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): June 6, 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 June 6, 2022, Windtree Therapeutics, Inc. (the "Company") updated information reflected in a slide presentation, which is attached as Exhibit 99.1 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	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: June 6, 2022

Windtree Therapeutics

Company Overview

June 5, 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.

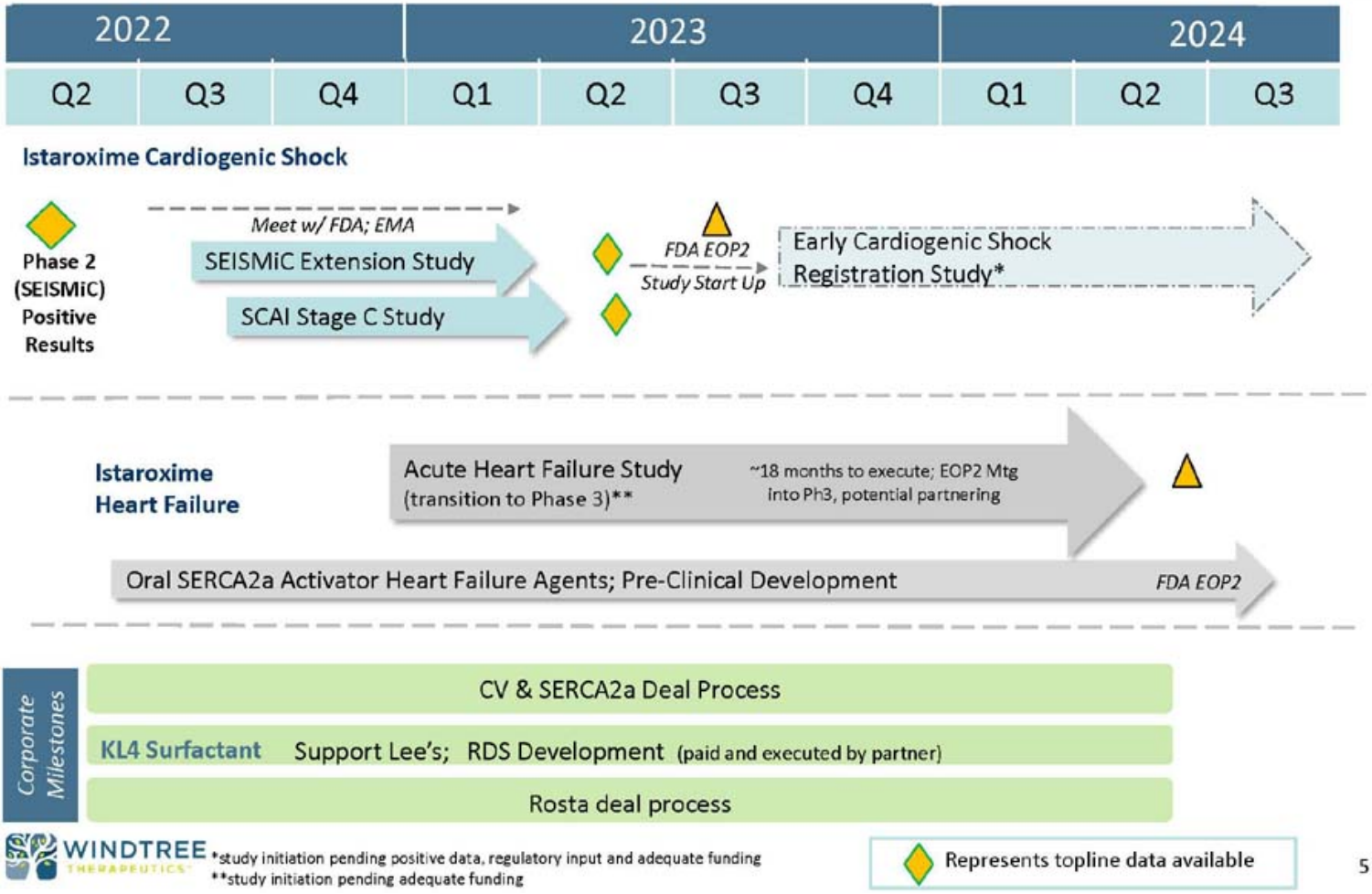
Windtree Therapeutics Highlights

- Biopharmaceutical company with **advanced clinical programs** spanning cardiovascular and respiratory disease states (NASDAQ: WINT)
- Clinical programs focused on **significant markets with high unmet needs and with supportive regulatory paths**:
  - One clinical program received both Fast Track and Orphan Drug designations; another clinical program received Fast Track designation with potential for Breakthrough designation
- **Recent positive Phase 2 study with istaroxime in early cardiogenic shock (ECS)** which can be a catalyst for the company; executing extension study for dose optimization as well as study in more severe patients and plan to meet with regulatory agencies in order to further define a potential development path to approval
- **Highly experienced** management team and company leadership

Windtree Therapeutics Pipeline

	Lead Products	Phase of Development	Current Status
FDA Fast Track Designation	**Istaroxime** (Acute Heart Failure)	Phase 2b	▪ Study start up ongoing for second Phase 2b clinical trial in ~300 patients targeted to start once clinical trial operations are fully funded
Potential for Breakthrough Designation	**Istaroxime** (Early Cardiogenic Shock)	Phase 2	▪ Positive Phase 2 study ▪ Windtree is planning the execution of the next studies and plans to meet with regulatory agencies regarding development path
	Oral SERCA2a Activators (Chronic HF; potentially HFpEF)	Preclinical	▪ Chronic and Acute Heart Failure ▪ Target for collaboration/partnership
FDA, EMA Orphan Drug for RDS	**KL4 Surfactant – COVID 19** (COVID 19 Pilot; Possible invasive Tx for RDS in neonates)	Phase 2	▪ Study completed; Results presented March 2022
FDA Fast Track Designation, Orphan Drug	**AEROSURF** (KL4 surfactant Drug/Device Tx for RDS)	Phase 2b	▪ Respiratory Distress Syndrome (RDS) development to be funded and executed by licensee
	Rostafuroxin (Genetically Associated HTN)	Phase 2b	▪ Out-licensing opportunity

