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): September 26, 2023

Windtree Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-39290**	**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 September 26, 2023, Windtree Therapeutics, Inc. (the "Company") updated information reflected in a slide presentation, which is filed herewith 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	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.

Dated: September 26, 2023

Windtree Therapeutics, Inc.

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

Exhibit 99.1


Windtree Therapeutics
Company Overview
September 2023
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 Company's most recent reports on Form 10-K, and any subsequent quarterly reports on Form 10-Q and current reports on 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.

Investment Highlights

- Clinical stage biopharmaceutical company focused on acute cardiovascular critical conditions with advanced stage programs intended to address large markets with significant unmet needs (NASDAQ: WINT)
- First in class, novel lead asset istaroxime has demonstrated positive efficacy and an attractive profile compared to currently available rescue medications in three Phase 2 global studies, highlighted by improvements in cardiac function and increases in blood pressure with favorable renal function profile
- Attractive cardiogenic shock development pathway with potential for relatively small, rapid, low-cost clinical studies with attractive primary endpoint (blood pressure)
- Advancing pipeline to generate several planned clinical milestones and readouts over the next 12-18 months. Company expects to be Phase 3 ready in cardiogenic shock in 2H 2024
- Focus on business development activities for potential deals with global partners or other strategic opportunities
- Lean, capital efficient operation led by a highly experienced management team

Multi-Asset / Indication Pipeline with Several Near-Term Milestones

Cardiogenic Shock with Istaroxime as Lead Program

Multi-asset Heart Failure platform for partnership

Product Candidates	Indication	Phase	Development Status / Plans
Priority Program **Istaroxime**	**Cardiogenic Shock**	**Phase 2**	• **Lead program** • **Positive Phase 2 study** • **Executing small follow-on studies with planned Q2'24 read-outs intended to transition to phase 3**
Istaroxime	Acute Heart Failure	Phase 2b (completed)	• Positive 2a and 2b data • Augment AHF data with cardiogenic shock data, if positive and adequate, for phase 3 for AHF with partnership
Oral SERCA2a Activators	Chronic Heart Failure, including potentially HFpEF	Preclinical	• Chronic and Acute Heart Failure • Target for collaboration/partnership
Rostafuroxin	Treatment Resistant Hypertension - Genetically Associated	Phase 2b	• Phase 2 data in hypertension and genetically associated hypertension • Company holding development to out-license and repositioned for the attractive and large Resistant Hypertension market
KL4 Surfactant and AEROSURF	KL4 surfactant Drug/Device Tx for RDS and potential other applications	Phase 2b	• Global out-license to Lee's Pharma • Lee's Pharma responsible for all costs of development

