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): May 23, 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 8.01 Other Events

On May 23, 2022, Windtree Therapeutics, Inc. (the "***Company***") issued a press release announcing the presentation of data from its positive SEISMiC Phase 2 study of istaroxime in early cardiogenic shock in a late-breaker presentation at the European Society of Cardiology Heart Failure Meeting in Madrid, Spain. A copy of the press release is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

In addition, on May 23, 2022, the Company presented a slide presentation as part of an investor conference call and webcast, which is attached as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

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 May 23, 2022, announcing the presentation of data from its positive SEISMiC Phase 2 study of istaroxime in early cardiogenic shock
99.2	Corporate 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: May 23, 2022

Exhibit 99.1

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

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

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

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

WARRINGTON, PA – **May 23, 2022** – Windtree Therapeutics, Inc. (NasdaqCM: WINT), a biotechnology company focused on advancing multiple late-stage interventions for acute cardiovascular and pulmonary disorders, today presented data from its positive Phase 2 study of istaroxime in early cardiogenic shock in a late-breaker presentation at the European Society of Cardiology Heart Failure Meeting in Madrid, Spain. The study met its primary endpoint of significantly improved SBP, the critical clinical objective in treating patients with cardiogenic shock, compared to the control group at 6 hours. The significant improvement in blood pressure profile persisted through 24 hours. The study met several other secondary endpoints including assessments of cardiac function.

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

Study results

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

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

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

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

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

Domestic:	+1-877-423-9813
International:	+1-201-689-8573
Conference ID:	13729315
Webcast link:	https://viavid.webcasts.com/starthere.jsp?ei=1544380&tp_key=29a0dff7b9

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

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

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

About Windtree Therapeutics
Windtree Therapeutics, Inc. is advancing multiple late-stage interventions for acute cardiovascular and acute pulmonary disorders to treat patients in moments of crisis. Using new scientific and clinical approaches, Windtree is developing a multi-asset franchise anchored around compounds with an ability to activate SERCA2a, with lead candidate, istaroxime, being developed as a first-in-class treatment for acute heart failure and for early cardiogenic shock. Windtree's heart failure platform includes follow-on oral pre-clinical SERCA2a activator assets as well. In pulmonary care, Windtree has focused on facilitating the transfer of the clinical development of AEROSURF®, to its licensee in Asia, Lee's HK. Included in Windtree's portfolio is rostafuroxin, a novel precision drug product targeting hypertensive patients with certain genetic profiles.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. The Company may, in some cases, use terms such as "predicts," "believes," "potential," "proposed," "continue," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Such statements are based on information available to the Company as of the date of this press release and are subject to numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from the Company's current expectations. Examples of such risks and uncertainties include: risks and uncertainties associated with the ongoing economic and social consequences of the COVID-19 pandemic, including any adverse impact on the Company's clinical trials, clinical trial timelines or disruption in supply chain; the success and advancement of the clinical development programs for istaroxime, KL4 surfactant and the Company's other product candidates; the impacts of political unrest, including as a result geopolitical tension, including escalation in the conflict between Russia and Ukraine and any additional resulting sanctions, export controls or other restrictive actions that may be imposed by the United States and/or other countries which could have an adverse impact on the Company's operations, including through disruption in supply chain or access to potential international clinical trial sites, and through disruption, instability and volatility in the global markets, which could have an adverse impact on the Company's ability to access the capital markets; the Company's ability to secure significant additional capital as and when needed; the Company's ability to access the debt or equity markets; the Company's ability to manage costs and execute on its operational and budget plans; the results, cost and timing of the Company's clinical development programs, including any delays to such clinical trials relating to enrollment or site initiation; risks related to technology transfers to contract manufacturers and manufacturing development activities; delays encountered by the Company, contract manufacturers or suppliers in manufacturing drug products, drug substances, aerosol delivery systems (ADS) and other materials on a timely basis and in sufficient amounts; risks relating to rigorous regulatory requirements, including that: (i) the FDA or other regulatory authorities may not agree with the Company on matters raised during regulatory reviews, may require significant additional activities, or may not accept or may withhold or delay consideration of applications, or may not approve or may limit approval of the Company's product candidates, and (ii) changes in the national or international political and regulatory environment may make it more difficult to gain regulatory approvals and risks related to the Company's efforts to maintain and protect the patents and licenses related to its product candidates; risks that the Company may never realize the value of its intangible assets and have to incur future impairment charges; risks related to the size and growth potential of the markets for the Company's product candidates, and the Company's ability to service those markets; the Company's ability to develop sales and marketing capabilities, whether alone or with potential future collaborators; and the rate and degree of market acceptance of the Company's product candidates, if approved. These and other risks are described in the Company's periodic reports, including the annual report on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, filed with or furnished to the Securities and Exchange Commission and available at www.sec.gov. Any forward-looking statements that the Company makes in this press release speak only as of the date of this press release. The Company assumes no obligation to update forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

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Windtree Therapeutics

Early Cardiogenic Shock Investor Call

May 23, 2022

(NASDAQ: WINT)

WINDTREE THERAPEUTICS™

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.

