March 4, 2025

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M. Marin
312-265-9211
mmarin@zacks.com

scr.zacks.com
10 S. Riverside Plaza, Chicago, IL 60606

Windtree Therapeutics (WINT-NASDAQ)

WINT: Advancing Lead Asset; Leveraging Strategic M&A to Potentially Shorten Timeline to Revenue Generation – Initiating Coverage

WINT is developing therapies for a range of cardiovascular & oncology treatments with significant unmet need. Its lead asset Istaroxime is a first-in-class, dual-acting agent being developed to improve blood pressure & cardiac function in patients with cardiogenic shock (CS). A 2nd indication is treatment of acute heart failure by improving cardiac function.

Current Price (3/3/25)	$2.91
Valuation	**$4.00**

OUTLOOK

In Sept. 2024, WINT reported positive Phase 2b study results of istaroxime in early CS patients. To position istaroxime for Phase 3 readiness, WINT is launching a small Phase 2 study in the more severe form of CS, SCAI Stage C. Additionally, under new CEO Jed Latkin, WINT recently embarked on a new strategy to become a revenue generating biotech through strategic M&A of small biotechs with FDA approved revenue generating assets. The company plans to use shares to fund potential transactions.

SUMMARY DATA

52-Week High	**N/A**
52-Week Low	**$2.08**
One-Year Return (%)	**-99**
Beta	**0.68**
Average Daily Volume (sh)	**171,204**
Shares Outstanding (mil)	**1**
Market Capitalization ($mil)	**$2**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**13**
Insider Ownership (%)	**1**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2024 Estimate	**N/A**
P/E using 2025 Estimate	**N/A**

Risk Level	**High**
Type of Stock	**Small-Value**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2023	0 A	0 A	0 A	0 A	0 A
2024	0 A	0 A	0 A	0.0E	0 E
2025					0 E

Loss Per Share*

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2023	($0.46)A	($0.73)A	($0.49)A	($0.57)A	($2.26)A
2024	($1.14)A	($1.34)A	($0.42)A	($0.64)E	($1.26)E
2025					($2.16)E

Quarters might not add to annual reflecting rounding

Disclosures on page 18 *Not PF

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KEY POINTS

- WINT's lead asset is Istaroxime, which addresses heart failure and cardiogenic shock (a severe form of heart failure) and has a first in class, dual mechanism of action that the company views as a key differentiator versus other treatments, as described in this report.

- Under new CEO Jed Latkin, the company has recently embarked on a new strategy to become a revenue generating biotech through strategic acquisitions of small biotechs with FDA approved assets generating revenue. The company plans to use shares to fund transactions. This plan is designed to shorten the timeline for WINT to reach revenue generation and positive cash flow generation.

- In September 2024, Windtree reported positive Phase 2b study results of Istaroxime in early cardiogenic shock (CS) patients. To position istaroxime for Phase 3 readiness, WINT is launching a small Phase 2 study in SCAI Stage C, administering istaroxime to patients with the more severe form of cardiac shock, SCAI Stage C.

- The company is in active discussions with pharmaceutical companies on licensing partnerships for its cardiovascular pipeline.

- Windtree has had success expanding its intellectual property rights for istaroxime, with recent patent awards in various markets, including the U.S., Japan, Hong Kong and mainland China, and multiple additional applications pending including prevention or reduction of arrhythmias.

COMPANY OVERVIEW

Multiple Programs Focus on Unmet Needs In Cardiogenic Shock & AHF

Pennsylvania-based Windtree Therapeutics, Inc. (NASDAQ:WINT) is a biopharmaceutical company developing therapies for a range of cardiovascular and oncology treatments characterized by significant unmet need. The company's lead indication area is cardiogenic shock (which is a severe form of heart failure). The company's lead asset, Istaroxime, is a first-in-class, dual-acting agent being developed to improve blood pressure and cardiac function in patients with cardiogenic shock. A second indication is treatment of acute heart failure by improving cardiac function.

New strategy to use shares to acquire FDA approved revenue generating assets

Under new CEO Jed Latkin, the company has recently embarked on a new strategy to acquire small biotechs with FDA approved assets to become a revenue generating biotech. The company intends to continue to develop its existing cardiovascular and oncology pipeline (see below). Windtree plans to become a parent company acquiring strategic subsidiaries with FDA-approved products and believes its management team has commercialization expertise in both large pharmaceutical and small biotech companies across multiple therapeutic areas. WINT expects that it will be able to leverage synergies among and optimize performance of potential acquired subsidiaries. WINT believes it can improve sales and lower costs and intends to use equity to acquire new subsidiaries. Management is optimistic that this new strategy can be transformative.