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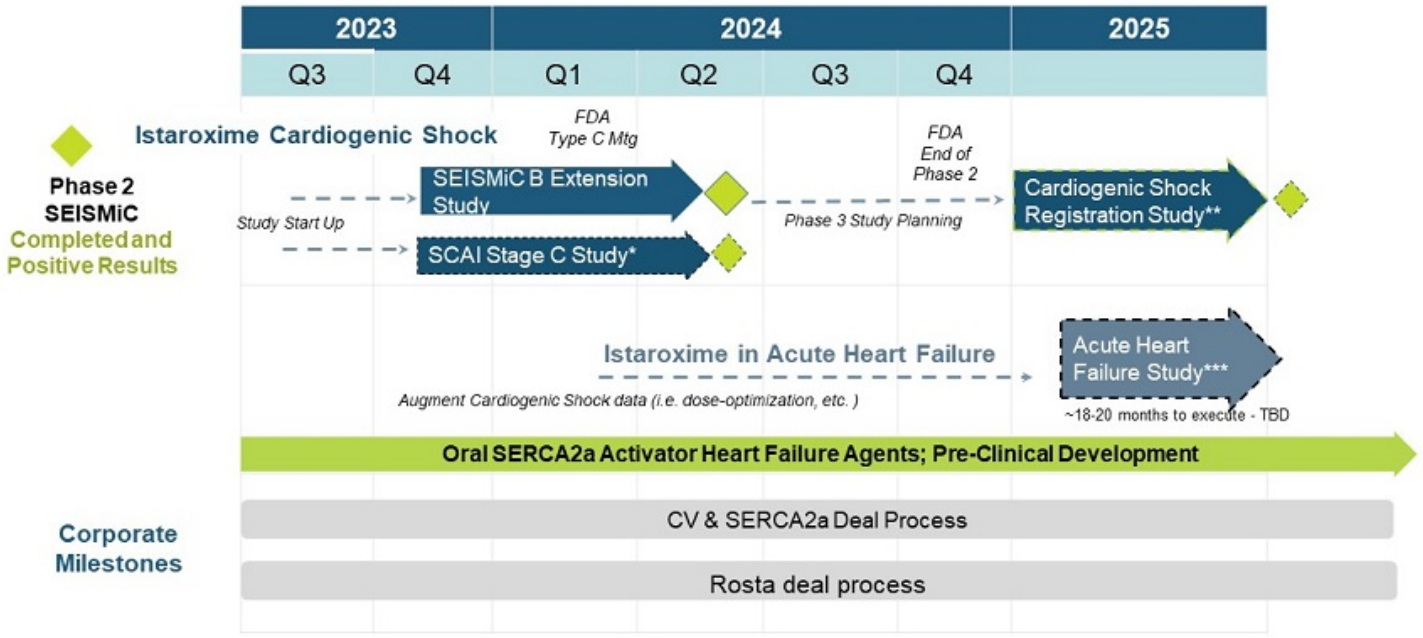
Istaroxime Milestones and Strategy for Value Creation



* Study start-up; initiation and guidance to be confirmed in Q4 2023
** Study and guidance pending positive EOP2 meeting and adequate funding
*** Study and guidance pending positive EOP2 meeting and adequate funding (via partnership)

◆ Represents planned topline data available

Istaroxime

Cardiogenic Shock

Potential to transform the standard of care for critical patients

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Cardiogenic Shock - *A Critical Condition Caused by a Failing Heart*

A severe presentation of heart failure characterized by **low blood pressure and inadequate blood flow to vital organs (hypoperfusion)** accompanied by congestion and high filling pressures of the heart. It **requires very urgent treatment.**

- Caused by severe impairment of cardiac function that results in diminished cardiac output, end-organ hypoperfusion and hypoxemia
- Most often requires pharmacological or mechanical intervention with key clinical objective to increase SBP to >90mmHg and improve tissue perfusion
- Cardiogenic shock patients typically require hospital intensive care and consume significant hospital resources
- High mortality (~30-40%) and substantial morbidity in survivors[1]
- US + EU markets represent an ~$1.0B market potential[2] with high unmet need

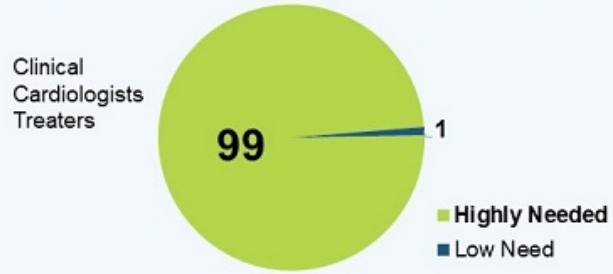
1) Kolte D, American Heart Association; 2014 Jan 13; (rates associated with classic, stage C shock)
2) Estimates from claims data and epi data September 2021, multiplied by assumed various regional prices

Significant Unmet Need and Reported Desire for Istaroxime

- **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"
- A therapy that can be used **earlier** to rapidly **improve blood pressure and cardiac function without unwanted side effects** is needed

