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): July 18, 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 July 18, 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: July 18, 2022


Windtree Therapeutics
Company Overview
July 18, 2022
WINDTREE
THERAPEUTICS
(NASDAQ: WINT)

Forward-Looking Statements

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

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

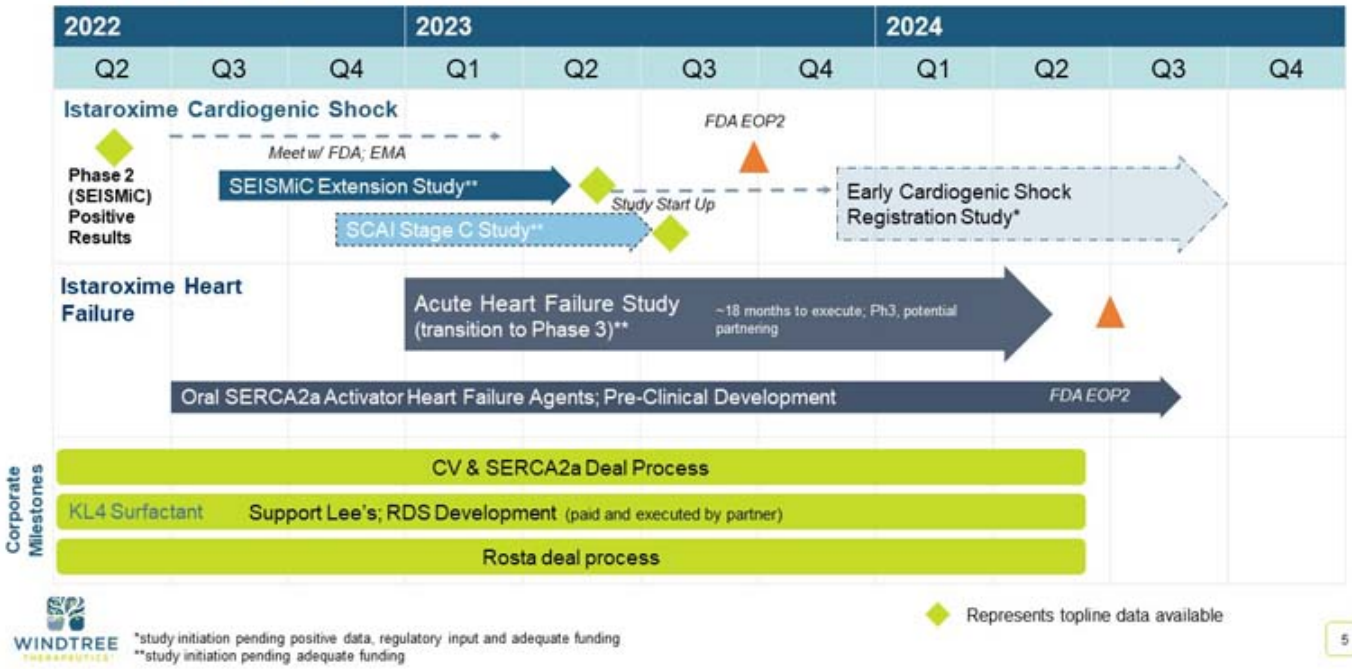
Windtree Therapeutics and Istaroxime Highlights

- **Biopharmaceutical company with advanced clinical focused on significant acute CV markets with high unmet needs and with supportive regulatory paths and designations** (NASDAQ: WINT)
- **Through three Phase 2 global studies, lead asset istaroxime has consistently demonstrated a highly unique and attractive profile**
  - It is the only acute heart failure or shock drug that has demonstrated both significant improvement in cardiac function of a failing heart, as well as rapid and significant improvement in blood pressure, with what so far has been a differentiating safety profile (avoiding many of the use-limiting side effects of existing therapies)
- **Recent positive Phase 2 study with istaroxime in early cardiogenic shock (ECS) paves the way for what we believe is a relatively fast and less expensive developmental and regulatory pathway**
  - Precedent shows blood pressure response can be acceptable as the primary endpoint in a pivotal shock study. Additionally, istaroxime demonstrated significant other benefits that we expect will continue to help us build a strong evidence-based position in the larger Phase 3 planned for 2023.
  - Given what we believe to be an attractive opportunity that may be pursued with less spend and have faster time to market, Cardiogenic shock has become the organization's priority and focus
- **Highly experienced management team and company leadership**

