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): April 3, 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 2.02 Results of Operations and Financial Condition

On April 3, 2023, Windtree Therapeutics, Inc. (the "Company") issued a press release announcing its financial results for the fourth quarter and fiscal year ended December 31, 2022. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

The information contained in this Item 2.02 (including Exhibit 99.1) is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section and shall not be deemed to be incorporated by reference in any filing under the Securities Act of 1933, as amended (the "Securities Act"), or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Item 7.01 Regulation FD Disclosure

On April 3, 2023, the Company updated information reflected in a slide presentation, which is furnished as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference. Representatives of the Company will use the updated presentation in various meetings with investors from time to time.

The information contained in this Item 7.01 (including Exhibit 99.2) is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities of that section and shall not be deemed to be incorporated by reference in any filing under the Securities Act or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

The following exhibits are being filed herewith:

Exhibit No.	Document
99.1	Press Release of Windtree Therapeutics, Inc., dated April 3, 2023, announcing financial results for the fourth quarter and fiscal year ended December 31, 2022, furnished herewith.
99.2	Investor Presentation of Windtree Therapeutics, Inc.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Windtree Therapeutics, Inc.

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

Date: April 3, 2023

Windtree Therapeutics Reports Fourth Quarter and Year-End 2022 Financial Results and Provides Key Business Updates

WARRINGTON, PA – April 3, 2023 – Windtree Therapeutics, Inc. (NasdaqCM: WINT), a biotechnology company focused on advancing multiple late-stage interventions for cardiovascular disorders, today reported financial results for the fourth quarter and fiscal year ended December 31, 2022 and provided key business updates.

"We continued to advance our cardiovascular platform during the fourth quarter of 2022 and early 2023 with study start up preparations for the istaroxime SEISMiC extension study in early cardiogenic shock, new patent issuances for istaroxime, new publications, and data presentations at scientific conferences," said Craig Fraser, President and Chief Executive Officer of Windtree. "We believe all these activities reflect the quality of the science, data, and opportunity with istaroxime and our next generation SERCA2a activators. We look forward to executing the extension study and planning for a potential Phase 3 study. Additionally, we have significantly reduced our company expenses and cash burn to create a leaner, capital-efficient organization while supporting our development programs. We remain focused on addressing our capital needs by exploring options for financing, as well as actively engaging in business development activities, including both licensing and strategic."

Key Business Update

- Issued a new patent for istaroxime that provides expanded patent coverage for istaroxime administration. The new U.S. patent, entitled: "*Istaroxime-Containing intravenous formulation for the treatment of acute heart failure (AHF)*," is a continuing patent following the expedited U.S. Track One filing by Windtree. The claims of the newly issued patent cover longer durations of istaroxime infusion for improved outcomes in treatment of acute heart failure. In particular, the claims are directed to an improvement in diastolic heart function following administration of istaroxime by intravenous infusion for 6 hours or more, which the Company attributes to the SERCA2a mechanism of action of istaroxime and its metabolites. Istaroxime is the Company's investigational drug candidate being studied in early cardiogenic shock and acute heart failure.

- Announced the publication of "*Istaroxime Metabolite PST3093 Selectively Stimulates SERCA2a and Reverses Disease-induced Changes in Cardiac Function*," in the Journal of Pharmacology and Experimental Therapeutics. The paper characterizes the pharmacokinetic and pharmacodynamic effects of PST3093, a pure SERCA2a activator and terminal metabolite of istaroxime. The paper describes pathophysiologic changes in SERCA2a activity and calcium distribution that occur in heart failure and how SERCA2a activation may reverse those effects and improve calcium handling in cardiac cells. Calcium abnormalities contribute to risk for arrhythmias and impaired cardiac muscle contractility/relaxation. The paper also explains why the effects of istaroxime may persist beyond the duration of the infusion because of the SERCA2a effect from PST3093. This data provides a foundation for the Company's preclinical family of assets that are selective for activation of SERCA2a.

- Presented two istaroxime presentations at the 2023 Technology and Heart Failure Therapeutics (THT) Conference held on March 20-22, 2023, in Boston, MA. The first presentation was on the istaroxime Phase 2 data in decompensated heart failure and early cardiogenic shock by Professor Alex Mebazaa, MD, PhD, FESC, Hôpital Lariboisière, Paris, France. The second presentation was an abstract and scientific presentation entitled: "*Safety and Efficacy of Istaroxime 1.0 and 1.5 mg/kg/min for Patients with Pre Cardiogenic Shock.*" The data presented are from the Company's Phase 2 SEISMiC study, an international randomized, double blind, placebo-controlled study that enrolled 60 patients to evaluate istaroxime for the treatment of early cardiogenic shock due to severe heart failure with SBP between 75-90 mmHg. The study met its primary endpoint, which was the difference in SBP area under the curve over six hours after initiating the infusion, with the pooled istaroxime treated group performing significantly better compared to the control group ($p=0.017$) and persisted through the 24-hour SBP profile measurement. Two target doses of istaroxime were studied compared to placebo. The data presented characterized the differences between doses and highlighted the favorable profile of the 1.0 µg/kg/min dose group on cardiovascular physiology, biomarkers and safety.

- Announced the results from a recently completed market study demonstrating the need and opportunity to address the very high costs associated with cardiogenic shock. The research showed that in 2020 the U.S. average cardiogenic shock patient length of stay in the hospital was 19.6 days with a median of 10 days. Additionally, the resources required to take care of these patients are substantial, with patients frequently requiring costly ICU or CCU care. The istaroxime program will be collecting and analyzing both clinical and pharmacoeconomic related data in the pursuit of addressing this significant need.

- Raised approximately $1.0 million in gross proceeds from the exercise of previously issued warrants in connection with warrant inducement offer letters with certain of the Company's warrant holders, and the issuance of new warrants to such warrant holders.