Market research shows need and enthusiasm for istaroxime profile

100 U.S. Cardiologists *questioned on degree of* ***unmet need for new innovative pharmacologic treatments for ECS[1]***



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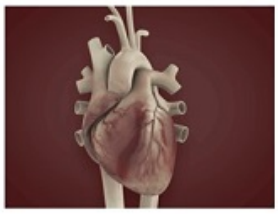
1) Market research conducted by Sermo, a leading provider of real time physician insights

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 **Increases the Force of Contraction**
via inhibition of the sodium-potassium pump and effects on the sodium-calcium exchanger

2 **Improves Cardiac Relaxation**
via stimulation of SERCA2a activity which enhances calcium reuptake

Impact on both systolic (contraction) and diastolic (relaxation) dysfunction

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Istaroxime Cardiogenic Shock Program Came from AHF Phase 2 Trials and the Potential Attractive Regulatory Pathway

Phase 2a and 2b data in AHF - istaroxime uniquely and significantly improved:

Cardiac Function
- increased stroke volume
- lowered cardiac filling pressures

Systolic Blood Pressure

Renal Function (eGFR)

Key Question that Windtree Decided to Answer with a Clinical Study:
Would istaroxime increase BP and improve cardiac function for early cardiogenic shock?

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

Positive Results in the Early Cardiogenic Shock Study

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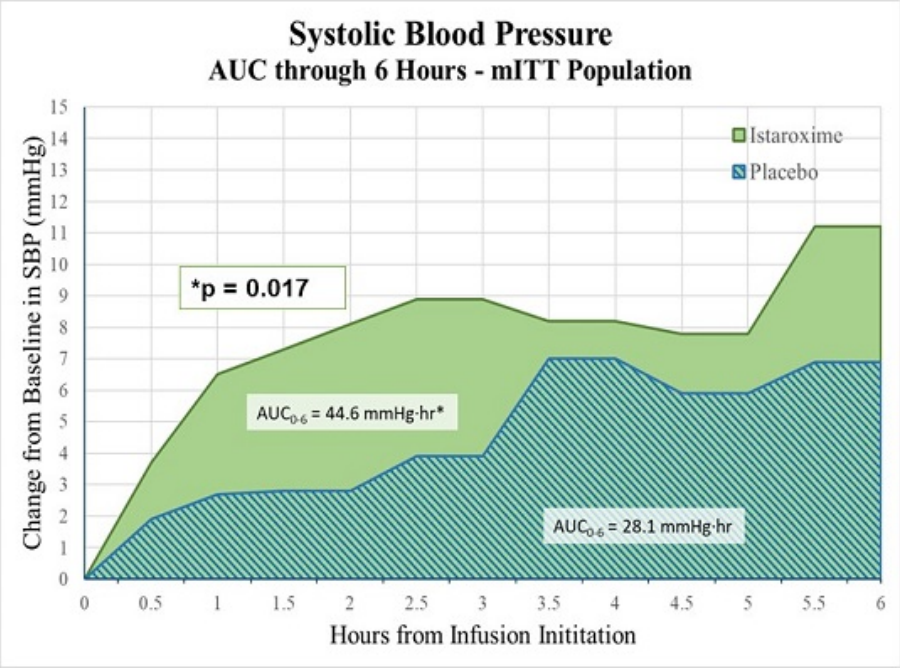
Istaroxime Achieved Positive Primary Endpoint