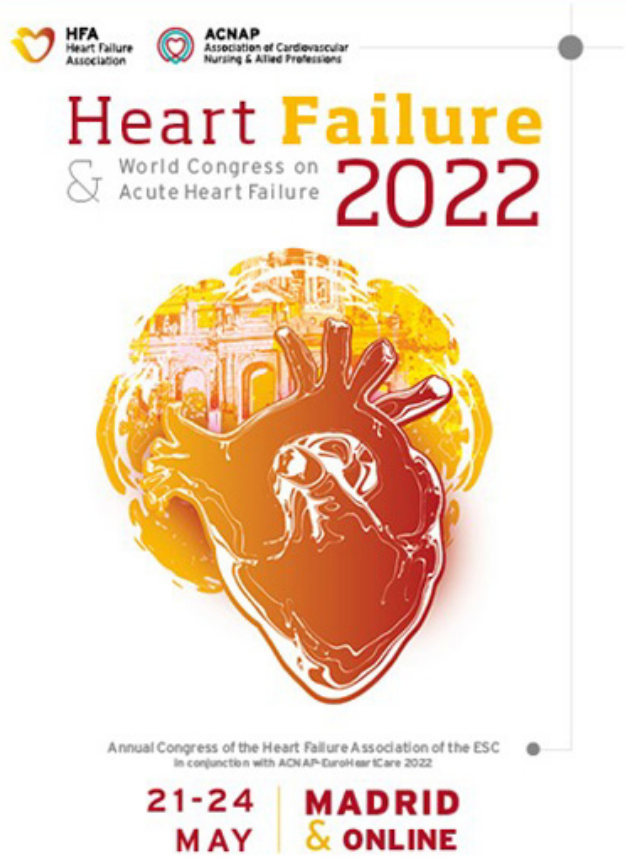
Under no circumstances shall this presentation be construed as an offer to sell or as a solicitation of an offer to buy any of the Company's securities. In addition, the information presented in this deck is qualified in its entirety by the Company Filings. The reader should refer to the Company Filings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

Istaroxime Early Cardiogenic Shock Update:
Live From ESC Heart Failure, Madrid Spain

Istaroxime early cardiogenic shock data from our SEISMiC Phase 2 study was presented at a late-breaker session earlier today here at the ESC Heart Failure meeting:

"The safety and efficacy of istaroxime for PreCardiogenic Shock"

Speaker: Marco Metra, MD (University of Brescia – Brescia, Italy)



WINDTREE THERAPEUTICS

Istaroxime – Novel First-in-Class Therapy

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

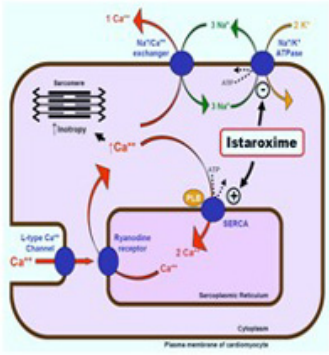
Dual Mechanism of Action

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 (greater fill volume) and subsequent contraction cycle

Impact on both systolic and diastolic dysfunction



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Istaroxime AHF Phase 2a & 2b Studies – Summary

Multicenter, double blind, placebo-controlled, parallel group in 240 patients

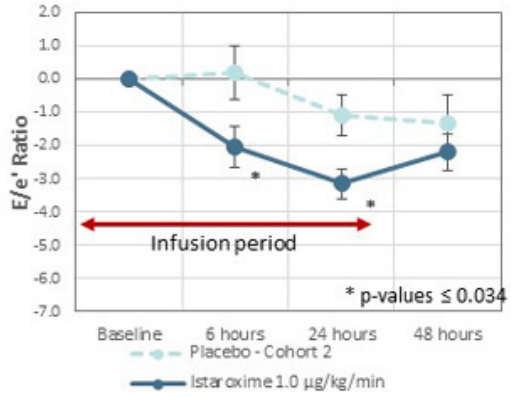
Phase 2a	n=**120** ADHF Patients	Dosing= **0.5, 1, 1.5** µg/kg/min	**6** hour Infusion
Phase 2b	n=**120** ADHF Patients (dyspnea plus need for IV furosemide ≥ 40mg)	Dosing= **0.5, 1.0** µg/kg/min	**24** hour Infusion