Select Fourth Quarter 2022 Financial Results

- Research and development expenses were $1.2 million for the fourth quarter of 2022, compared to $4.5 million for the fourth quarter of 2021. The decrease in research and development expenses was primarily due to (i) a decrease of $2.1 million related to the KL4 surfactant platform as the Company continues to focus its resources on the development of its istaroxime pipeline; (ii) a decrease of $0.5 million following the completion of enrollment in the SEISMiC study in March 2022; (iii) a decrease of $0.4 million for expenditures related to the development of istaroxime for AHF primarily due to toxicology studies performed in 2021; and (iv) a decrease of $0.3 million in non-cash stock-based compensation expense due to granting two option grants to employees during 2021 compared to one option grant in 2022.

- General and administrative expenses for the fourth quarter of 2022 were $2.2 million, compared to $3.0 million for the fourth quarter of 2021. The decrease in general and administrative expenses is primarily due to (i) a decrease of $0.5 million in personnel costs and (ii) a decrease of $0.4 million in non-cash, stock-based compensation expense due to granting two option grants to employees during 2021 compared to one option grant in 2022.

- For the fourth quarter ended December 31, 2022, the Company reported an operating loss of $10.8 million, compared to an operating loss of $14.7 million in the fourth quarter of 2021. Included in operating loss for the fourth quarter of 2022 is non-cash expense of $6.8 million related to the impairment of the Company's rostafuroxin intangible asset and non-cash expense of $0.5 million related to the impairment of goodwill. Included in operating loss for the fourth quarter of 2021 is non-cash expense of $7.3 million related to the impairment of our rostafuroxin intangible asset.

- The Company reported a net loss of $9.7 million ($13.01 per basic share) on 0.7 million weighted-average common shares outstanding for the quarter ended December 31, 2022, compared to a net loss of $13.1 million ($23.22 per basic share) on 0.6 million weighted average common shares outstanding for the comparable period in 2021.

Select 2022 Year-End Financial Results

- Research and development expenses were $11.1 million for the year ended December 31, 2022, compared to $17.8 million for the year ended December 31, 2021. The decrease in research and development expenses is primarily due to (i) a decrease of $4.0 million related to the KL4 surfactant platform as the Company continues to focus its resources on the development of its istaroxime pipeline; (ii) a decrease of $2.0 million in non-cash stock-based compensation expense due to granting two option grants to employees during 2021 compared to one option grant in 2022; and (iii) a decrease of $0.8 million for expenditures related to the development of istaroxime for AHF primarily due to toxicology studies performed in 2021.

- General and administrative expenses for the year ended December 31, 2022 were $10.8 million, compared to $14.5 million for the year ended December 31, 2021. The decrease in general and administrative expenses is primarily due to (i) a decrease of $2.0 million in non-cash, stock-based compensation expense due to granting two option grants to employees during 2021 compared to one option grant in 2022 and (ii) a decrease of $1.6 million in professional fees.

- For the year ended December 31, 2022, the Company reported an operating loss of $41.3 million, compared to an operating loss of $77.3 million for the year ended December 31, 2021. Included in operating loss for the year ended December 31, 2022 is non-cash expense of $12.6 million related to the impairment of goodwill and non-cash expense of $6.8 million related to the impairment of our rostafuroxin intangible asset. Included in operating loss for the year ended December 31, 2021 is non-cash expense of $45.0 million related to the impairment of our rostafuroxin intangible asset.

- The Company reported a net loss of $39.2 million ($62.23 per basic share) on 0.6 million weighted-average common shares outstanding for the year ended December 31, 2022, compared to a net loss of $67.6 million ($136.64 per basic share) on 0.5 million weighted average common shares outstanding for the comparable period in 2021.

- As of December 31, 2022, the Company reported cash and cash equivalents of $6.2 million, which is expected to be sufficient to fund operations into the second quarter of 2023.

Readers are referred to, and encouraged to read in its entirety, the Company's Annual Report on Form 10-K for the year ended December 31, 2022, which will be filed with the Securities and Exchange Commission on March 31, 2023, and includes detailed discussions about the Company's business plans and operations, financial condition, and results of operations.

About Windtree Therapeutics
Windtree Therapeutics, Inc. is advancing multiple late-stage interventions for cardiovascular disorders to treat patients in moments of crisis. Using new scientific and clinical approaches, Windtree is developing a multi-asset franchise anchored around compounds with an ability to activate SERCA2a, with lead candidate, istaroxime, being developed as a first-in-class treatment for acute heart failure and for early cardiogenic shock. Windtree's heart failure platform includes follow-on oral pre-clinical SERCA2a activator assets as well. In pulmonary care, Windtree has focused on facilitating the transfer of the KL4 surfactant platform, to its licensees, Lee's Pharmaceutical (HK) Ltd. and Zhaoke Pharmaceutical (Hefei) Co. Ltd. Included in Windtree's portfolio is rostafuroxin, a novel precision drug product targeting hypertensive patients with certain genetic profiles.

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

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

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

WINDTREE THERAPEUTICS, INC. AND SUBSIDIARIES
Consolidated Balance Sheets

(in thousands, except share and per share data)

	December 31, 2022	December 31, 2021
ASSETS		
Current Assets:		
Cash and cash equivalents	$ 6,172	$ 22,348
Prepaid expenses and other current assets	1,205	1,143
Total current assets	7,377	23,491
Property and equipment, net	262	1,011
Restricted cash	154	154
Operating lease right-of-use assets	1,853	2,381
Intangible assets	25,250	32,070
Goodwill	3,058	15,682
Total assets	$ 37,954	$ 74,789
LIABILITIES, MEZZANINE EQUITY & STOCKHOLDERS' EQUITY		
Current Liabilities:		
Accounts payable	$ 249	$ 693
Accrued expenses	1,552	3,408
Operating lease liabilities - current portion	404	528
Loans payable - current portion	252	294
Total current liabilities	2,457	4,923
Operating lease liabilities - non-current portion	1,624	2,071
Restructured debt liability - contingent milestone payments	15,000	15,000
Other liabilities	3,800	3,800
Deferred tax liabilities	5,061	7,114
Total liabilities	27,942	32,908
Mezzanine Equity:		
Series A redeemable preferred stock, $0.001 par value; 40,000 and 0 shares authorized; 38,610.119 and 0 shares issued and outstanding at December 31, 2022 and 2021, respectively	-	-
Stockholders' Equity:		
Preferred stock, $0.001 par value; 4,960,000 and 5,000,000 shares authorized; 0 shares issued and outstanding at December 31, 2022 and 2021, respectively	-	-
Common stock, $0.001 par value; 120,000,000 shares authorized; 772,203 and 565,379 shares issued at December 31, 2022 and 2021, respectively; 772,202 and 565,378 shares outstanding at December 31, 2022 and 2021, respectively	-	-
Additional paid-in capital	837,598	830,259
Accumulated deficit	(824,532)	(785,324)
Treasury stock (at cost); 1 share	(3,054)	(3,054)
Total stockholders' equity	10,012	41,881
Total liabilities, mezzanine equity & stockholders' equity	$ 37,954	$ 74,789