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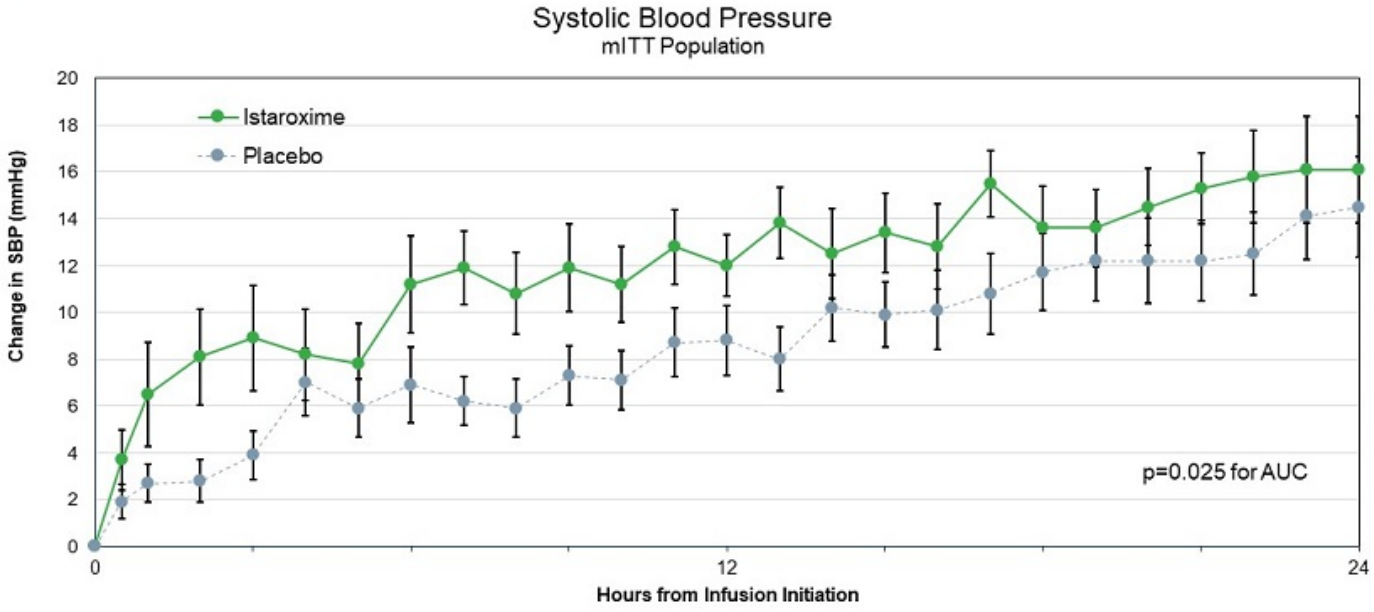
Systolic BP Improvements Persisted over 24 Hours



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Cardiac Function Improvement

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

- ✓ **Cardiac index (amount of output from the heart over a minute) significantly increased**
- ✓ **Stroke volume (amount of blood from the heart with each heartbeat) substantially increased**
  - (4 mL/m^2) approaching statistical significance
- ✓ **The strength and cardiac geometry of the heart improved including:**
  - Left atrial area was reduced
  - Left ventricular end systolic volume was reduced
  - Left ventricular end diastolic volume was reduced