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

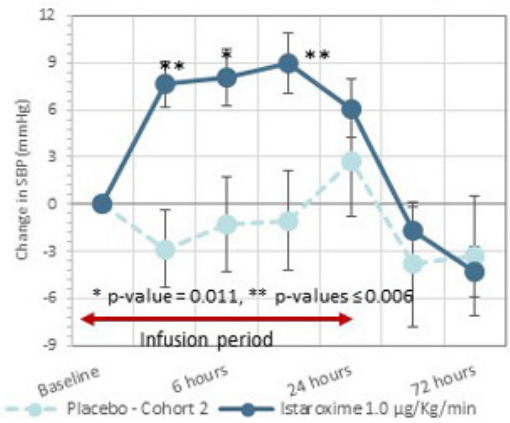
Acute Heart Failure Phase 2b

Significant Improvements in E/e', Stroke Volume and Blood Pressure along with a Favorable Renal Profile

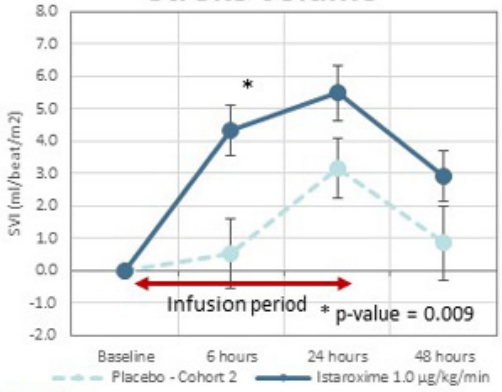
E/e'



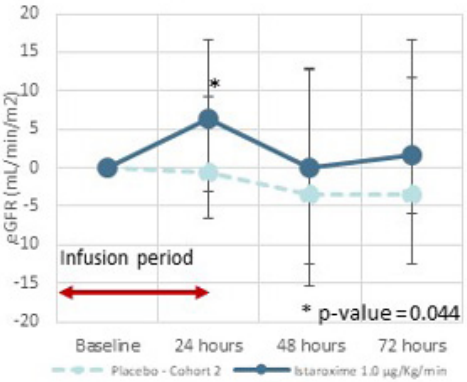
Systolic Blood Pressure (SBP)



Stroke Volume



GFR (Renal Function)



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

SEISMiC Study

Istaroxime in Early Cardiogenic Shock

Additional potential indication in active clinical development

WINDTREE THERAPEUTICS

Cardiogenic Shock

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

- 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]

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

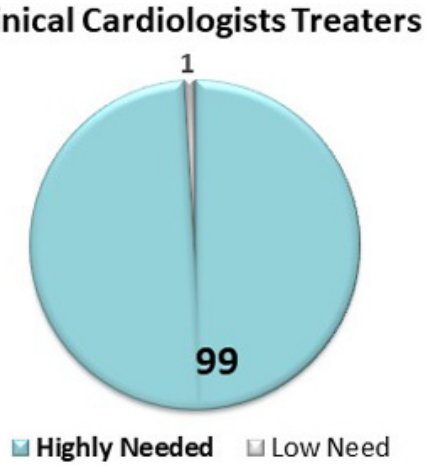
Early Cardiogenic Shock Treatment

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**

Market Research[1]

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

1) Market research conducted by Sermo, a leading provider of realtime physician insights

Early Cardiogenic Shock Treatment

Istaroxime Potential Opportunity for Accelerated Pathway

FDA Regulatory Commentary and Precedent

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 for 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 indicates potential accelerated regulatory pathway and review opportunities

Potential for a complementary program that may have a scale which is faster and less expensive than the fundamental, larger AHF development program

WINDTREE THERAPEUTICS

1) Kosaraju A, Hai O. Cardiogenic Shock. [Updated 2019 Jan 25]. In: https://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