WINDTREE THERAPEUTICS, INC. AND SUBSIDIARIES
Consolidated Statements of Operations

(in thousands, except per share data)

	Three Months Ended December 31,		Year Ended December 31,	
	2022	2021	2022	2021
Expenses:				
Research and development	$ 1,216	$ 4,476	$ 11,099	$ 17,787
General and administrative	2,242	2,966	10,790	14,473
Loss on impairment of goodwill	534	-	12,624	-
Loss on impairment of intangible assets	6,820	7,250	6,820	45,020
Total operating expenses	10,812	14,692	41,333	77,280
Operating loss	(10,812)	(14,692)	(41,333)	(77,280)
Other income (expense):				
Interest income	52	1	109	91
Interest expense	(13)	(13)	(53)	(114)
Other expense, net	(286)	(24)	702	(320)
Total other income (expense), net	(247)	(36)	758	(343)
Loss before income taxes	(11,059)	(14,728)	(40,575)	(77,623)
Deferred income tax benefit	1,367	1,655	1,367	9,987
Net loss	$ (9,692)	$ (13,073)	$ (39,208)	$ (67,636)
Net loss per common share				
Basic and diluted	$ (13.01)	$ (23.22)	$ (62.23)	$ (136.64)
Weighted average number of common shares outstanding				
Basic and diluted	745	563	630	495


Windtree Therapeutics
Company Overview
April 3, 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.

Windtree Therapeutics and Istaroxime Highlights

- **Biopharmaceutical company with advanced clinical focus 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**
  - An acute heart failure and cardiogenic shock drug candidate that has demonstrated both significant improvement in cardiac function as well as rapid and significant improvement in blood pressure, with favorable effect on myocardial oxygen demand and renal function and what so far has been a differentiating safety profile (avoiding many of the use-limiting side effects of existing therapies)
- **Recent positive Phase 2 study with istaroxime in early cardiogenic shock (ECS) paves the way for what we believe is a relatively fast and less expensive developmental and regulatory pathway**
  - Precedent shows blood pressure response can be acceptable as the primary endpoint in a pivotal shock study. Additionally, istaroxime is demonstrating other significant benefits that we plan to build upon in the larger Phase 3 to create a strong, evidence-based clinical and pharmacoeconomic positioning
- **Highly engaged in business development activities - including exploring strategic opportunities**
- **Lean, capital efficient operation led by a highly experienced management team**

Pipeline

Lead Products	Indication	Phase	Development Status	Regulatory Status
Istaroxime	Cardiogenic Shock	Phase 2	• Positive Phase 2 study • Planning the execution of the next study and plans to meet with regulatory agencies regarding development path	*Executed Phase 2 in early cardiogenic shock,*
Istaroxime	Acute Heart Failure	Phase 2b	• Augment AHF data with the efficacy, safety and dosing from the extension and other studies in the severe AHF patients experiencing cardiogenic shock. If positive and adequate, move istaroxime into phase 3 for AHF with partnership	*FDA Fast Track Designation*
Oral SERCA2a Activators	Chronic Heart Failure, including potentially HFpEF	Preclinical	• Chronic and Acute Heart Failure • Target for collaboration/partnership	*IND-enabling studies*
Rostafuroxin	Treatment Resistant Hypertension - Genetically Associated	Phase 2b	• Phase 2 data in hypertension and genetically associated hypertension • Company repositioned for the attractive and large Resistant Hypertension market • Out-licensing opportunity	*Ex-U.S. filings* *Open U.S. IND*
KL4 Surfactant and AEROSURF	KL4 surfactant Drug/Device Tx for RDS and potential other applications	Phase 2b	• Global out-license to Lee's Pharmaceuticals	*FDA Fast Track Designation, Orphan Drug*

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Istaroxime

Cardiogenic Shock

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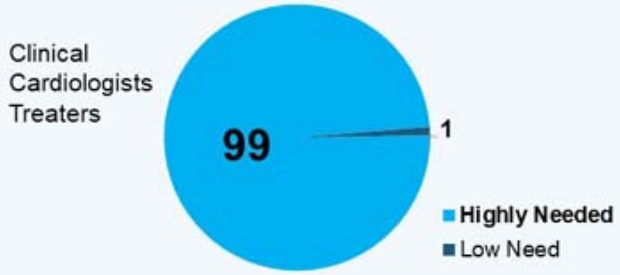
1) Kolte D, American Heart Association; 2014 Jan 13
2) Estimates from claims data and epi data September 2021, multiplied by assumed various regional prices

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

Istaroxime – Novel First-in-Class Therapy

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

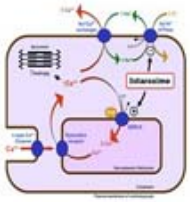
Dual Mechanism of Action

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

Istaroxime

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

Impact on both systolic and diastolic dysfunction



WINDTREE THERAPEUTICS

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

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

- **Cardiac Function**
  - increased stroke volume
  - lowered cardiac filling pressures
- **Dose Related Increases in Systolic Blood Pressure**
- **Increased Renal Function (eGFR)**

WINDTREE THERAPEUTICS

Cardiogenic Shock Treatment
Istaroxime Potential Opportunity for Regulatory Pathway

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

FDA Regulatory Pathway Assumptions

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]

End of Phase 2 meeting will confirm requirements for Phase 3:

- Endpoint is blood pressure increase
- Superior mortality over control group endpoint is not required
- Smaller number of subjects required than typical cardiovascular clinical trials