Pipeline

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

Early Cardiogenic Shock

Additional potential indication in active clinical development

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Cardiogenic Shock

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

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

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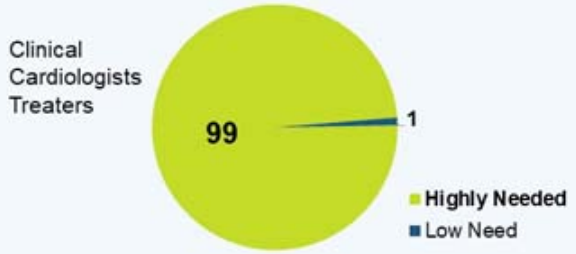
1) Kolte D, American Heart Association; 2014 Jan 13
2) Estimates from claims data and epi data September 2021, multiplied by assumed various regional prices

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

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

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

Early Cardiogenic Shock Treatment
Istaroxime Potential Opportunity for Accelerated Pathway

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

FDA Regulatory Commentary with Break-Through Therapy Designation Potential

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

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

1) Kosaraju A, Hai O. Cardiogenic Shock. [Updated 2019 Jan 25]. In: www.ncbi.nlm.nih.gov/books/NBK482255/ CSRC Think Tank - July 24, 2019
2) Senatore et al., Am J Cardiovasc Drugs, February 2019, Volume 19, Issue 1, pp 11–20 (https://doi.org/10.1007/s40256-018-0297-9)

Istaroxime – Novel First-in-Class Therapy

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

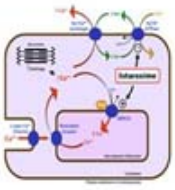
Dual Mechanism of Action

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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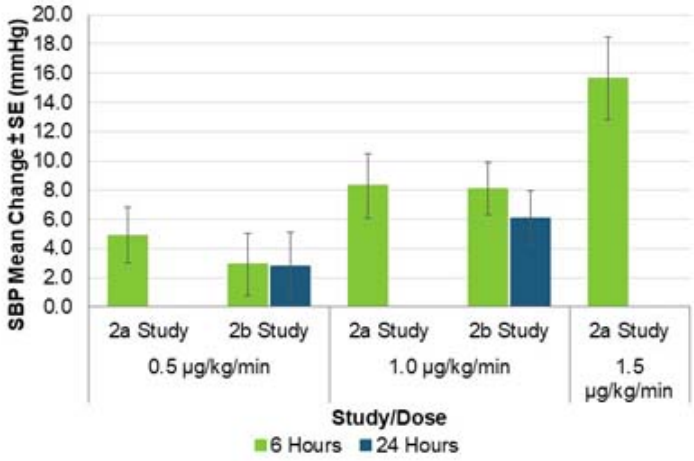
Rationale for Istaroxime in Cardiogenic Shock

Based on Phase 2 Studies in Acute Heart Failure

In the positive Phase 2a and Phase 2b studies in Acute Heart Failure, istaroxime demonstrated:

- ✓ Significantly improved cardiac function
- ✓ Significantly improved systolic blood pressure
- ✓ Attractive tolerability profile including maintained or increased renal function



Mean SBP at Baseline ~112 mmHg

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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

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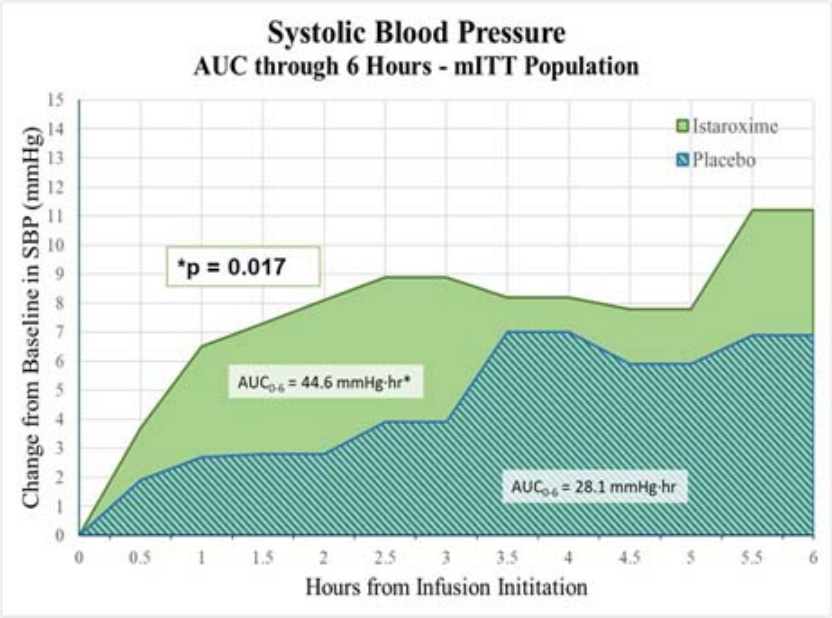
Difference in SBP Profile