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

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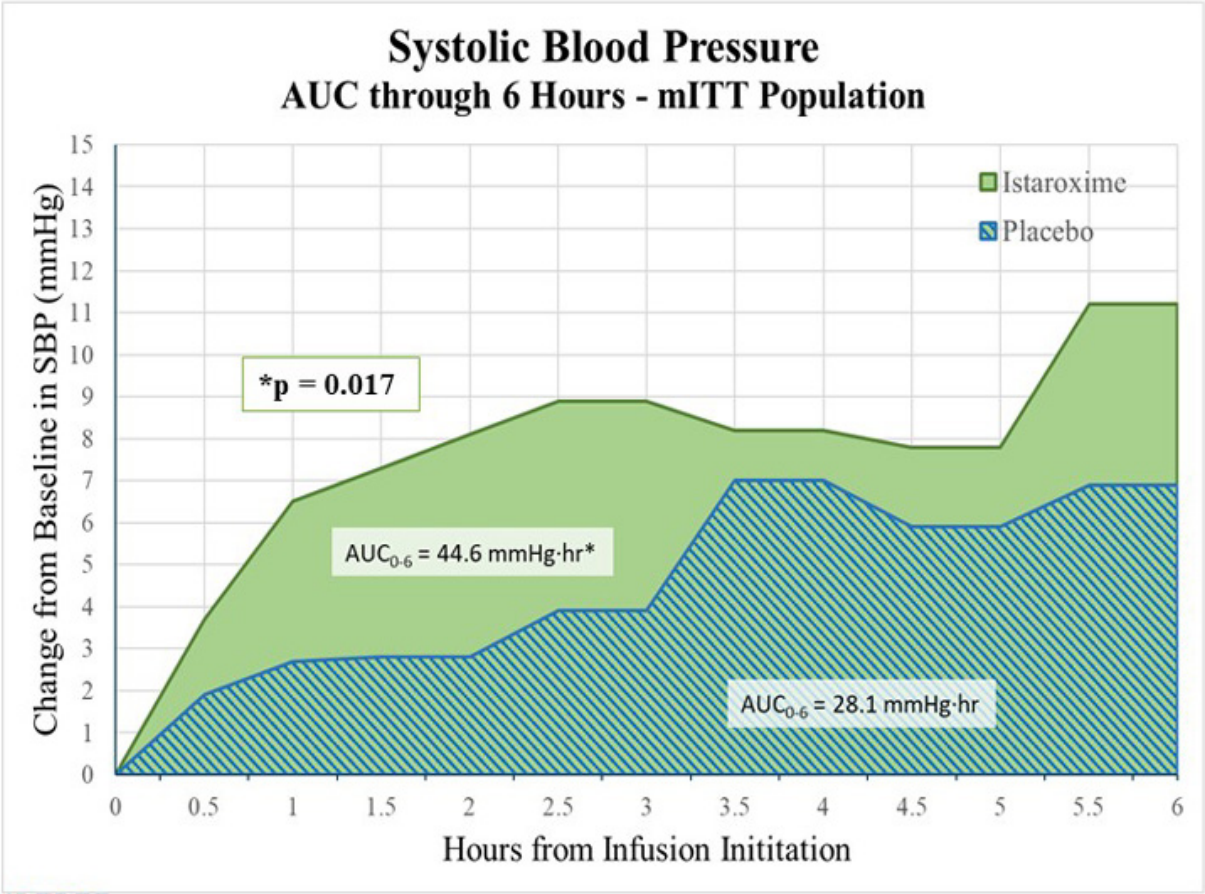
SEISMiC Results Summary

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)
- Key secondary endpoints of systolic and diastolic cardiac function and performance were significantly 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 treatment for AHF as well as enable us to continue to progress the program in cardiogenic shock

Primary Endpoint –
Difference in SBP Profile



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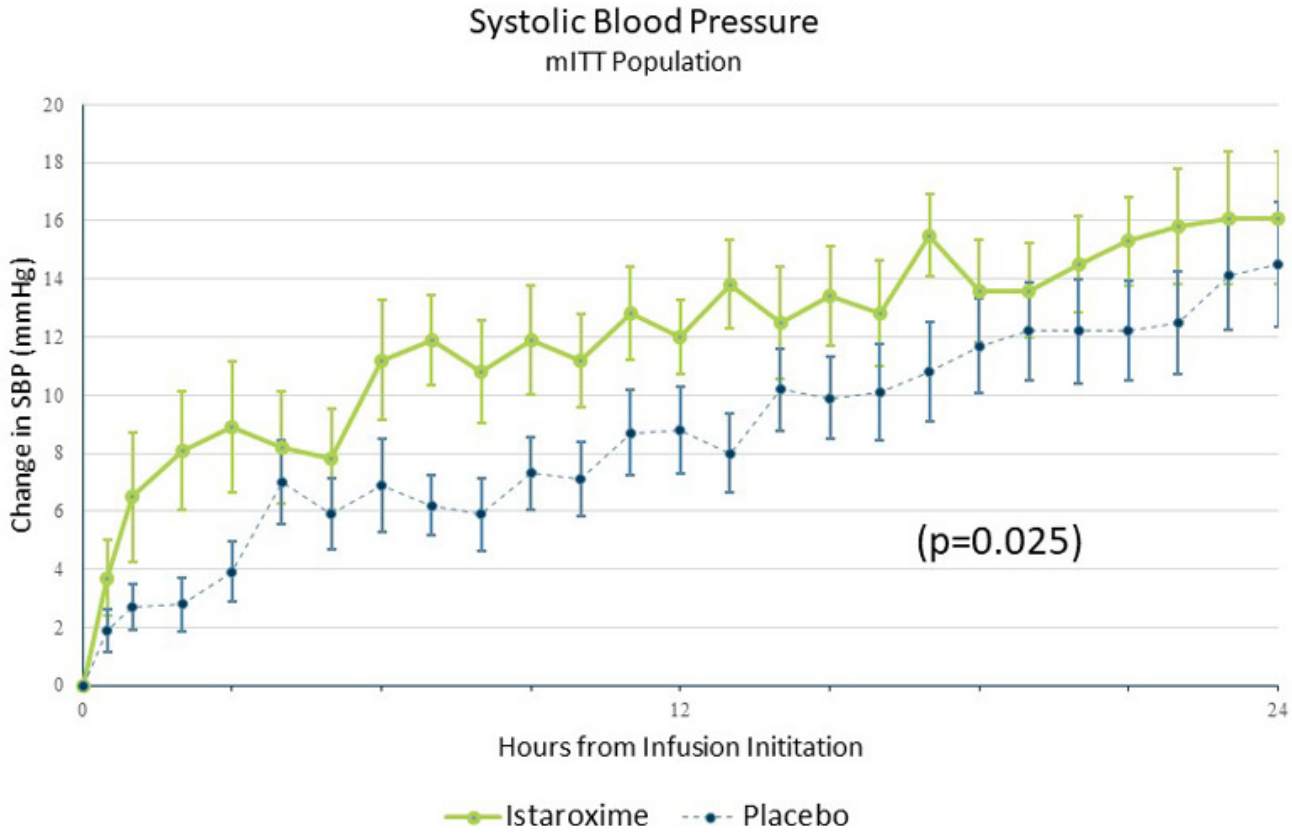
Secondary Results -
Systolic BP Improvements Persisted over 24 Hours