Strategy for Value Creation



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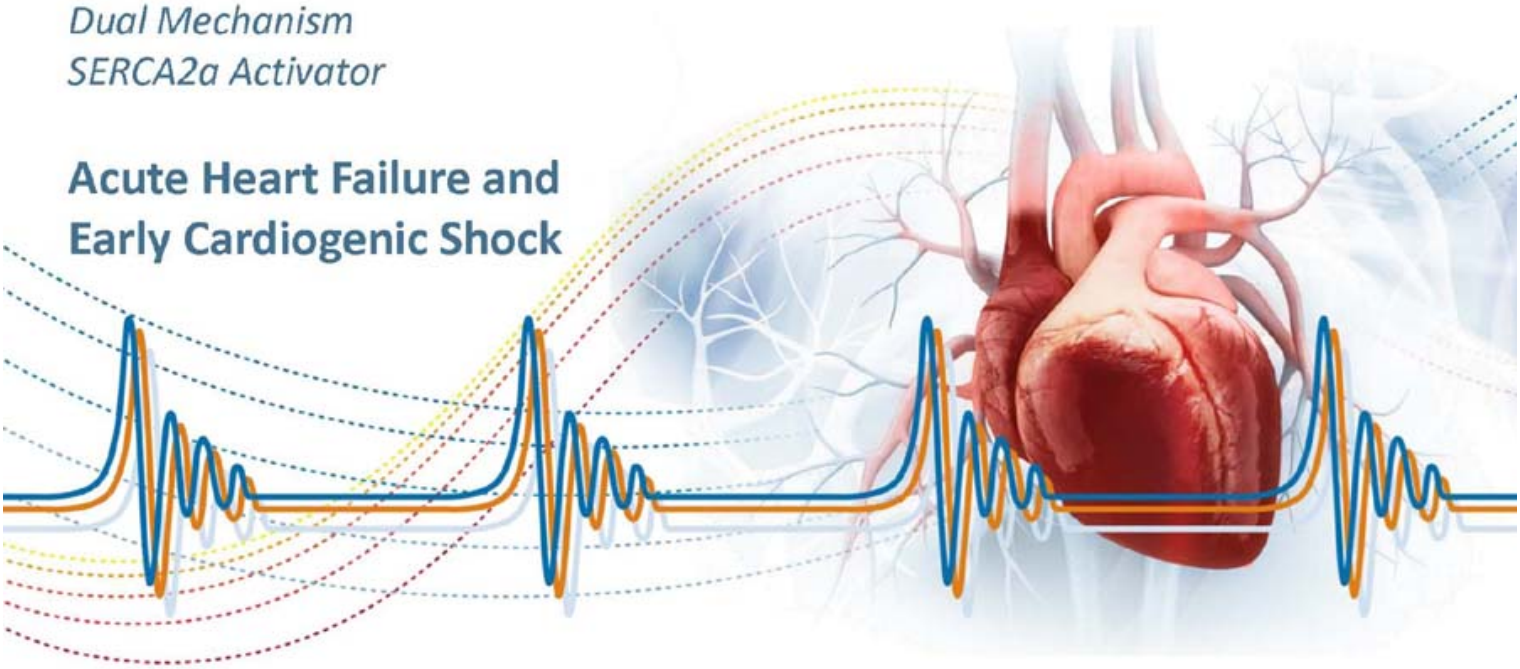
*study initiation pending positive data, regulatory input and adequate funding
**study initiation pending adequate funding

Represents topline data available

Istaroxime

Dual Mechanism
SERCA2a Activator

Acute Heart Failure and Early Cardiogenic Shock



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Heart Failure – Large, Growing Market But Underserved

The prevalence and mortality of heart failure is high and increasing

- 6M U.S., 20M+ worldwide patients
- #1 cause of U.S. hospitalization in patients > 65 years old;
  > 1.3M admissions annually (U.S.) ~1.5M admissions annually (E.U.)
- In-patient mortality up to 7%; 30-day mortality can exceed 10%
- Most expensive of the Medicare diagnoses; U.S. hospitals >$18B annually
- There has not been meaningful 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

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Sources: American Heart Association; DRG Data

Acute Heart Failure – Significant Unmet Clinical Need

- **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 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**

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

Istaroxime – Novel First-in-Class Therapy

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

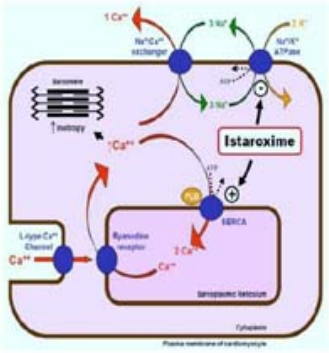
Dual Mechanism of Action

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

- 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

- Primary: E/e' (echocardiographic assessment of PCWP) was significantly improved by both doses
- Heart rate decreased and stroke volume increased
- Istaroxime maintained / increased systolic blood pressure
- Renal function tended to improve
- No evidence for increased risk of arrhythmia or increases in troponin
- Generally well tolerated (nausea and infusion site discomfort were most common AEs)