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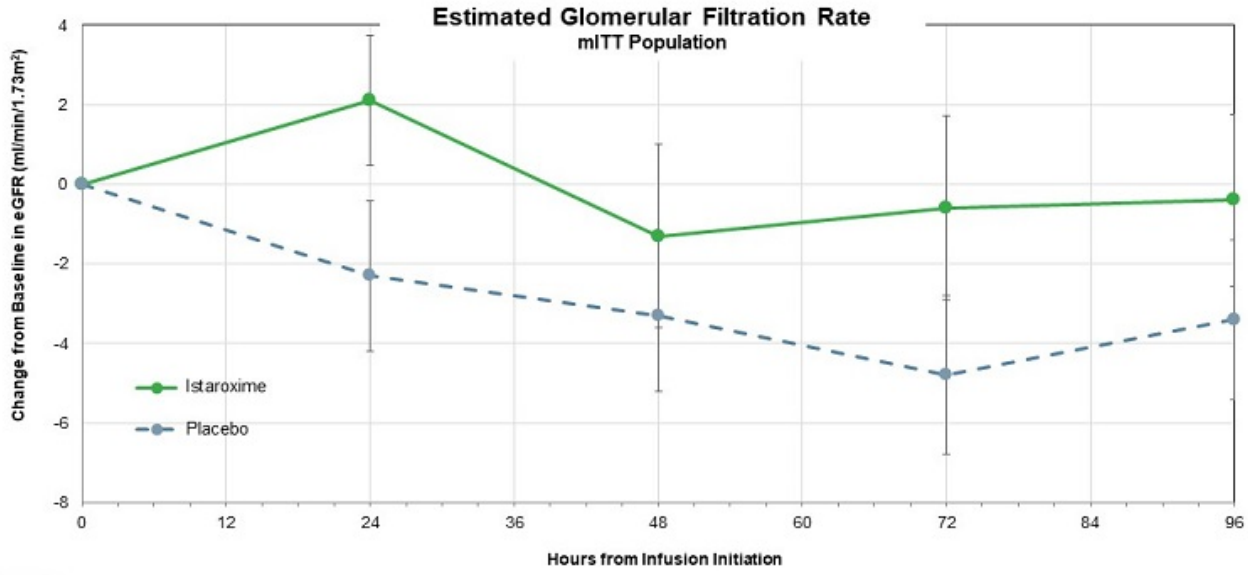
Treatment was Associated with a Favorable Renal Profile

Renal function was not decreased in istaroxime treated patients



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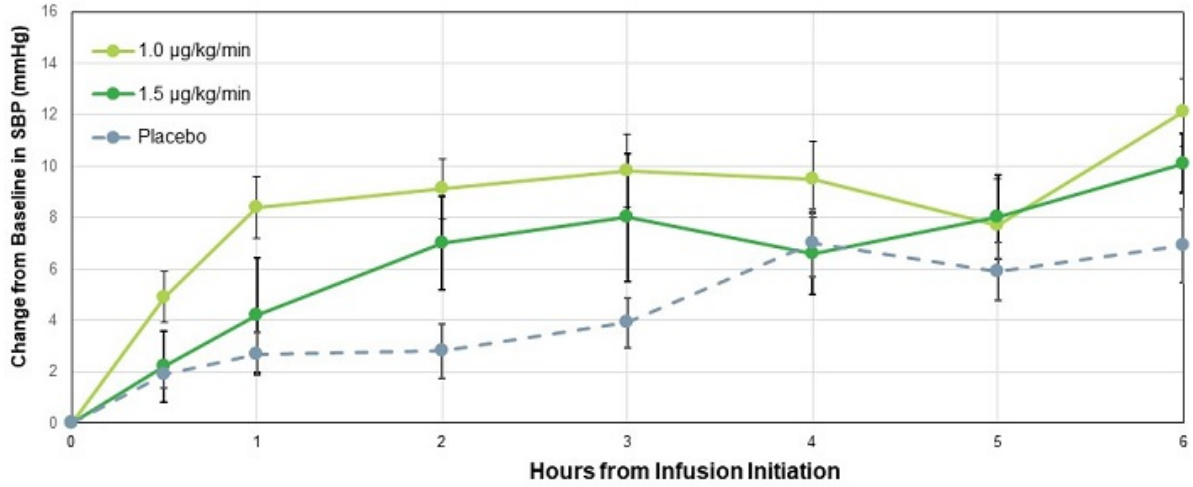
Data shown as means and standard errors