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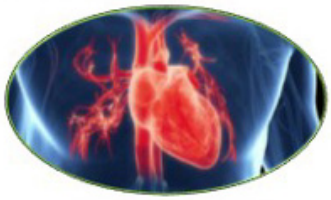
Cardiac Function Improvement

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

- Cardiac index significantly increased
- Stroke volume substantially increased and approached statistical significance
- Other echocardiographic measurements significantly improved
  - Left atrial area was reduced
  - Left ventricular end systolic volume was reduced
  - Left ventricular end diastolic volume was reduced



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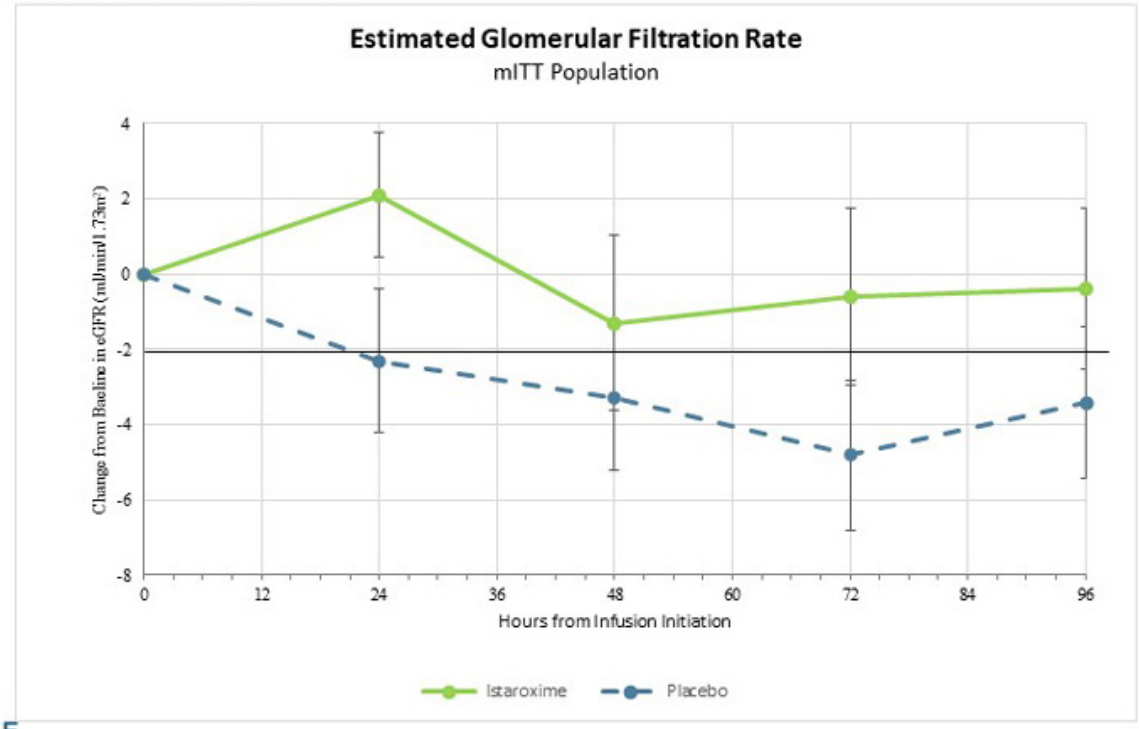
Treatment was Associated with a Positive Renal Profile