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

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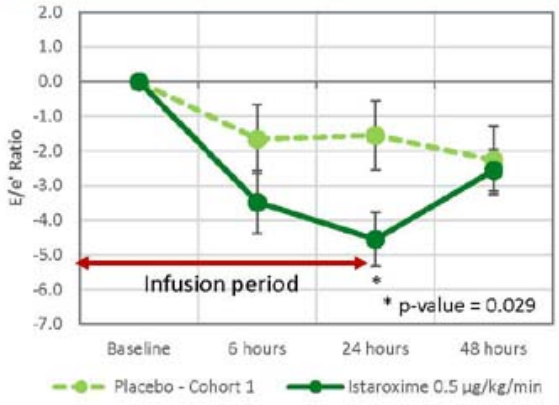
Primary Endpoint Achieved

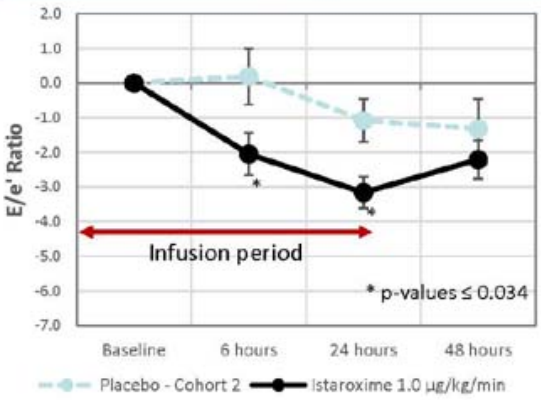
Significant Changes in E/e' Ratio[1] and Stroke Volume

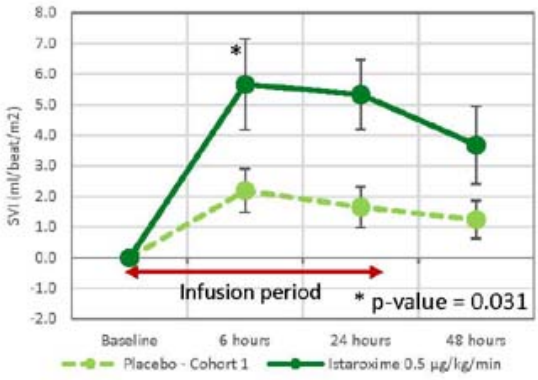
Istaroxime 0.5 µg/kg/min vs. placebo



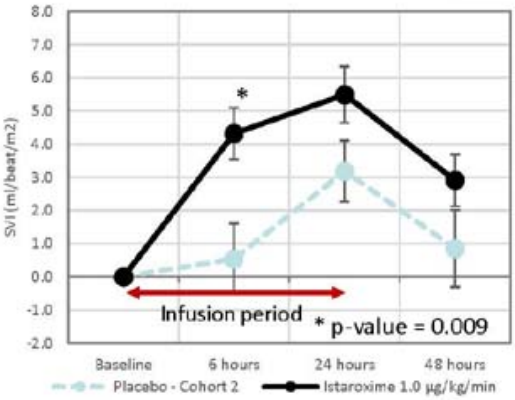
E/e'

Istaroxime 1.0 µg/kg/min vs. placebo





Stroke Volume



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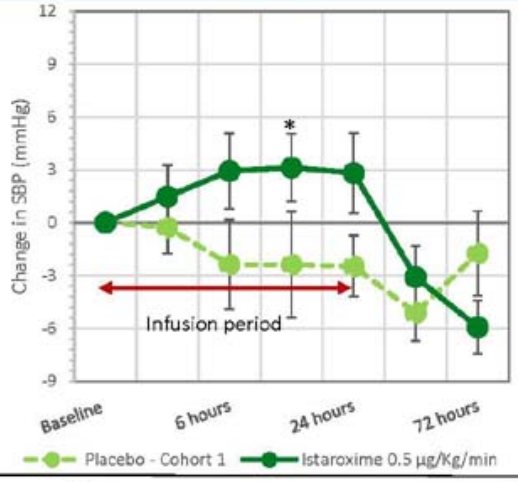
1) E/e' echocardiographic assessment of PCWP; Note: Data shown as means and standard errors

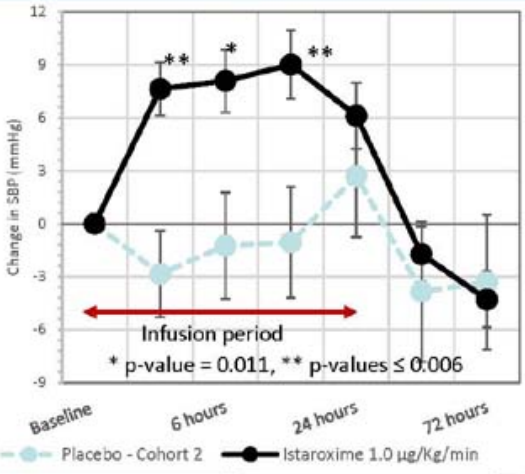
Systolic Blood Pressure Increased During Treatment and Renal Function Tended to Improve

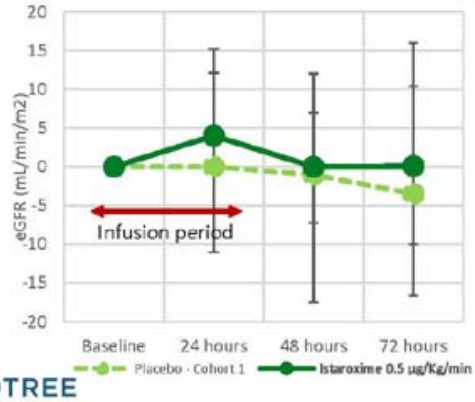
Istaroxime 0.5 µg/kg/min vs. placebo



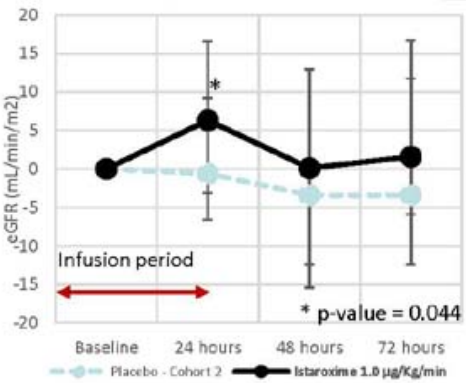
Systolic Blood Pressure (SBP)