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



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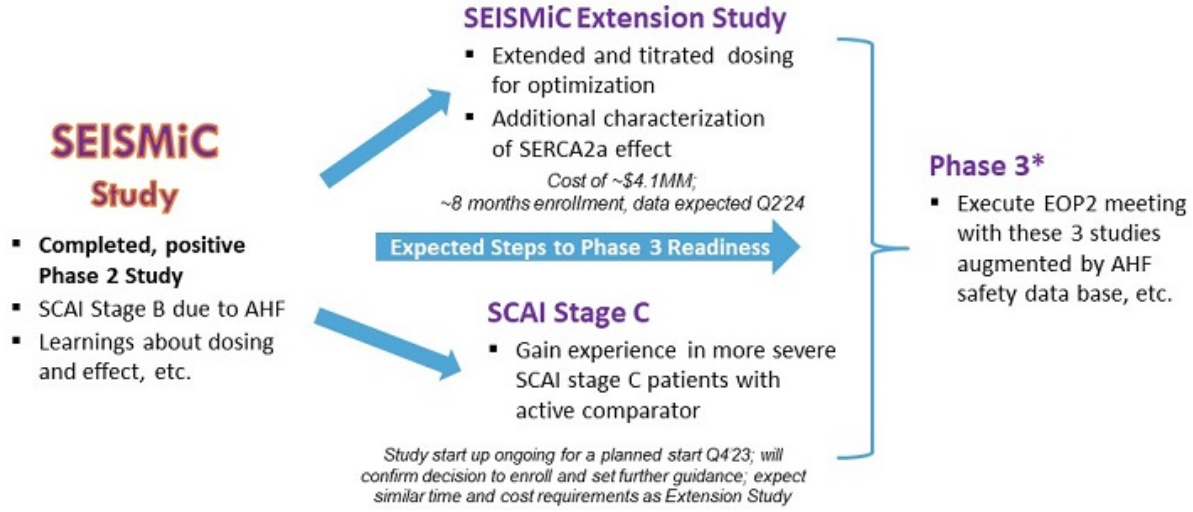
All Subjects (n=60)

SEISMiC Study Results Summary

- ✓ 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 align with the existing data from the program in AHF

Cardiogenic Shock Development Strategy

Focus on thoroughness, speed and relatively low cost of trials



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

Istaroxime Cardiogenic Shock Studies

Expected Steps to Phase 3 Readiness

Dose Optimization – Extension Study

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

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

Two istaroxime doses versus placebo. Istaroxime dosed for up to 60-hours, decreasing the dose over time

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

SCAI Stage C Study

Study Objectives:

- Gain experience with istaroxime in SCAI stage C patients experiencing hypotension effects on organs
- Study istaroxime in a setting which has active background therapy (pressors) present

20 patients with SCAI Stage C shock due to ADHF: Hypotension + hypoperfusion. (Protocol will allow additional enrollment after this review)

Istaroxime or placebo will be added to initial standard of care shock therapy (blinded)

Hold shock therapies constant for 6 hours to assess the primary BP endpoint, changes are allowed if the patient's condition dictates. Thereafter, taper the initial shock therapy with istaroxime supporting the patient

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

Plan allows the potential for more subjects to be added to the study

Cardiogenic Shock Represents a Significant Opportunity for Istaroxime and Windtree

DRIVERS OF OPPORTUNITY AND COMMERCIAL VALUE

- ✓ Very long average length of hospital stay (~ 19.5 days[1]) means high cost of hospital care (estimated >$175k[2]) and creates opportunity for pharmacoeconomic benefits
- ✓ Currently available pharmacologic treatments have undesirable side effects and poor outcomes
- ✓ Lack of competition in development or in the market
- ✓ Attractive valuation of commercial market potential versus time and cost of development

[1] US Hospital Claims Data, 2022
[2] Healthcare.gov, Department of Health & Human Services , estimated from average cost of hospital stay
[3] Long et al, USC Cardiology Review, Describing and Classifying Shock: Recent Insights, Sept 2021

STRATEGIC POSITIONING

Covers ~85%* of Addressable Market[3]