- Renal function was not decreased with istaroxime infusion
- Istaroxime treated patients also had greater diuresis with less cumulative diuretic use



WINDTREE THERAPEUTICS

Data shown as means and standard errors

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%)

Note: data shown as n (%); patients can have more than one event during the 30-day follow up period

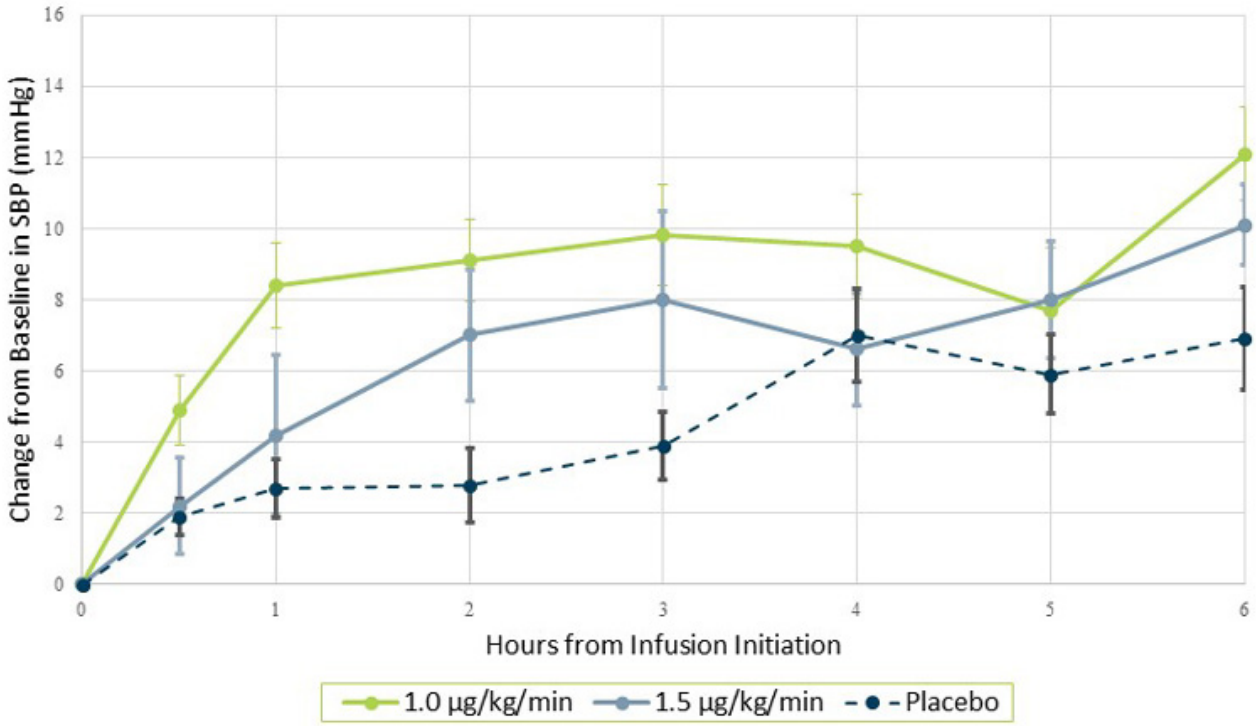
† Adverse drug reactions are AEs possibly related or related to study drug

‡ Most common - nausea, vomiting

WINDTREE THERAPEUTICS

Comparison of Doses

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



All Subjects (n=60)

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:

- Attractive 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.