Istaroxime 1.0 µg/kg/min vs. placebo





GFR (Renal Function)



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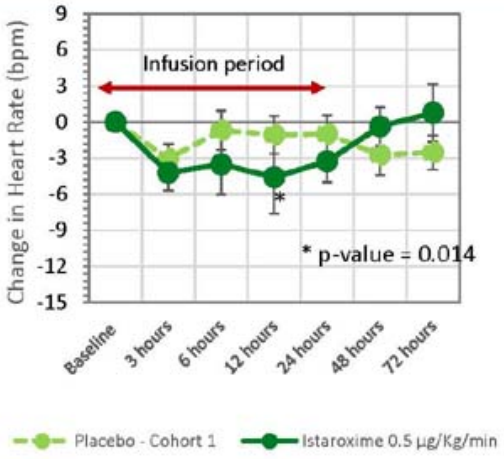
Data shown as means and standard errors

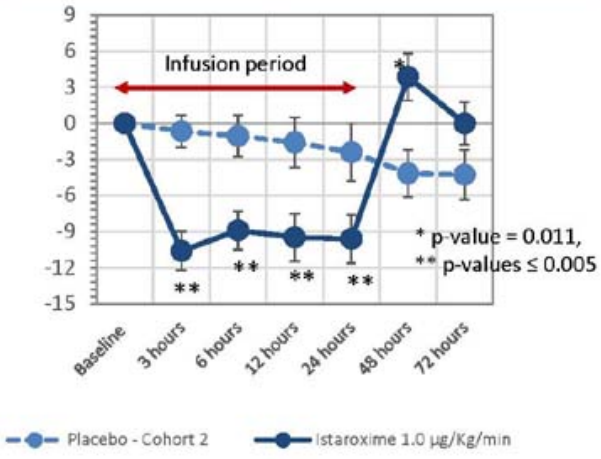
Heart Rate Decreased and No Increases in Cardiac Troponins

Istaroxime 0.5 µg/kg/min vs. placebo



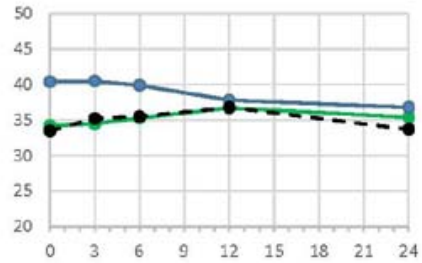
Heart Rate

Istaroxime 1.0 µg/kg/min vs. placebo

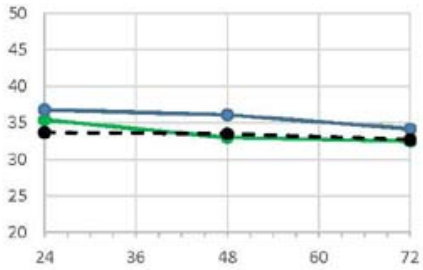


Cardiac TnT (Myocardial Damage)

cTnT – 0 to 24 hours



cTnT – 24 to 72 hours



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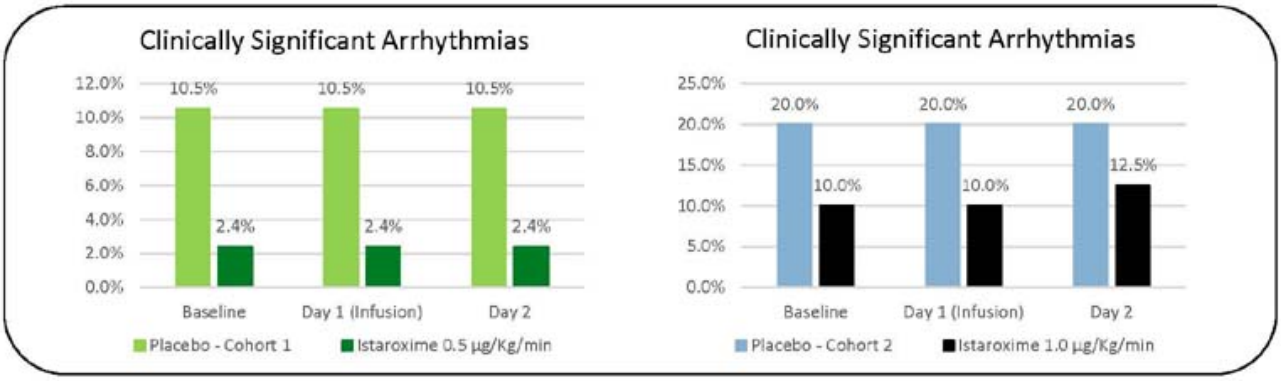
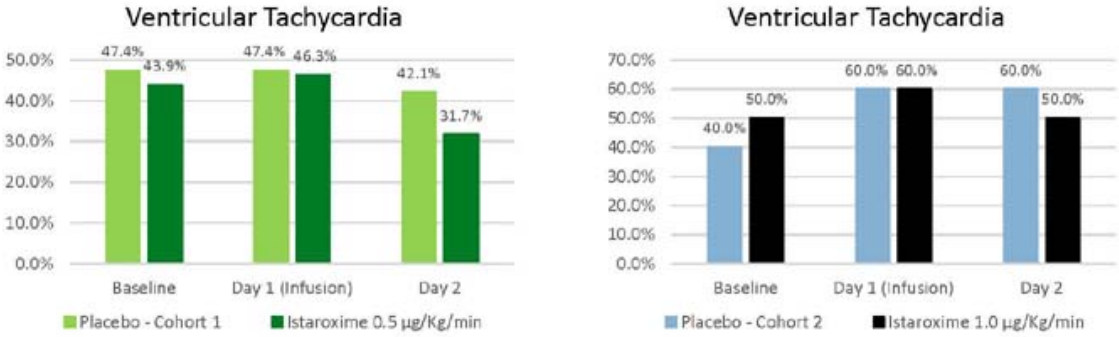
Favorable Profile Observed with 24-hour Holter Monitoring