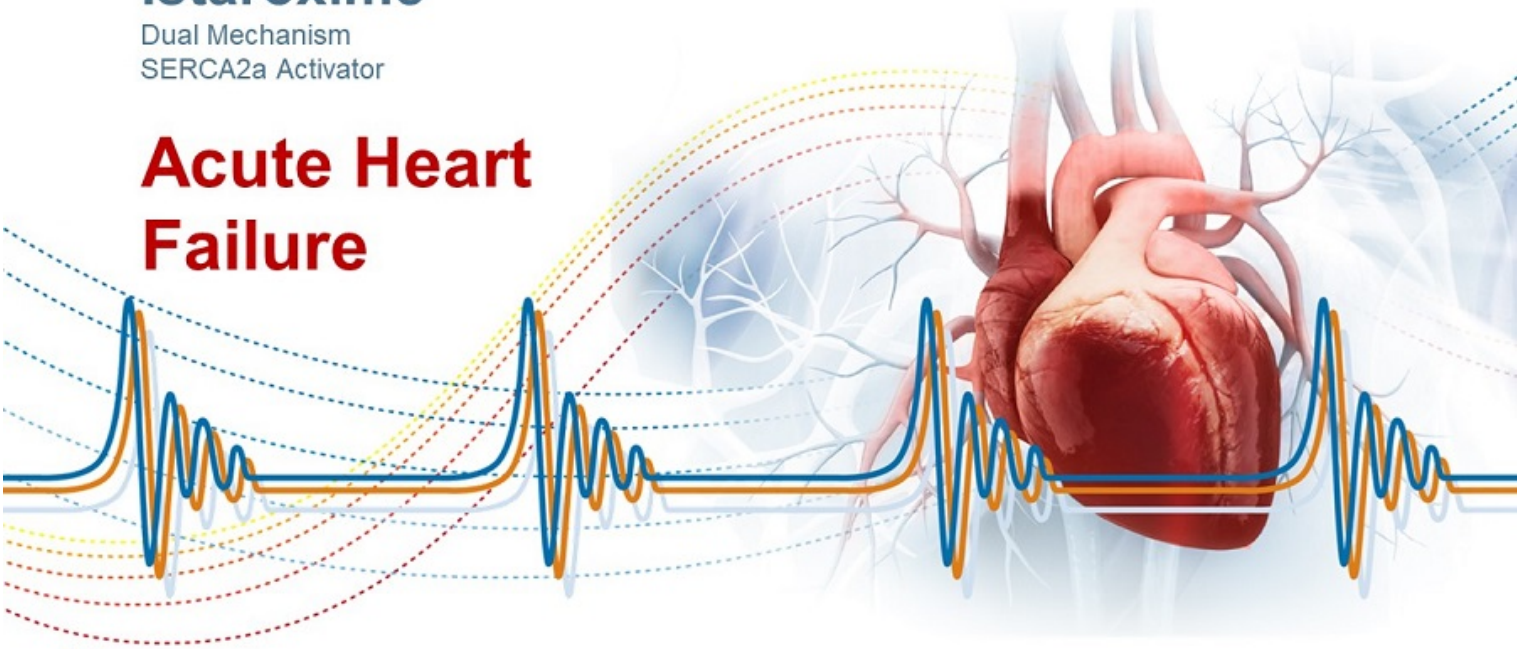
1. **Expand the Market due to Profile:** SCAI Stage B / Early Cardiogenic Shock (where vasopressors are reserved) to help stabilize the patient and prevent deterioration
2. **Become the Preferred Agent:** Preferred agent with first line use in SCAI Stage C / Classic Cardiogenic Shock

*Calculation removes SCAI Stage A

Istaroxime

Dual Mechanism
SERCA2a Activator

Acute Heart Failure



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Heart Failure –
A Large and Growing Market with Significant Mortality and Unmet Need

#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

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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**

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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**

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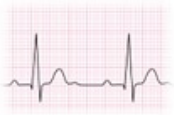
Istaroxime in AHF Phase 2b – Results Summary

Cardiac Function Improved with Both Doses

- Significant increase in stroke volume (amount of blood expelled with each heartbeat)
- Lowered cardiac filling pressures

Increased in Systolic Blood Pressure

Increased Renal Function (eGFR)



Heart Rate Decreased

Favorable Heart Rhythm Profile Observed

- No increase in clinically significant arrythmias or ventricular tachycardia

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Istaroxime – Acute Heart Failure

Objective: Evaluate potential Phase 3 AHF program based on data from our cardiogenic shock program

Potential Phase 3 AHF Program

Augment our data from the positive phase 2a and phase 2b AHF studies with the efficacy, safety and dosing and characterization learnings from the extension and other studies in the severe AHF patients experiencing early cardiogenic shock. If positive and adequate, move istaroxime into phase 3 for AHF.