SEISMiC Results Summary

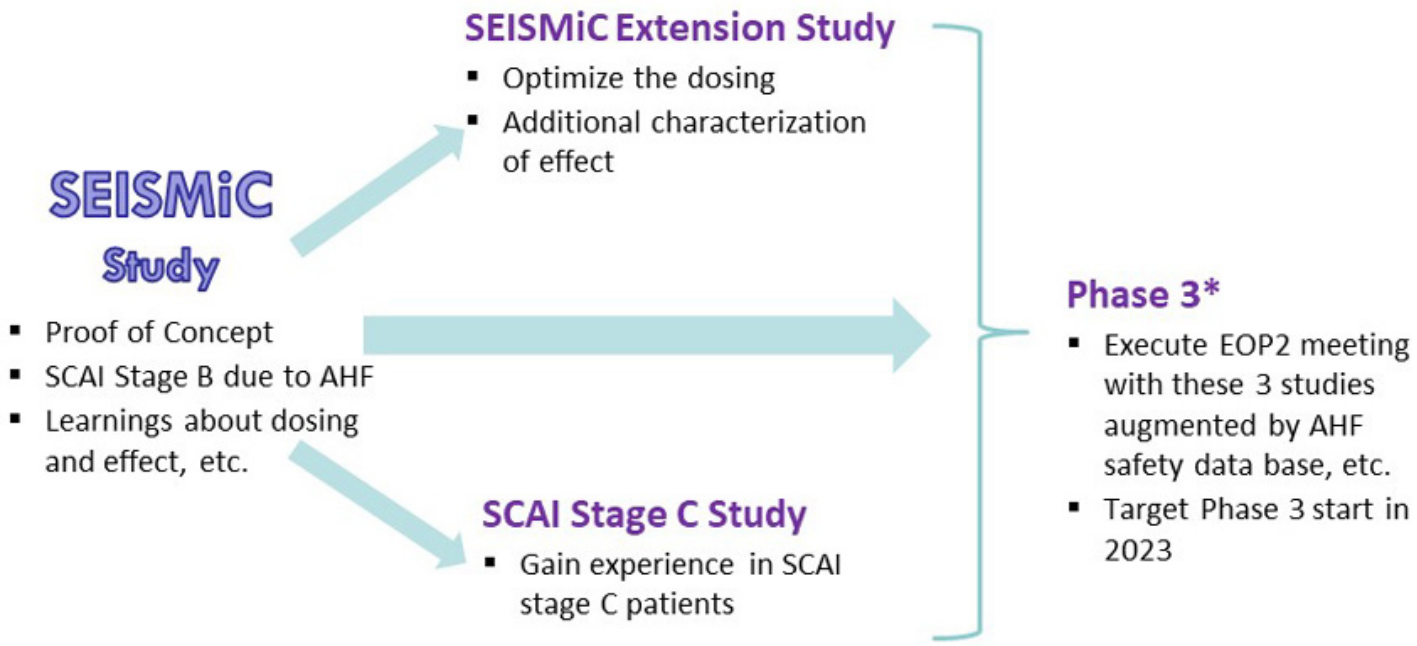
SEISMiC was a positive study in early cardiogenic shock patients

- 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 and istaroxime treated patients tended to experience greater diuresis than placebo
- SEISMiC provided valuable information for optimizing our dose moving forward
- These data substantiate and advance the rationale for istaroxime as a treatment for AHF as well as enable us to continue to progress the program in cardiogenic shock

SEISMiC Trial – Relevance to the Acute Heart Failure (AHF) Program

- The early cardiogenic shock trial results are consistent with Windtree's Phase 2 AHF studies and complementary to further advancement in AHF.
- While SEISMiC was an early cardiogenic shock study, the patients studied had very severe AHF providing valuable insight into treating more severe AHF patients.
- As an acute cardiac treatment:
  Istaroxime has the potential to effectively improve cardiac function without reducing SBP and or renal function (common side effects of currently available agents)

Cardiogenic Shock Development Strategy



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** Progression to Phase 3 dependent upon trial results, regulatory alignment and resourcing*

SEISMiC Extension Study (amendment to the ECS 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

Study 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

1) 1.0 µg/kg/min for 24 hours, titrated down to 0.5 µg/kg/min for 24 hours, titrated to 0.25 µg/kg/min for 12 hours or
2) 1.0 µg/kg/min for 12 hours, titrated to 0.5 µg/kg/min for 36 hours, or
3) Placebo control

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

Planned SCAI Stage C Cardiogenic Shock Patient Study

While a smaller group than SCAI stage B, given positive results in early cardiogenic shock, the strategy is to gain experience in more severe, SCAI stage C patients to support both regulatory, development and commercial strategies

Study objectives:

- ✓ Gain experience in SCAI Stage C patients
- ✓ Support regulatory and clinical strategy