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

Istaroxime – Acute Heart Failure

Next Steps

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**

Study start up underway with initiation pending adequate funding; ~18 months to execute

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* Estimates

Istaroxime

Early Cardiogenic Shock

Additional potential indication in active clinical development

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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]

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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***

Clinical Cardiologists Treaters

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

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

Early Cardiogenic Shock Treatment

Istaroxime Potential Opportunity for Accelerated 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 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

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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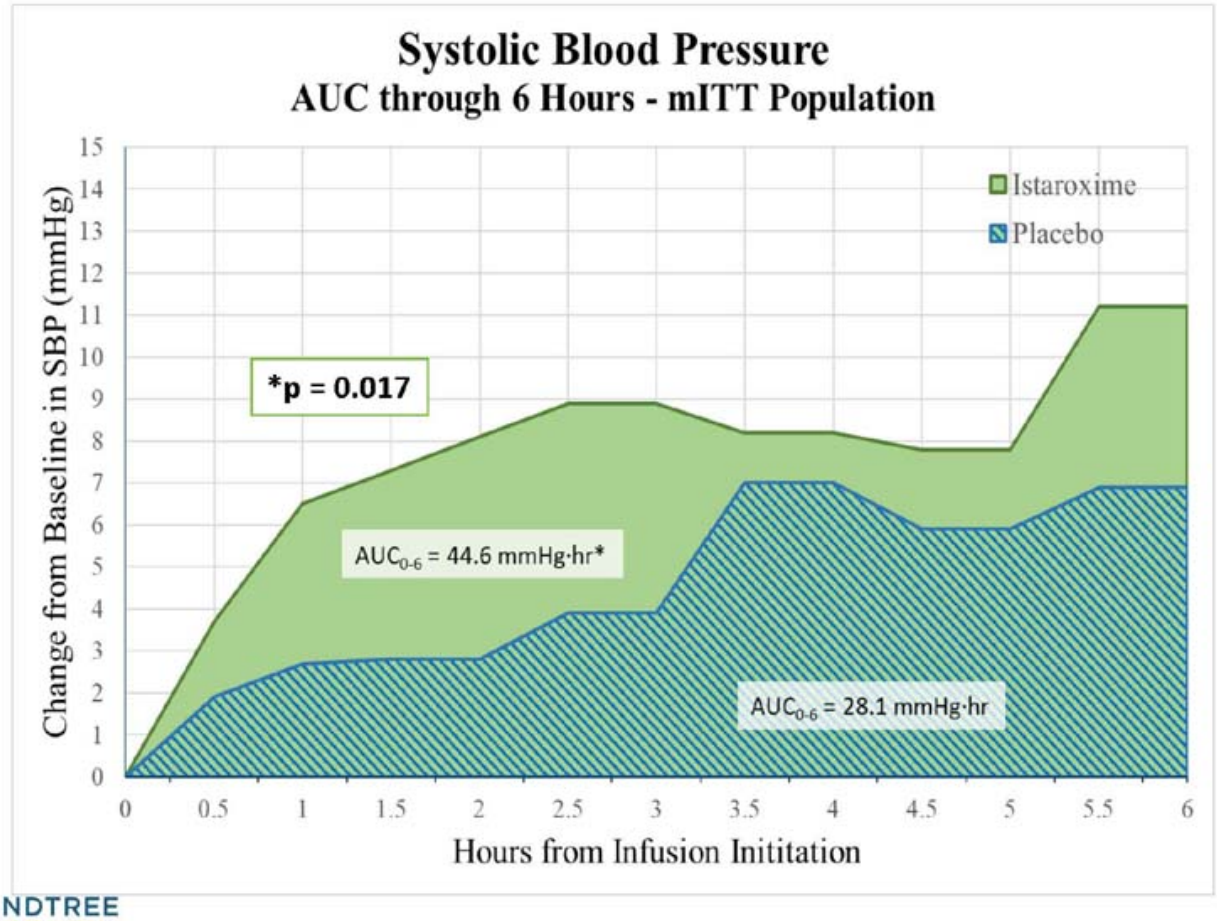
Primary Endpoint –
Difference in SBP Profile