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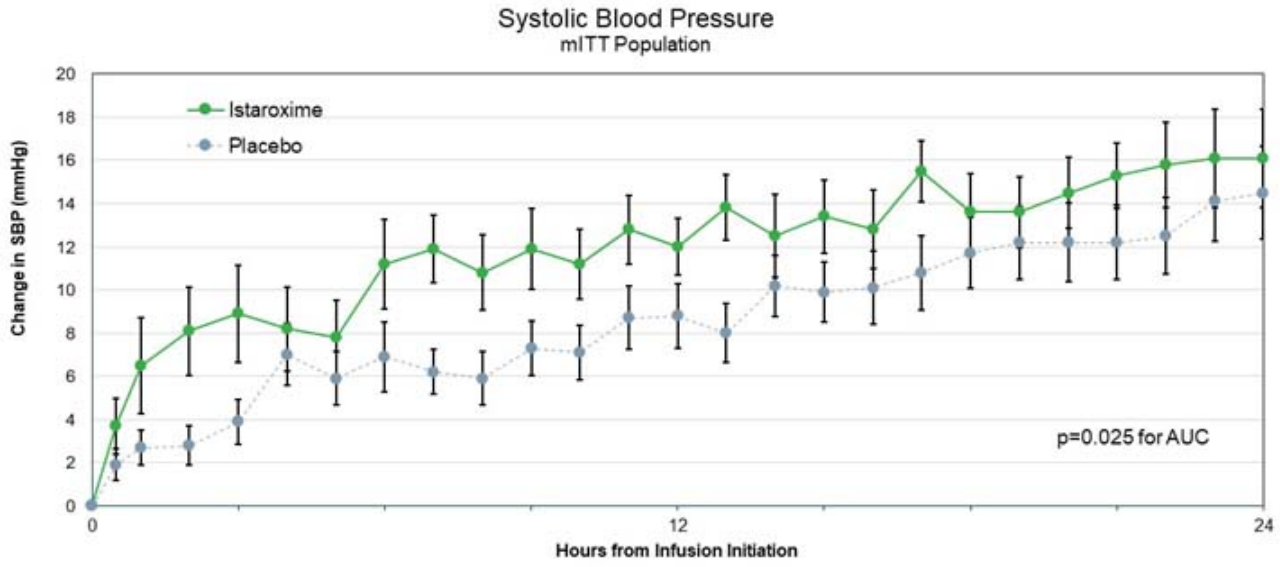
Systolic BP Improvements Persisted over 24 Hours