WINDTREE THERAPEUTICS

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

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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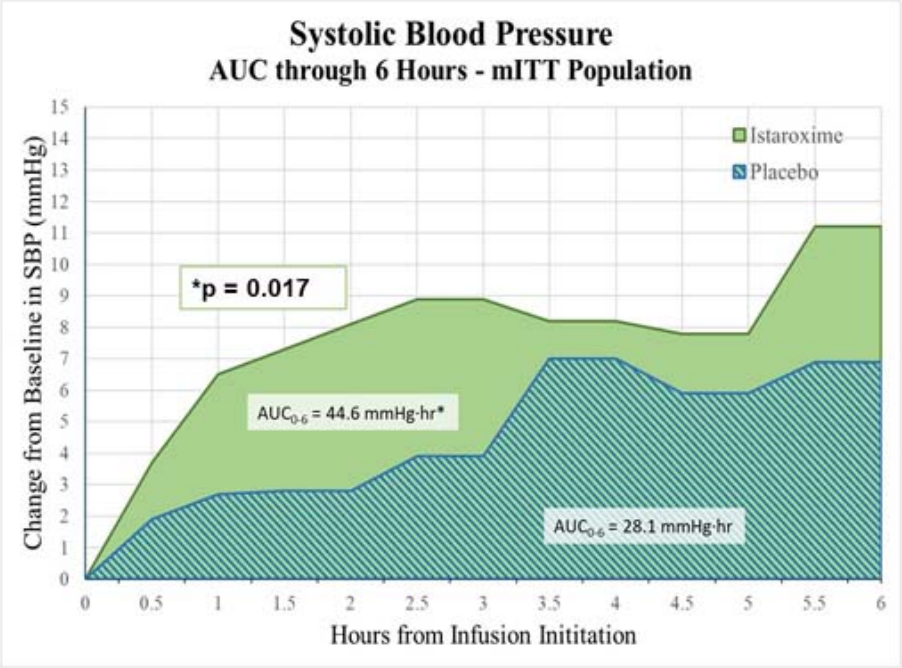
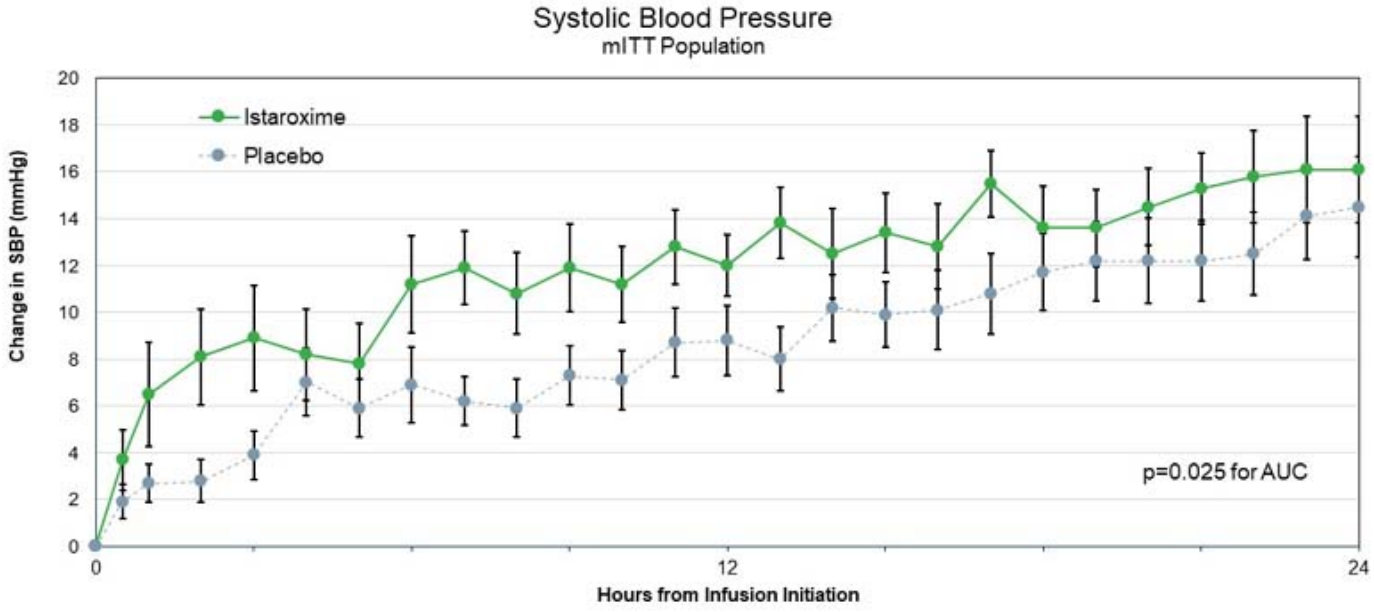
Difference in SBP Profile