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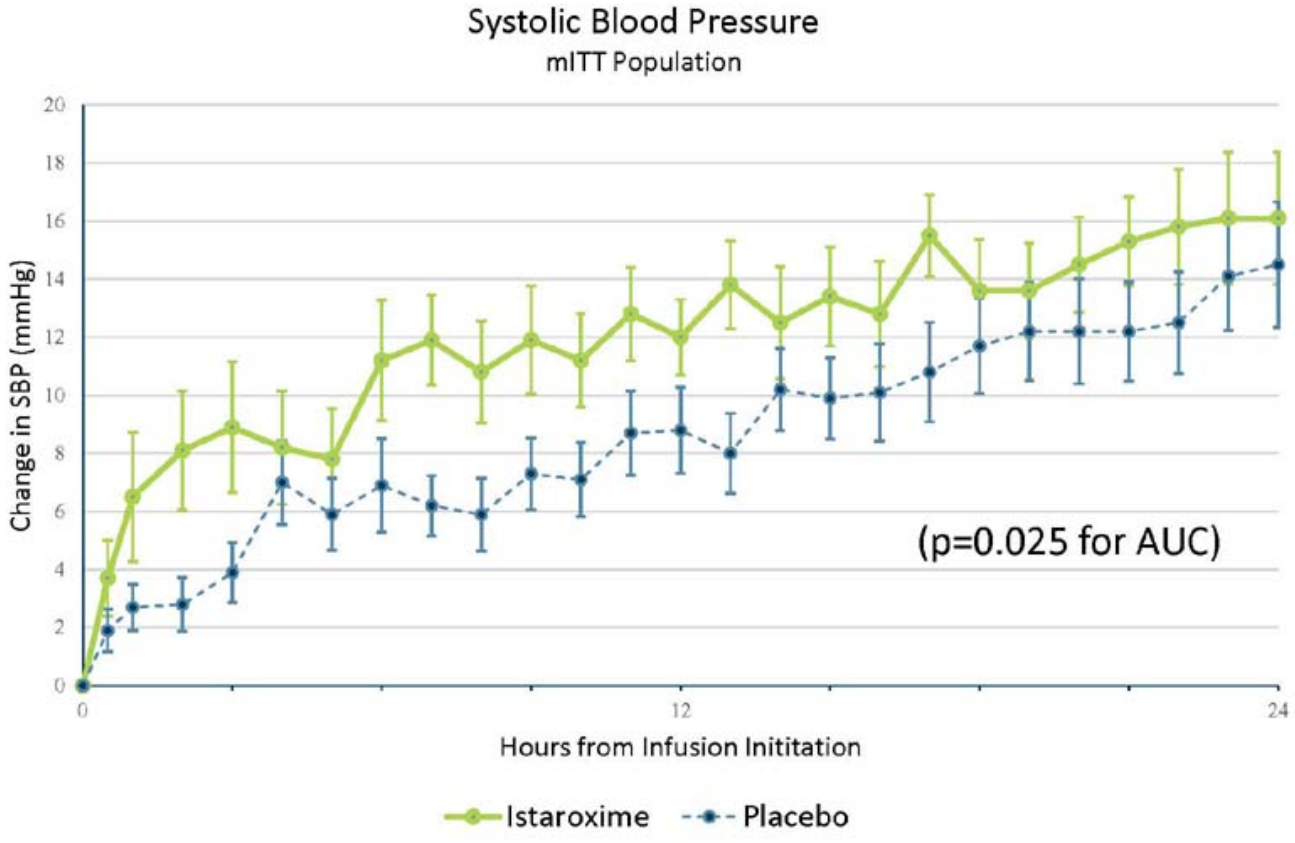
Secondary Results -
Systolic BP Improvements Persisted over 24 Hours



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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 index substantially increased 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

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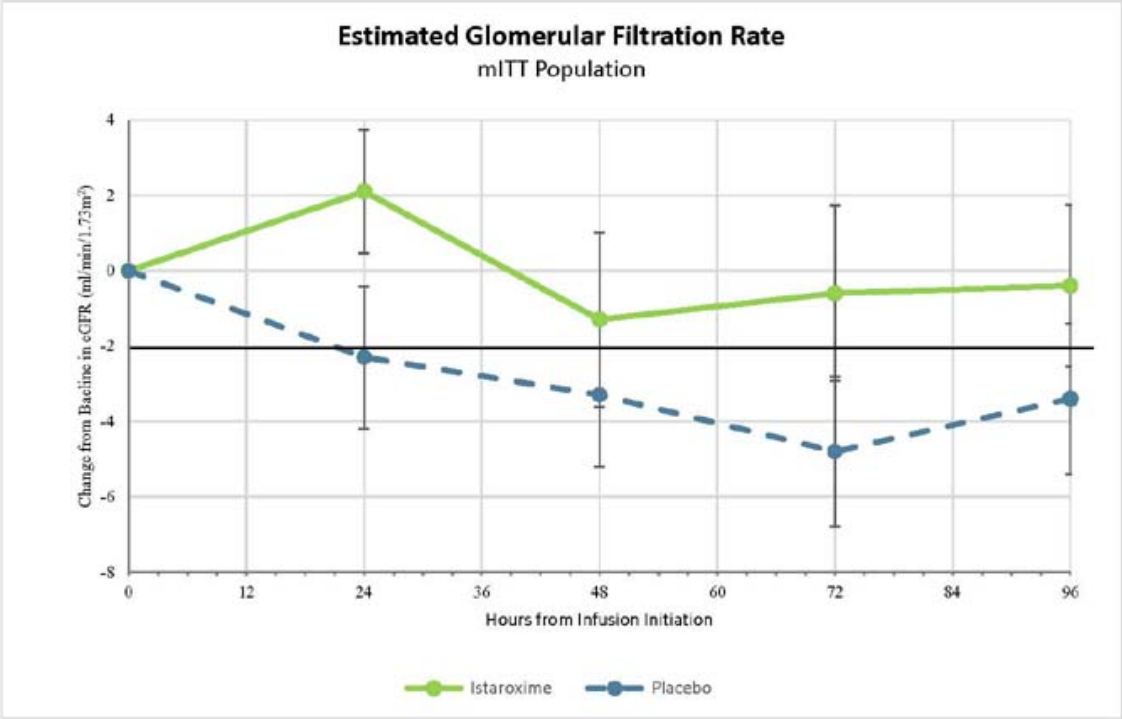
Treatment was Associated with a Positive Renal Profile