Cardiac Function Improvement

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

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

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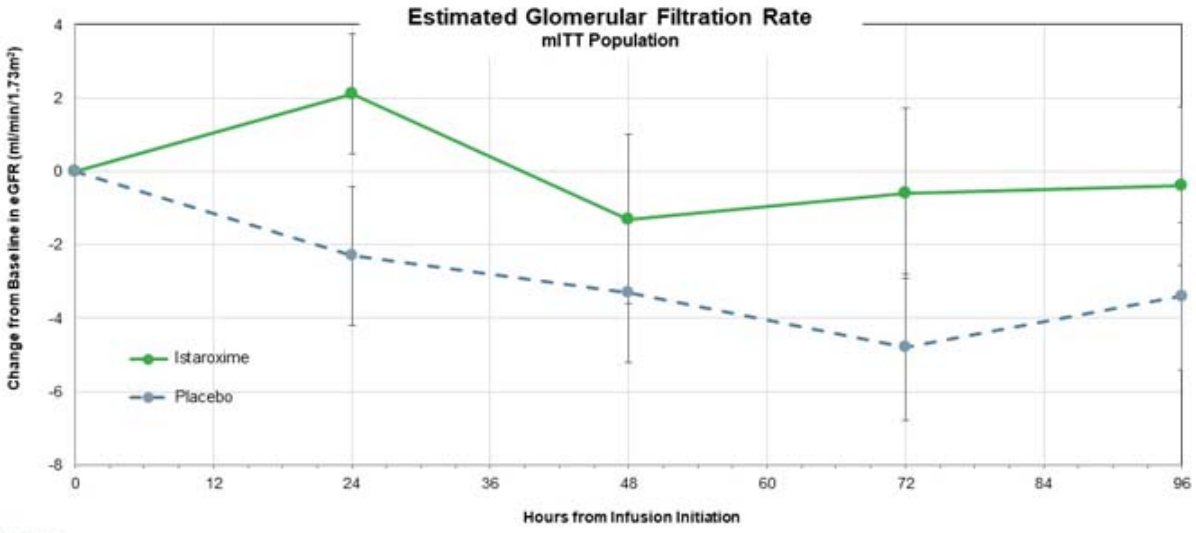
Treatment was Associated with a Favorable Renal Profile

Renal function was not decreased in istaroxime treated patients



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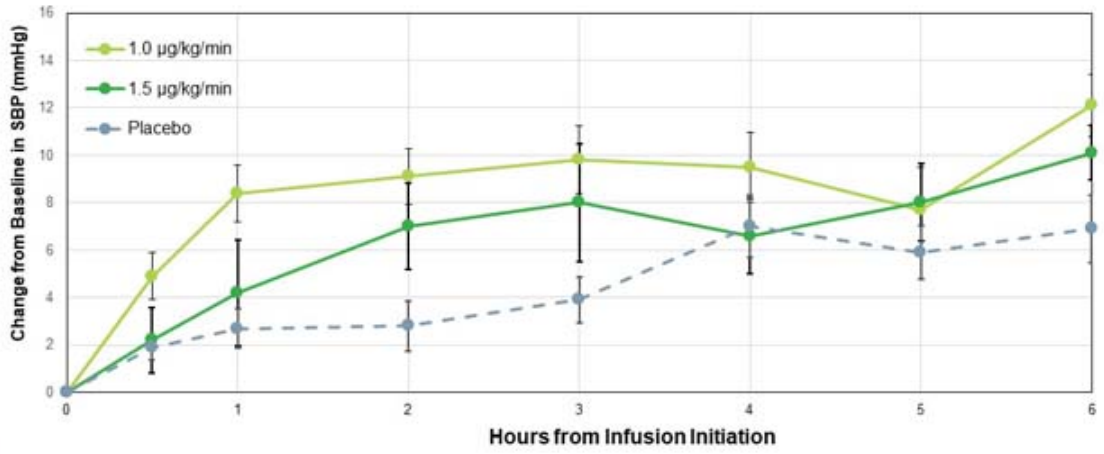
Data shown as means and standard errors

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 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

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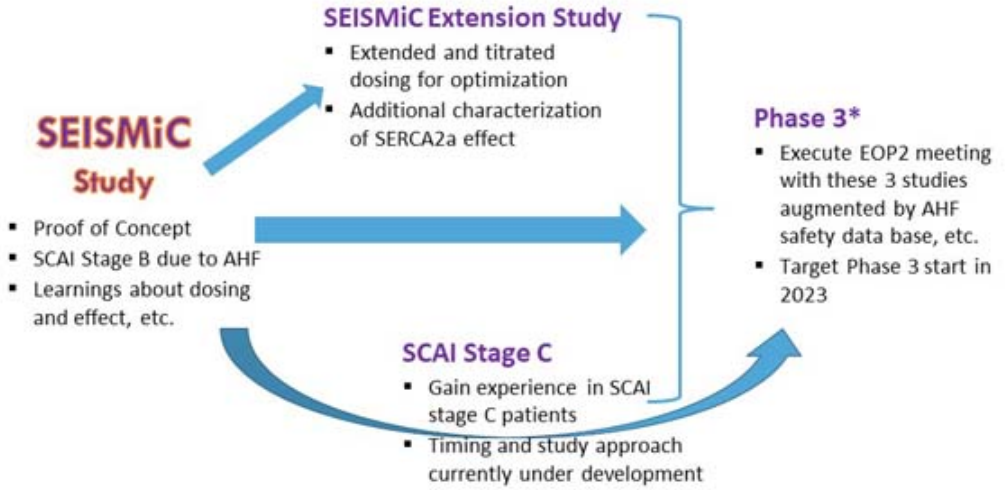
Relevance to the Acute Heart Failure (AHF) Program

