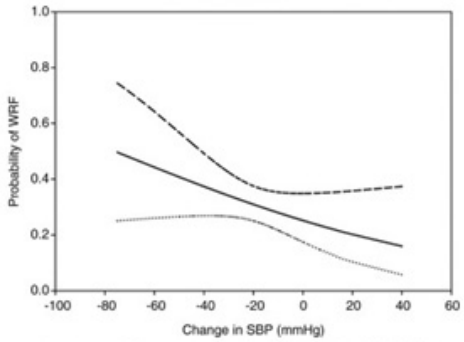
- Patients with low blood pressure (SBP) and peripheral hypoperfusion are high risk, challenging patients. These patients are also generally resistant to diuretic therapy and often discharged in a sub-optimal state.
  - Low SBP in-patient mortality approximately two-fold greater than normal/high SBP[1]
  - There is a direct relationship between early drop in SBP and worsening renal function in acute heart failure2

In-Hospital Mortality Rates by Admission Systolic Blood Pressure Deciles (n = 48,567)



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

Early drop in systolic blood pressure and worsening renal function in Acute Heart Failure: renal results of Pre-RELAX-AHF Study



Voors, A. et al. European Journal of Heart Failure 2011; 13; 961-967

WINDTREE THERAPEUTICS

1) ADHERE Registry, n=48,567; JAMA 2006
2) European Journal of Heart Failure; Voors, PRE-RELAX AHF Study; 2011; 13