- Renal function was not decreased in istaroxime treated patients



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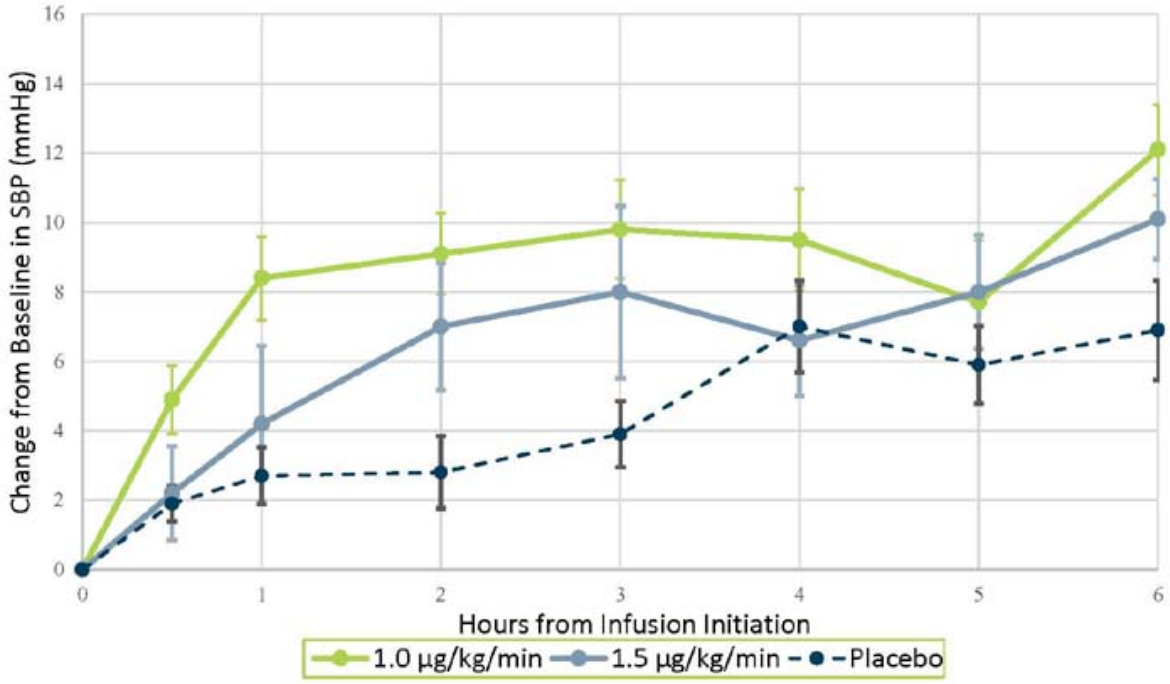
Data shown as means and standard errors

Comparison of Doses

1.0 ug/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 parameters of cardiac function
- More favorable adverse event, serious adverse event and clinical event profile



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 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 rescue agents)

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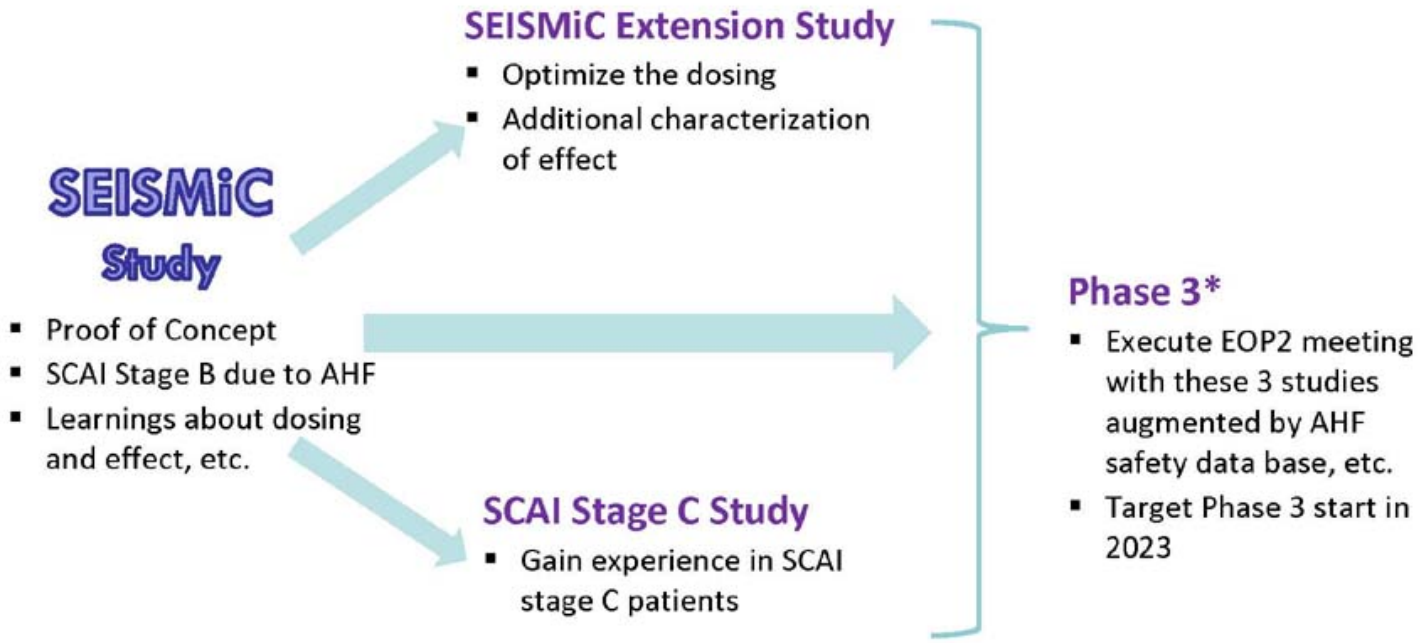
Cardiogenic Shock Development Strategy