WINDTREE THERAPEUTICS

Systolic BP Improvements Persisted over 24 Hours



WINDTREE THERAPEUTICS

Cardiac Function Improvement

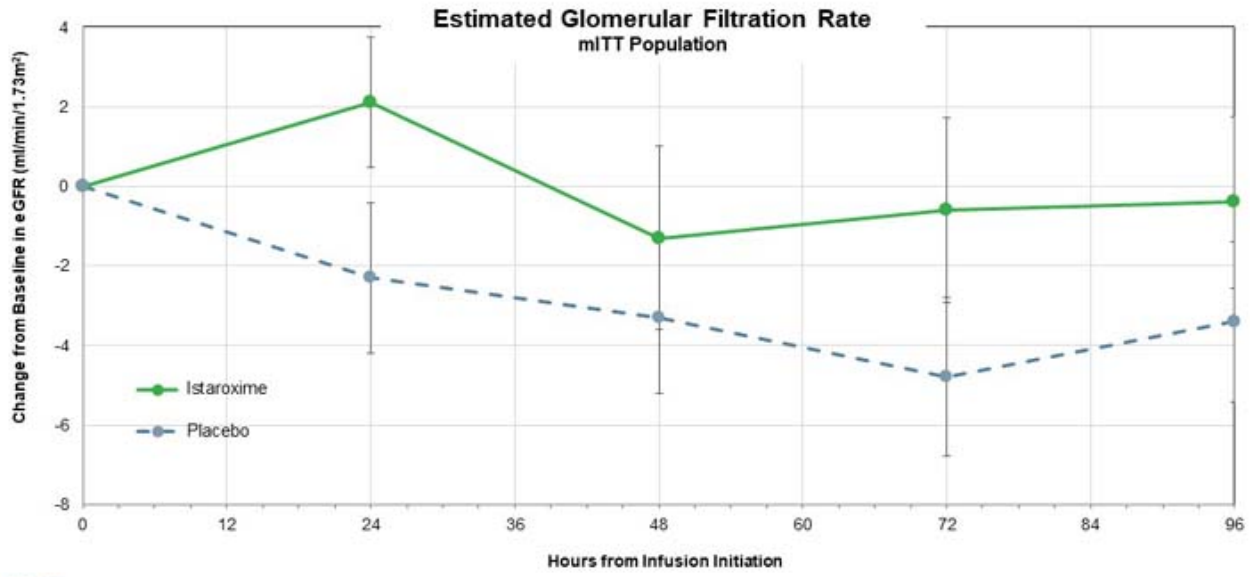
Echocardiography demonstrated improvements in key systolic and diastolic cardiac function measures including:

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

WINDTREE THERAPEUTICS

Treatment was Associated with a Favorable Renal Profile

Renal function was not decreased in istaroxime treated patients



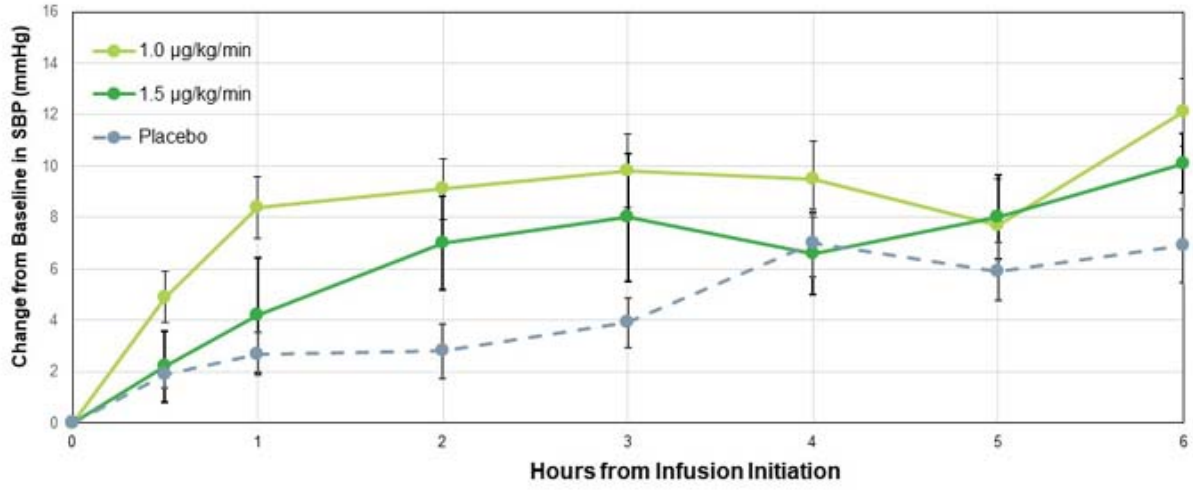
WINDTREE THERAPEUTICS

Data shown as means and standard errors

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

1.0 µg/kg/min dosing was associated with:

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



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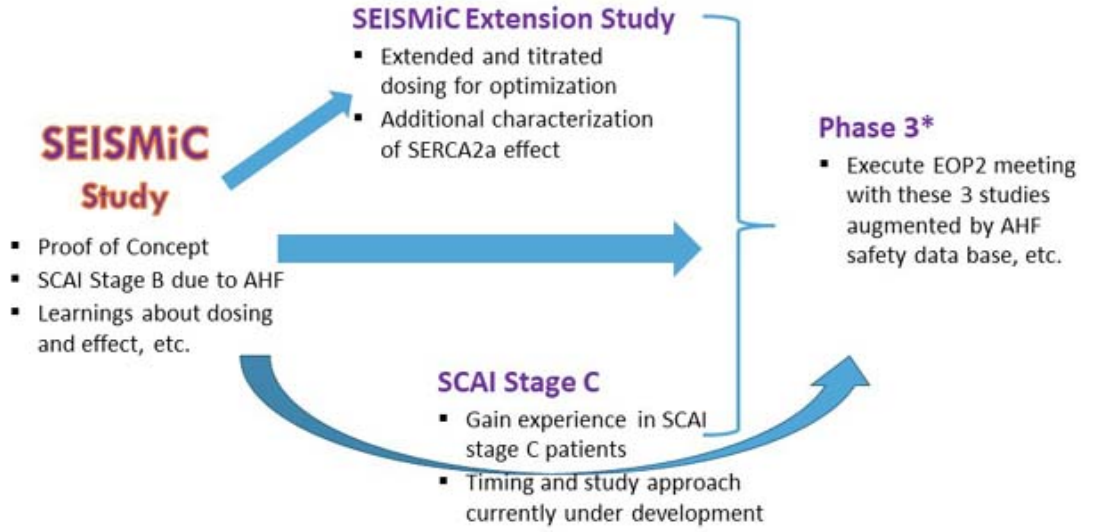
All Subjects (n=60)

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 potential treatment for cardiogenic shock and support the existing data from the program in AHF

Cardiogenic Shock Development Strategy



WINDTREE THERAPEUTICS

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

Plan for Dose Optimization – Extension Study

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

Study objectives:

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

Current study plan design:

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

Istaroxime dosed for up to 60-hours

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

~8 months to execute enrollment and $3.5MM
Study plans and progression dependent upon regulatory alignment and capital resourcing

Cardiogenic Shock Opportunity

INTENDED TARGET THERAPEUTIC PROFILE

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

OPPORTUNITY DRIVERS

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

INTENDED POSITIONING:

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

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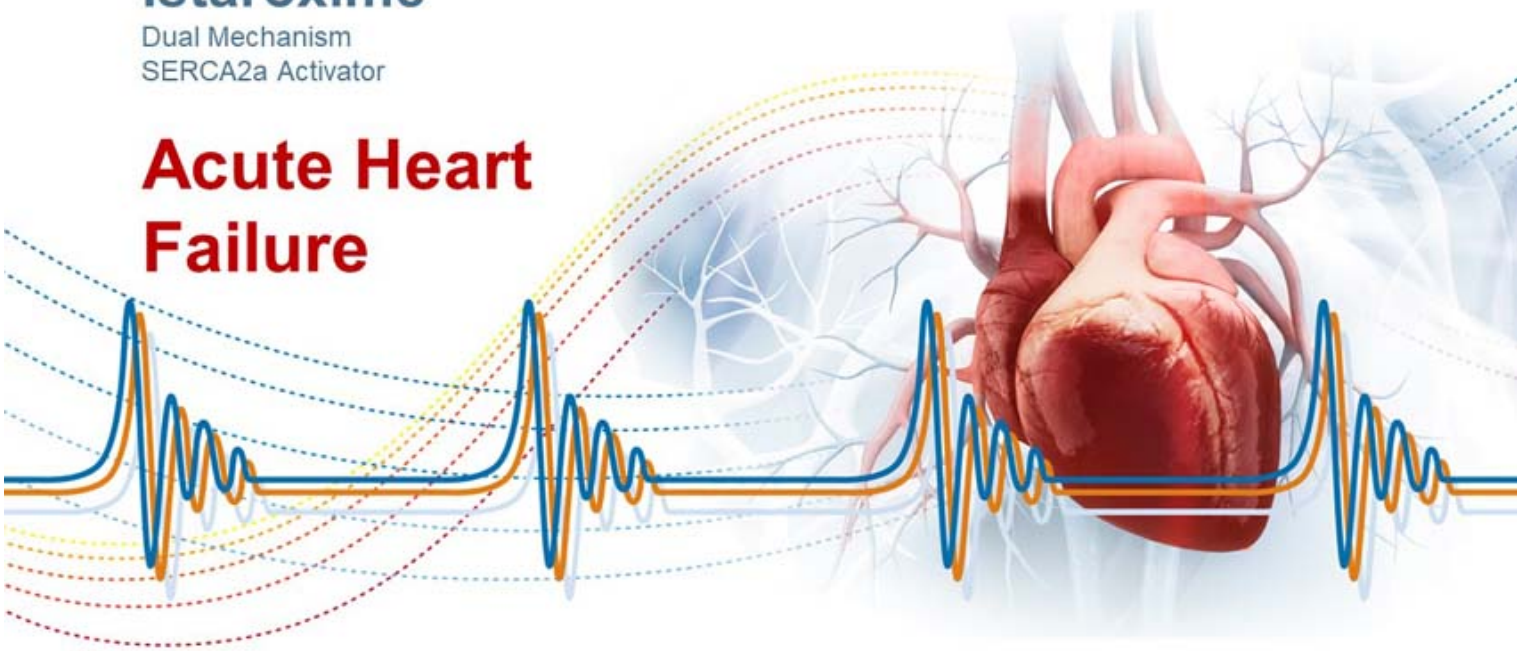
Istaroxime

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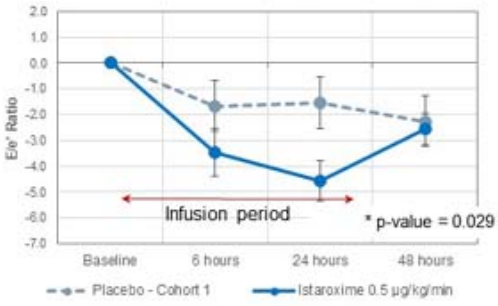
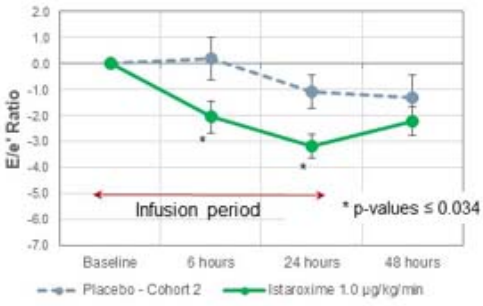
Primary Endpoint Achieved
Significant Changes in E/e' Ratio[1] and Stroke Volume

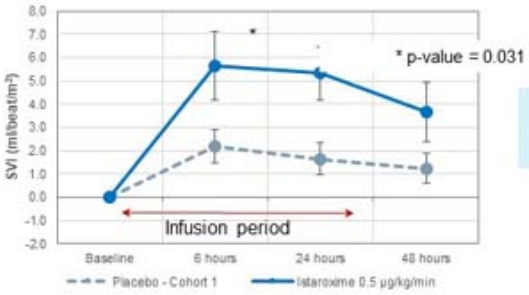
Istaroxime 0.5 µg/kg/min vs. placebo



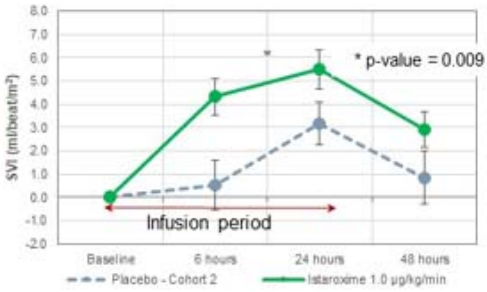
E/e'

Istaroxime 1.0 µg/kg/min vs. placebo





Stroke Volume



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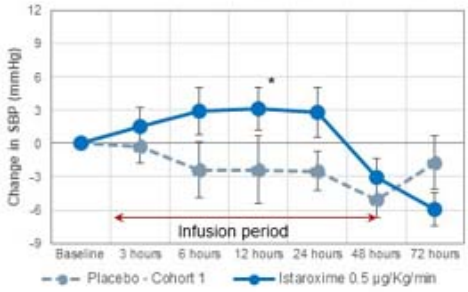
1) E/e' echocardiographic assessment of PCWP; Note: Data shown as means and standard errors