- 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)

Cardiogenic Shock Development Strategy



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

Plan for Dose Optimization – Extension Study

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

Study objectives:

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

Current study plan design:

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

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

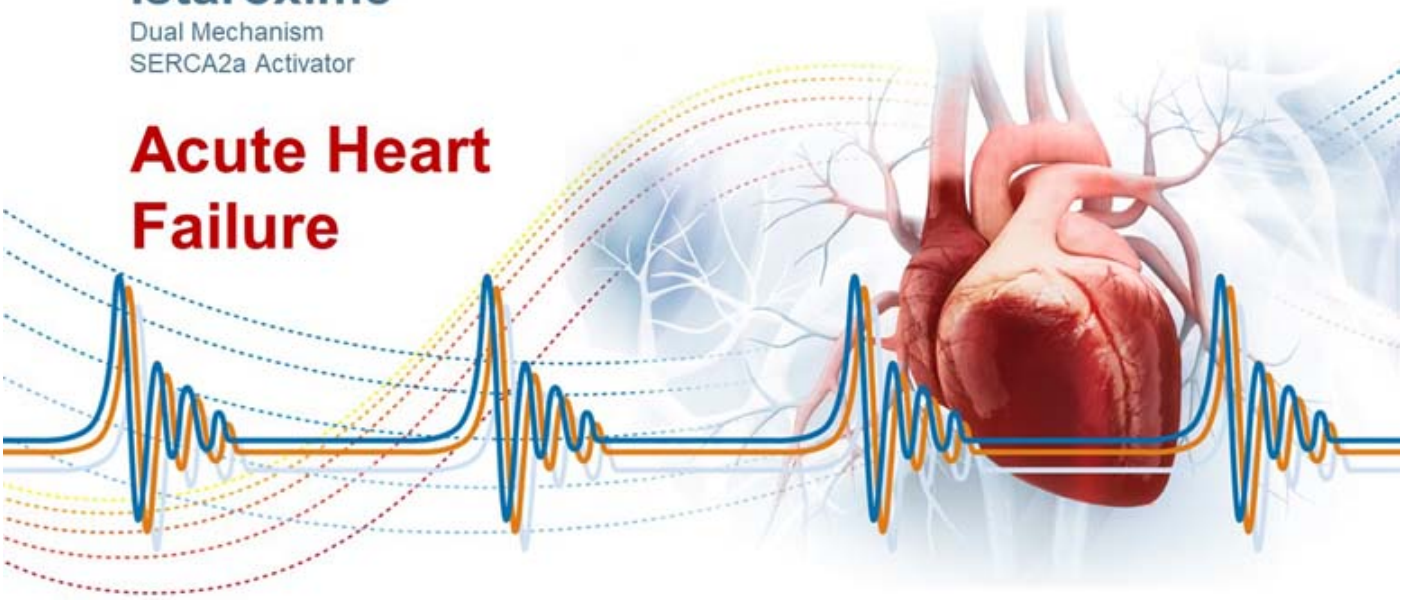
Multiple physiologic measures associated with cardiac function, blood pressure and safety
Approximately 6 months of recruitment

** Study plans and progression dependent upon regulatory alignment and resourcing*

Istaroxime

Dual Mechanism
SERCA2a Activator

Acute Heart Failure



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Heart Failure – Large, Growing Market But Underserved

The prevalence and mortality of heart failure is high and increasing

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

Annual Admissions
~1.3M U.S.
~1.5M E.U.