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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

~$4MM and
6 months to execute;
Data expected Q2 2023

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 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

~$3MM and
6 months to execute;
Data targeted late Q2 2023

WINDTREE THERAPEUTICS

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 -
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

Financial Summary & Capitalization as of March 31, 2022

- Cash & Equivalents of ~$15.5 million

Securities	Common Equivalents as of May 5, 2022
Common Stock	29,406,172
Options (WAEP $7.81)	4,163,934
Restricted Stock Units	554,000
Warrants (WAEP $9.43)	16,628,802
Fully Diluted Equivalents	50,752,908

Strategy for Value Generation

WINDTREE THERAPEUTICS

- **Communicate Our Milestones**: Share the results from our late-stage clinical programs for achievement of milestones and news flow that may be growth catalysts - set new milestones for the future
- **Transactions**:
  - Secure focused BD transactions for deal revenue and non-dilutive financial support of clinical development
  - Progress heart failure platform to an attractive and valuable position for global partnership (while retaining US co-promotion rights)
- **Optimization**: Bring in new, well-suited development opportunities and transactions

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Windtree Therapeutics

"Striving to Deliver Hope for a Lifetime!"

WINDTREE THERAPEUTICS

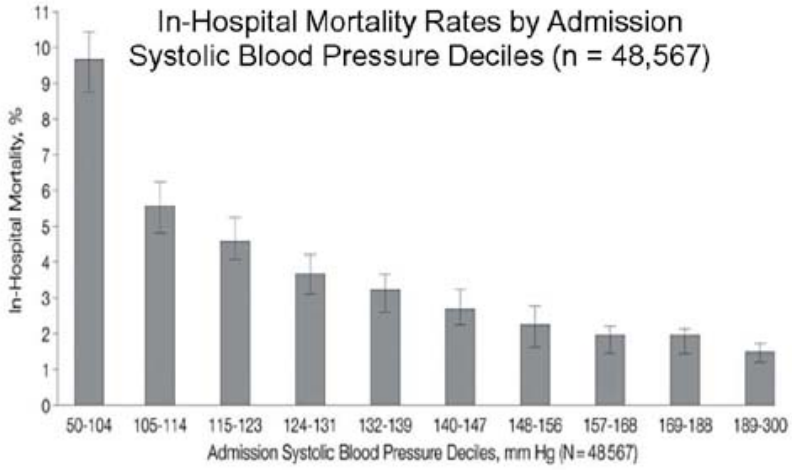
Appendix

WINDTREE THERAPEUTICS

Acute Heart Failure

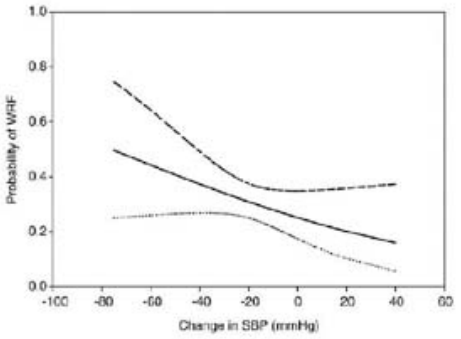
Significant Healthcare Issue with Significant Unmet Clinical Need

- **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 failure[2]



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

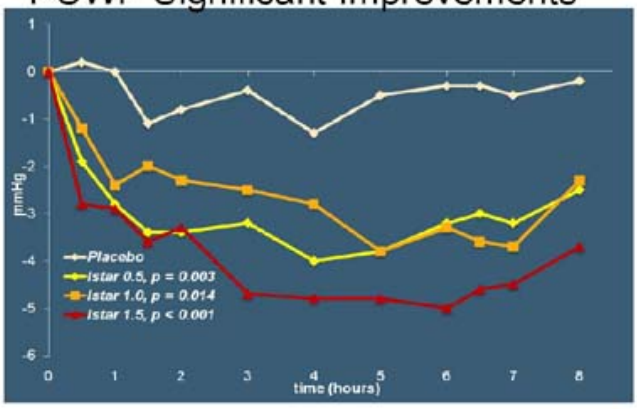
1) ADHERE Registry, n=48,567; JAMA 2006
2) European Journal of Heart Failure; Voors, PRE-RELAX AHF Study; 2011; 13

Istaroxime Phase 2a (HORIZON-HF) Study

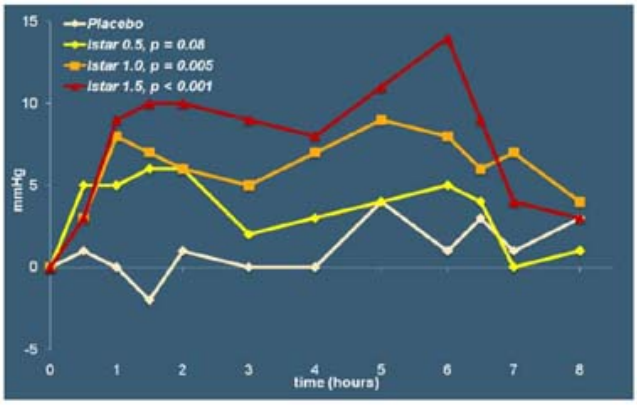
- Multicenter, double blind, placebo-controlled, doses 6-hour infusion of istaroxime 0.5, 1.0, 1.5 ug/kg/min, conducted in the EU
- Hospitalized with AHF, with criteria including:
  - LVEF ≤ 35%
  - SBP 90-150 mmHg
- N=120 (30/group)
- Significant improvement in PCWP, SBP, heart rate was lower. Istaroxime 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%)

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

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%)

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