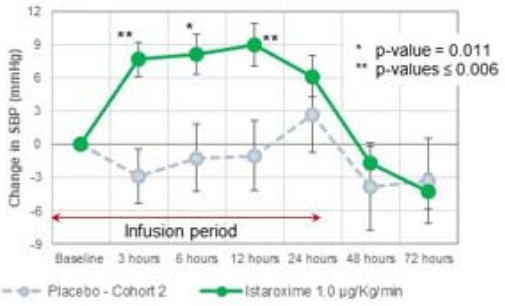
Systolic Blood Pressure Increased During Treatment and Renal Function Tended to Improve

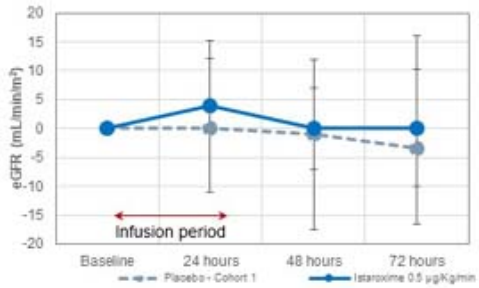
Istaroxime 0.5 µg/kg/min vs. placebo



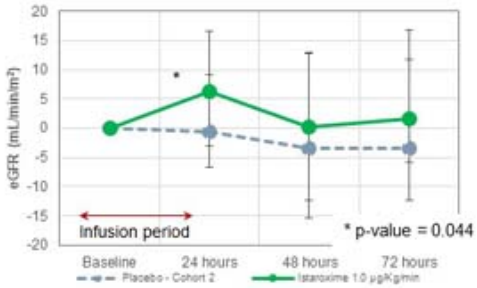
Systolic Blood Pressure (SBP)

Istaroxime 1.0 µg/kg/min vs. placebo





GFR (Renal Function)

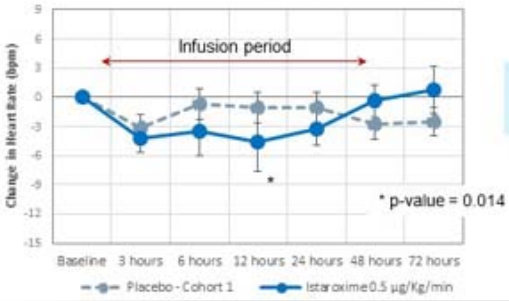


WINDTREE THERAPEUTICS

Data shown as means and standard errors

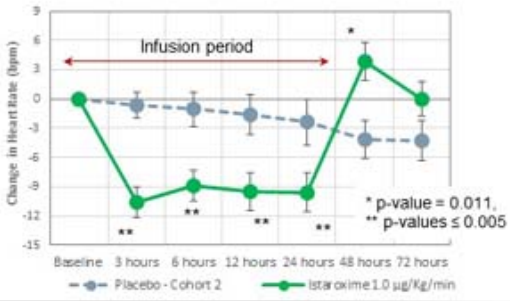
Heart Rate Decreased and No Increases in Cardiac Troponins

Istaroxime 0.5 µg/kg/min vs. placebo

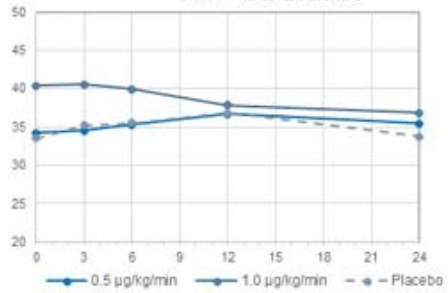


Heart Rate

Istaroxime 1.0 µg/kg/min vs. placebo

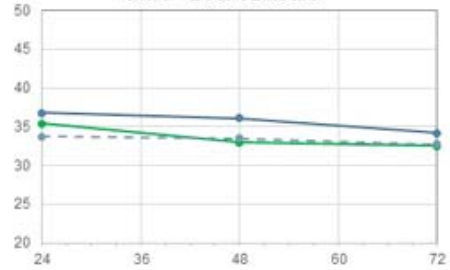


cTnT – 0 to 24 hours



Cardiac TnT (Myocardial Damage)

cTnT – 24 to 72 hours



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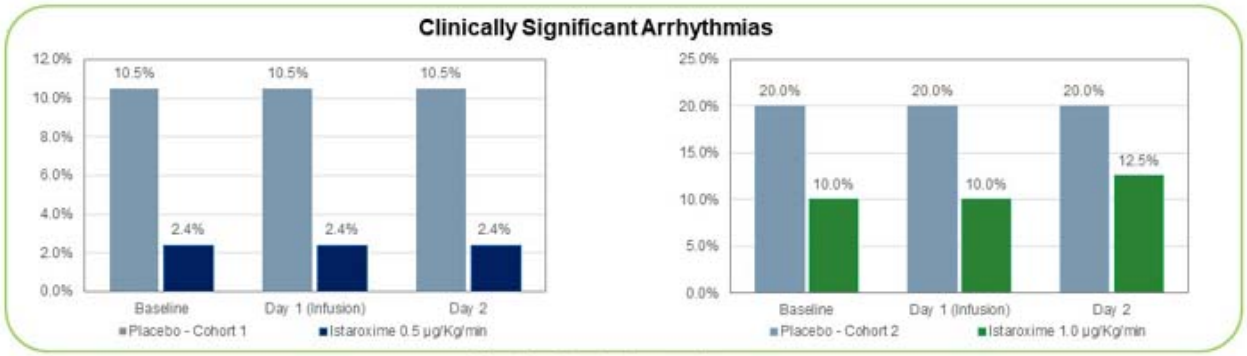
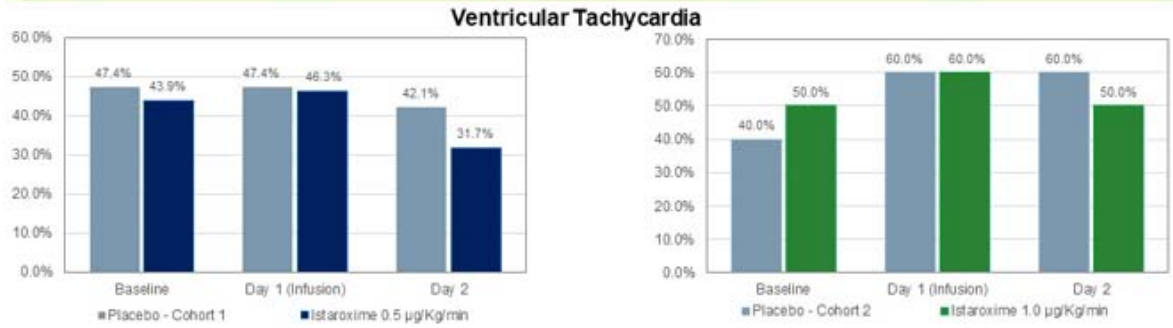
Favorable Profile Observed with 24-hour Holter Monitoring





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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: 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.