Patients
7M U.S.,
25M+ worldwide

~7%
In-patient mortality
30-day mortality can exceed 10%

>$18B
annual U.S. hospital costs
Most expensive of the Medicare diagnoses

0
New pharmacologic advancements in acute heart failure for decades

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

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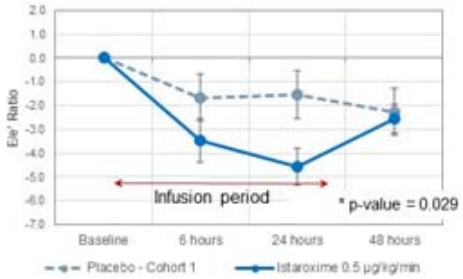
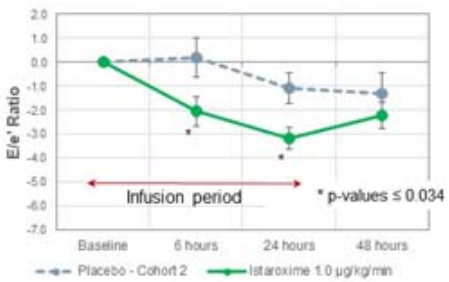
Primary Endpoint Achieved
Significant Changes in E/e' Ratio[1] and Stroke Volume

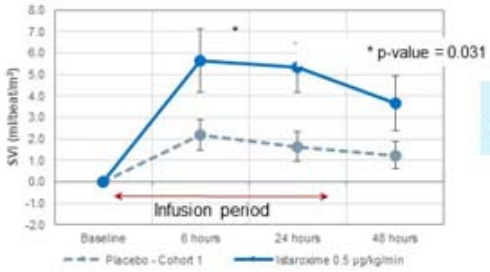
Istaroxime 0.5 µg/kg/min vs. placebo



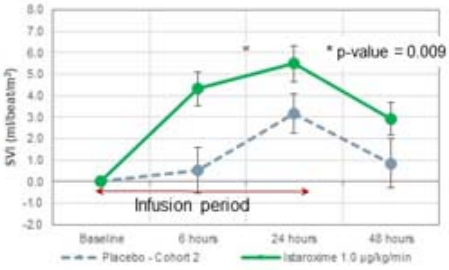
Istaroxime 1.0 µg/kg/min vs. placebo



E/e'



Stroke Volume



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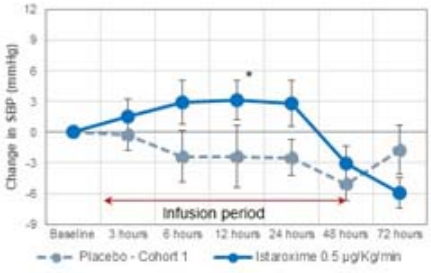
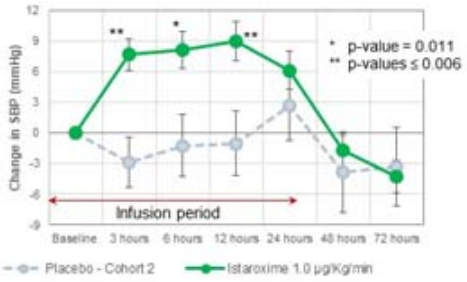
1) E/e' echocardiographic assessment of PCWP; Note: Data shown as means and standard errors

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

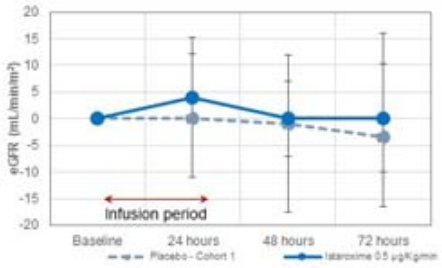
Istaroxime 0.5 µg/kg/min vs. placebo

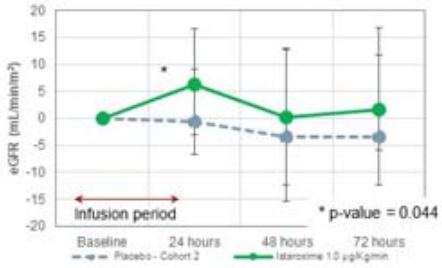


Istaroxime 1.0 µg/kg/min vs. placebo



Systolic Blood Pressure (SBP)





GFR (Renal Function)