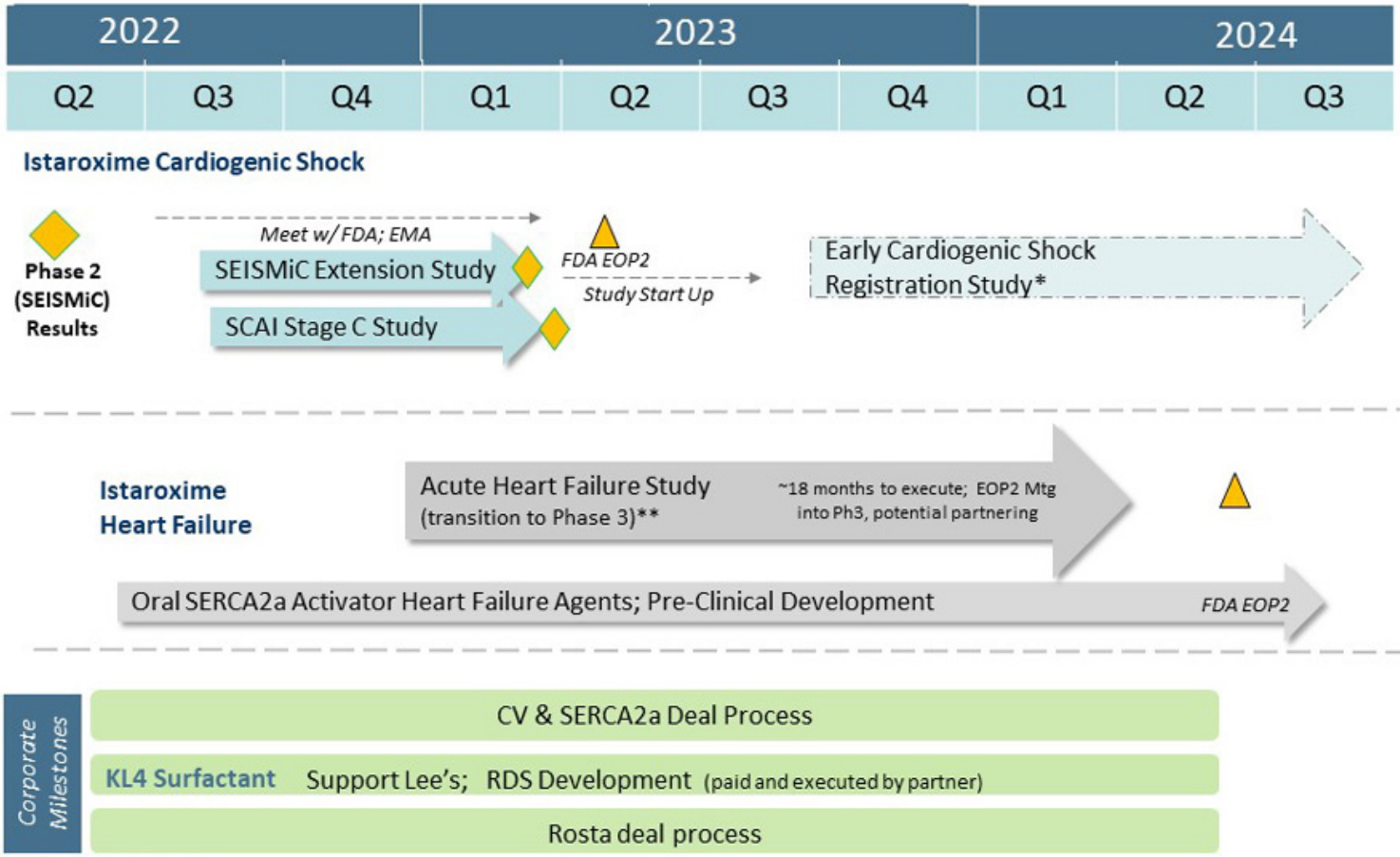
Study design:

Initial study in ~15-20 patients in the US with very low SBP and identified hypoperfusion that requires inotropic support.

Istaroxime infusions at 1.0 µg/kg/min, then titrated down
Non-responders can move to an approved inotrope, vasopressors

Blood pressure profile
Need for rescue medicine and devices / procedures
Safety and tolerability

Strategy for Value Creation



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*study initiation pending positive data, regulatory input and adequate funding

**study initiation pending adequate funding

Summary -
Potential to Create Value

- Istaroxime has been successfully studied in 7 clinical trials (3 being Phase 2 trials) with approximately 300 patients treated with istaroxime to date (and plans to grow)
- Istaroxime has positive Phase 2a and 2b results demonstrating:
  - ✓ Improved cardiac function – without coming at the expense of….
  - ✓ Uniquely improved SBP and renal function
  - ✓ Favorable safety tolerability profile compared to existing therapies
- Early Cardiogenic Shock has significant unmet need and the positive results in our Phase 2 trial has created a valuable, additional program and option for the company. Pathway to approval and launch is expected to be both faster and cost less with a scale fitting of Windtree with an indication that is complimentary to AHF
- The AHF program will proceed with the sourcing of additional resources and/or non-dilutive support afforded by business development (which remains the ultimate, pre-phase 3 strategy for Istaroxime) while also advancing the next generation, oral SERCA2a activators for chronic and acute HF including HFpEF

Windtree Therapeutics

Q & A

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