Our strategy is to focus on treating heart failure patients with low blood pressure, who also tend to be diuretic resistant, as a patient population that we believe could particularly benefit from the unique profile and potential ability of istaroxime to increase cardiac function and increase blood pressure while maintaining or improving renal function.

Currently seeking partnership to execute this clinical trial

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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

- **Potential Oral & i.v.** therapies for chronic heart failure (CHF) and AHF
- Attractive approach for **heart failure with preserved ejection fraction (HFpEF) -** which represents nearly half of heart failure** and is underserved

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

- **"Next generation istaroxime"** as oral/i.v. for **in-patient acute and out-patient chronic use**
- **Granted patent for composition of matter** from the European Patent Office and issued patent from the US Patent and Trademark Office

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

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**American Heart Association, Circulation Research, Vol. 124, No. 11, Heart Failure with Preserved Ejection Fraction in Perspective, May 2019

Active Engagement in BD Opportunities

Goal: Non-Dilutive Resourcing and Creating Shareholder Value

Global / Regional Licensing

COMPLETE

AEROSURF / KL4 Platform –

- Exclusive global license to Lee's Pharm and Zhaoke. Potential proceeds:
  - Up to $78.9 million in potential milestone payments, low double-digit % royalties
  - *WINT no longer responsible for any costs for KL4 platform*

Licensing opportunities

- Istaroxime – AHF and Cardiogenic Shock
- SERCA2a Activators – Chronic and Acute Heart Failure
- Rostafuroxin – Treatment Resistant Hypertension

Strategic Transaction

- Acquisition by a pharmaceutical company
- Merger if it creates more shareholder value

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Milestones and Financial Summary

Cash

June 30, 2023	$11.5M

Driving Capital Efficiency to Program Investment

Significantly reduced company expenses and cash burn via out-licensing KL4 platform, focused resources on lead priority program

- **44%** Total Company Burn / Month Reduction 1H'22 vs. 1H'23
- **43%** Non-Program Burn / Month Reduction 1H'22 vs. 1H'23
- **55%** FTE Reduction 1H'22 vs. 1H'23

In the near term, the Company plans to maintain the lower non-program cash burn that was achieved during 1H'23.

Anticipated Events / Milestones
for the next 4-6 quarters

- ✓ Extension Study – first patient enrolled
- ✓ Stage C Study – first patient enrolled*
- ✓ Oral SERCA2a advancement (i.e., patent, pubs)
- ✓ **Extension Study Data**
- ✓ **Stage C Study Data***
- ✓ Regulatory interactions (i.e., End of Phase 2, etc.)
- ✓ Potential for Business Development (ongoing)

** Stage C Study start up ongoing for a planned start Q4 2023; will confirm decision to enroll and set further guidance*

Strategy for Value-Creation -
Focus for the Next 4-6 Quarters

Clinical Milestones
- Strong trial execution of Cardiogenic Shock Extension and SCAI Stage C
- Enable transition to EOP2/Ph3
- Execute select CMC actions

Transformative BD
- Licensing and partnership for non-dilutive value
- Strategic: Increase value, portfolio with enhanced opportunities and mitigated risk

WINDTREE THERAPEUTICS

High IR/PR Communication
- Deliverables and news, dedicated media, etc.

WINT Team

Retention, Motivation and Performance Culture


WINDTREE
THERAPEUTICS