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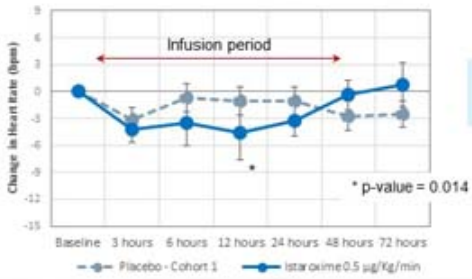
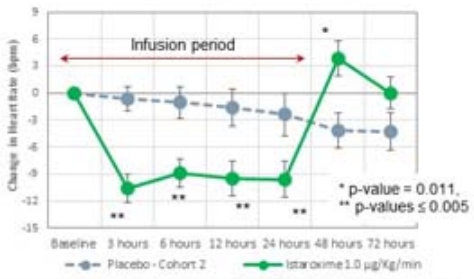
Data shown as means and standard errors

Heart Rate Decreased and No Increases in Cardiac Troponins

Istaroxime 0.5 µg/kg/min vs. placebo

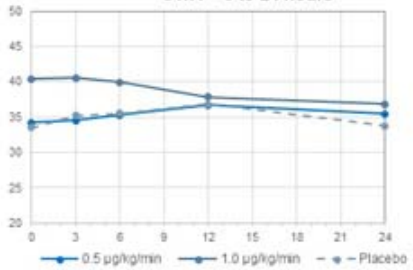


Istaroxime 1.0 µg/kg/min vs. placebo

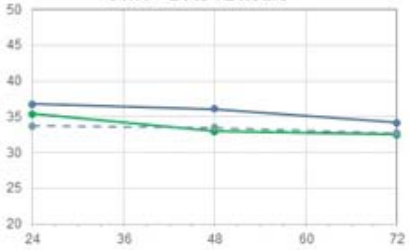


Heart Rate

cTnT – 0 to 24 hours



cTnT – 24 to 72 hours



Cardiac TnT (Myocardial Damage)

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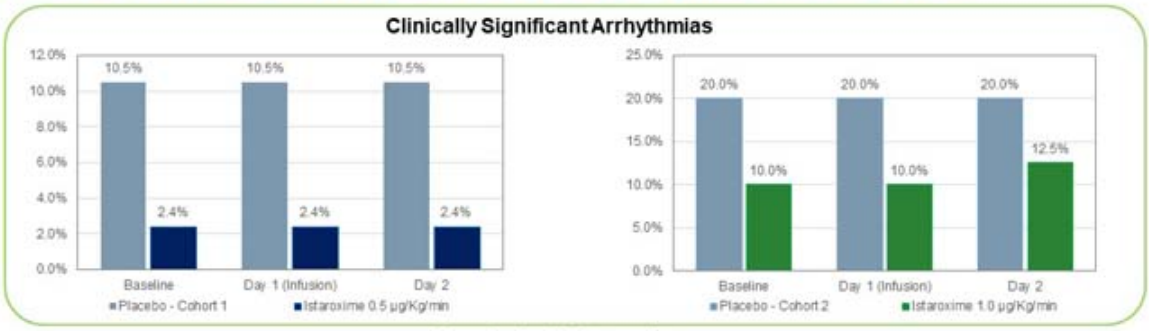
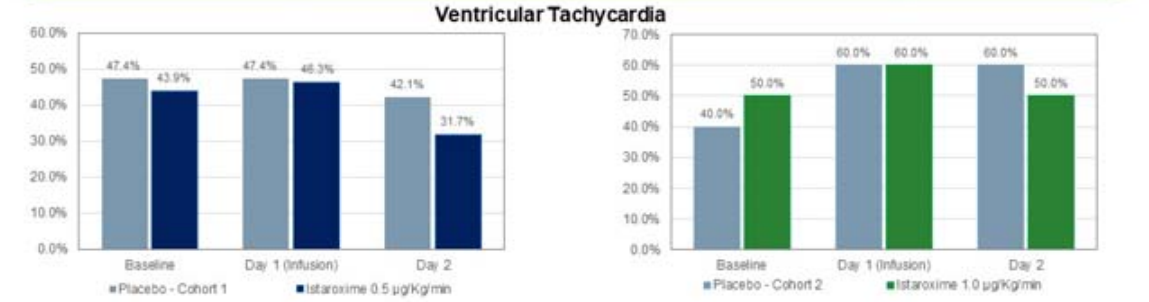
Favorable Profile Observed with 24-hour Holter Monitoring