We currently seek partnership to execute this clinical trial

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

- Istaroxime has produced positive, differentiating data in three Phase 2 studies for two separate and complementary indications. These markets have significant unmet needs, and no known other late-stage programs in development to address the acute decompensated patient
  - The data is consistent, across all regions/populations and across many endpoints (including many in early cardiogenic shock despite small trial)
- Istaroxime has demonstrated a highly unique and desirable profile as compared to existing therapies:
  - Improved cardiac function **and** SBP while maintaining renal function and overall safety profile
- Recent positive Phase 2 study with istaroxime in early cardiogenic shock (ECS) paves the way for what we believe is a relatively fast and less expensive developmental and regulatory pathway
- Few opportunities have the unmet need of serious diseases, favorable regulatory environment and market size of the istaroxime opportunity

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Rostafuroxin – A Potential New Treatment for Resistant Hypertension (RHTN)

Rostafuroxin

Specifically displaces ouabain binding from the high affinity Na+–K+ATPase isoform present in the caveolae, antagonizing all the functional effects of ouabain

Studies have reported a correlation of ouabain and aldosterone* (the target of the Cincor and Mineralys Phase 2 studies) in patients with RHTN

There have been seven clinical studies of rostafuroxin in treatment naïve hypertension (patients without any treatment), including 4 Phase 2 studies which examined the antihypertensive effect, safety and tolerability

*Rossi G, Manunta P, Hamlyn JM, et al. Immunoreactive endogenous ouabain primary aldosteronism and essential hypertension: relationship with plasma renin, aldosterone and blood pressure levels. *J Hypertens* 1995;13(10):1181.

*Borrio G, Tentori S, Faroffi F, et al. Endogenous ouabain and aldosterone are coelevated in the circulation of patients with essential hypertension. *Intern Emerg Med* 2022;1.

*Manunta P, Hamlyn JM, Simonini M, et al. Endogenous ouabain and the renin-angiotensin-aldosterone system: distinct effects on Na handling and blood pressure in human hypertension. *J Hypertens* 2011;29(2):349.

High Potential Value in Treatment Resistant Hypertension Market

Large Market with Significant Unmet Need

- Treatment resistant hypertension
  - An estimated 10% to 20% of hypertensive patients have resistant hypertension, defined as having controlled or uncontrolled blood pressure with the use of ≥ 3 medications that includes a diuretic*
- Effective hypertension treatment is critical to reducing cardiovascular and renal disease; yet millions of hypertensive patients in the United States are not at goal despite treatment

Significant Value Potential

- Two biotech companies have demonstrated the significant value the market is placing on RHTN with Phase 2 results
- Cincor acquisition by AstraZeneca (Jan 9, 2023)
  - Total consideration would be approximately $1.8 billion (a 206% premium over CinCor's closing market price on January 6, 2023)
- Mineralys executes IPO and raises $192MM (Feb 13, 2023)

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*Carey RM, Sakhuja S, Calhoun DA, Whelton PK, Muntner P. Prevalence of Apparent Treatment-Resistant Hypertension in the United States. *Hypertension* 2019;73:424.; AHA. High Blood Pressure Among Black People. <https://www.heart.org/en/health-topics/high-bloodpressure/why-high-blood-pressure-is-a-silent-killer/high-blood-pressure-and-african-americans> (2022).; *Roberie DR, Elliott WJ. What is the prevalence of resistant hypertension in the United States? *Curr Opin Cardiol* 2012;27(4):385.; *Sim JJ, Bhandari SK, Shi J, et al. Characteristics of resistant hypertension in a large, ethnically diverse hypertension population of an integrated health system. *Mayo Clin Proc* 2013 ;88(10):1099 *Calhoun DA, Jones D, Textor S, et al. Resistant hypertension: diagnosis, evaluation, and treatment: a scientific statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research. *Circulation* 2008;117(25):e510-526

Active Engagement in Out-License and Partnership Opportunities

Global / Regional Licensing

- ✓ **AEROSURF / KL4 Platform** – Exclusive global license to Lee's Pharm (SEHK:950) and Zhaoke. Potential proceeds:
  - Up to $78.9 million in potential milestone payments
  - Low double-digit % royalties
  - *WINT no longer carries any costs for KL4 platform*

Potential licensing opportunities

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

Strategic Transaction

Mergers & Acquisitions

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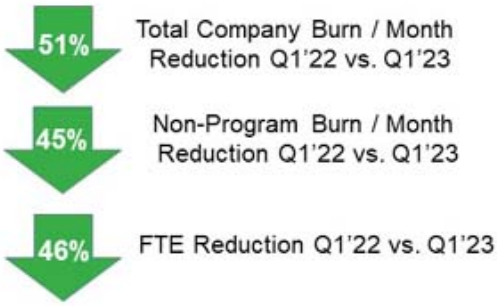
Financial Summary & Capitalization

Securities	Common Equivalents as of February 28, 2023
Common Stock	904,459
Options (WAEP $389.91)	73,789
Restricted Stock Units	9,594
Warrants (WAEP $179.56)	449,345
Fully Diluted Equivalents	1,437,187

Driving Capital Efficiency to Program Investment

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



While the Company has plans to start new studies, it plans to also continue to lower non-program cash burn moving forward

WINDTREE THERAPEUTICS

Strategy for Value Generation

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