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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

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

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

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

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

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

Pending adequate funding; ~18 months to execute

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* Estimates

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

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

Selective SERCA2a Activators

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

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

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

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

Summary

- ✓ Istaroxime has produced positive, differentiating data in three Phase 2 studies for two separate and complementary indications. These markets have significant unmet needs, and no known other late-stage programs in development to address the acute decompensated patient
  - The data is consistent, across all regions / populations and across many endpoints (including many in early cardiogenic shock despite small trial).
- ✓ Istaroxime has demonstrated a highly unique and desirable profile:
  - Improved cardiac function *without coming at the expense of:*
  - Improved SBP and renal function
  - Favorable safety tolerability profile compared to existing therapies
    The recent very positive data in cardiogenic shock paves the way for a relatively fast and inexpensive developmental and regulatory pathway
- ✓ Recent positive Phase 2 study with istaroxime in early cardiogenic shock (ECS) paves the way for what we believe is a relatively fast and less expensive developmental and regulatory pathway
- ✓ The AHF program will proceed with business development (which remains a pre-Phase 3 strategy for istaroxime) and/or additional resourcing while also advancing the next generation, oral SERCA2a activators for chronic and acute HF including HFpEF

Financial Summary & Capitalization

Cash & Equivalents of ~$15.5 million as of March 31, 2022

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

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Appendix

Istaroxime Unique Opportunity With Attractive Risk / Return Profile

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

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

Istaroxime: Attractive Risk, Time, Cost and Return Profile

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

5. Long, successful history of CMC

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

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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

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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%)

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

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

1.0 µg/kg/min dosing was associated with:

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%)

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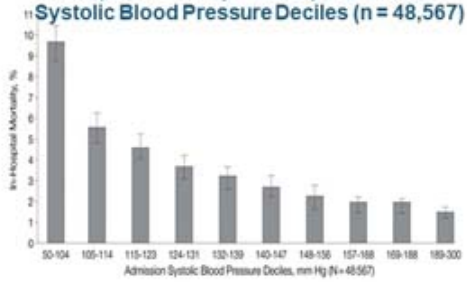
* LS-Means and associated p-values from ANCOVA model adjusted for pooled site, treatment, and baseline systolic BP.

Acute Heart Failure

Significant Healthcare Issue with Significant Unmet Clinical Need

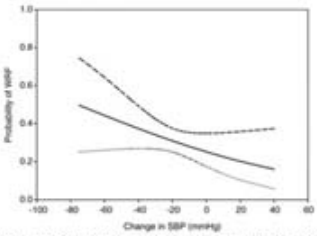
- Patients with low blood pressure (SBP) and peripheral hypoperfusion are high risk, challenging patients. These patients are also generally resistant to diuretic therapy and often discharged in a sub-optimal state.
  - Low SBP in-patient mortality approximately two-fold greater than normal/high SBP[1]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

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



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

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



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

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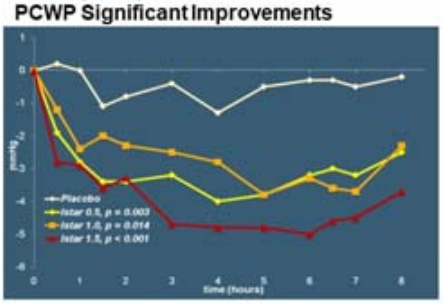
1) ADHERE Registry, n=48,567; JAMA 2005
2) European Journal of Heart Failure; Voors, PRE-RELAX AHF Study; 2011; 13

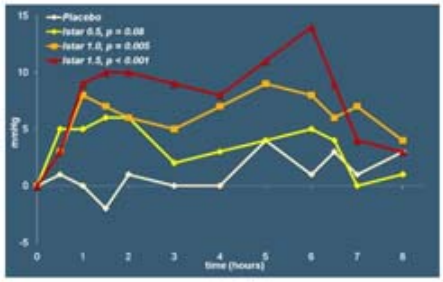
Istaroxime Phase 2a (HORIZON-HF) Study

- 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



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