Lead Asset Istaroxime has Fast Track Therapy Designation

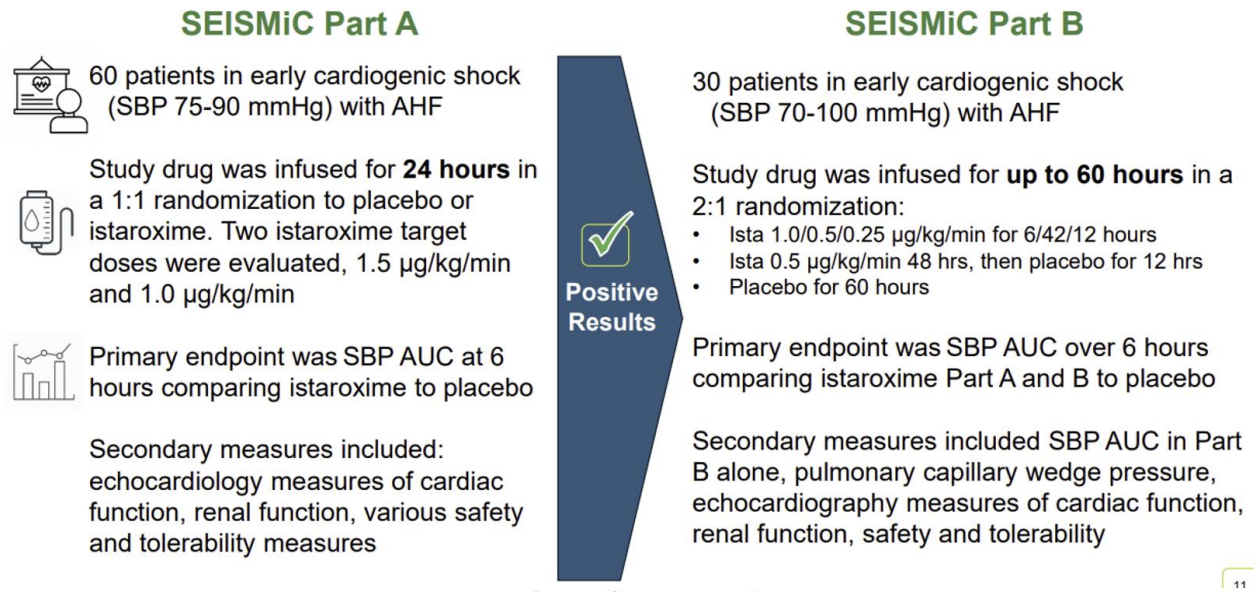
Istaroxime has been granted FDA Fast Track designation for the treatment of AHF. Fast track could lead to an expedited FDA review of istaroxime to treat AHF, potentially shortening the clinical timeline and time to commercialization. Once an asset receives Fast Track designation, it is potentially eligible for, among other factors:

- More frequent communication and meetings with the FDA to discuss development plans
- Accelerated approval and priority review depending on when/if relevant criteria are met

Windtree recently reported positive Phase 2b clinical trial data in early cardiogenic shock. To position istaroxime for Phase 3 readiness, WINT is also enrolling a small Phase 2 study in SCAI Stage C, administering istaroxime to patients with the more severe form of cardiac shock, SCAI Stage C. WINT is also developing next generation therapies called SERCA2a activators in areas for acute and chronic cardiovascular disease.

Results of Phase 2b istaroxime study in early cardiogenic shock promising

The company recently conducted a Phase 2b SEISMiC extension study of istaroxime in early cardiogenic shock in the U.S., Europe and Latin America that enrolled hospitalized patients with SCAI Stage B cardiogenic shock with persistent hypotension due to acute heart failure. WINT recently released positive topline data from both Part A and Part B of this extension study that support further clinical efforts. Istaroxime was shown to significantly improve the primary endpoint of the systolic blood pressure profile over six hours. This is a critical clinical objective in treating patients in early cardiogenic shock due to heart failure. Istaroxime also demonstrated significant improvements in many secondary endpoints. These results follow positive results in a previous Phase 2 SEISMiC trial. It also provided information to help further inform dose optimization and the characterization of istaroxime's mechanism of action including potential benefits of SERCA2a activation.



Source: Company reports

The trial evaluated two different dose regimens of istaroxime compared to placebo. Patients received infusions of istaroxime for up to 60 hours. By comparison, treatment in prior studies was limited to 24 hours. The extended treatment time was designed to determine the potential for additional benefit at longer dosing. The trial had one cohort that received a decreasing istaroxime dose over the period and the other cohort received a constant istaroxime dose. It aggregated data related to both cardiac and renal function and additional safety information on cardiac arrhythmias. Importantly, the study results were consistent with results of prior clinical activity, indicating that istaroxime is not related to increased cardiac arrhythmias. WINT believes this is a potentially important differentiating characteristic compared to commonly used current drug therapies. The company recently presented an istaroxime presentation featuring positive data from its Phase 2b SEISMiC study at the Technology and Heart Failure Therapeutics Conference.

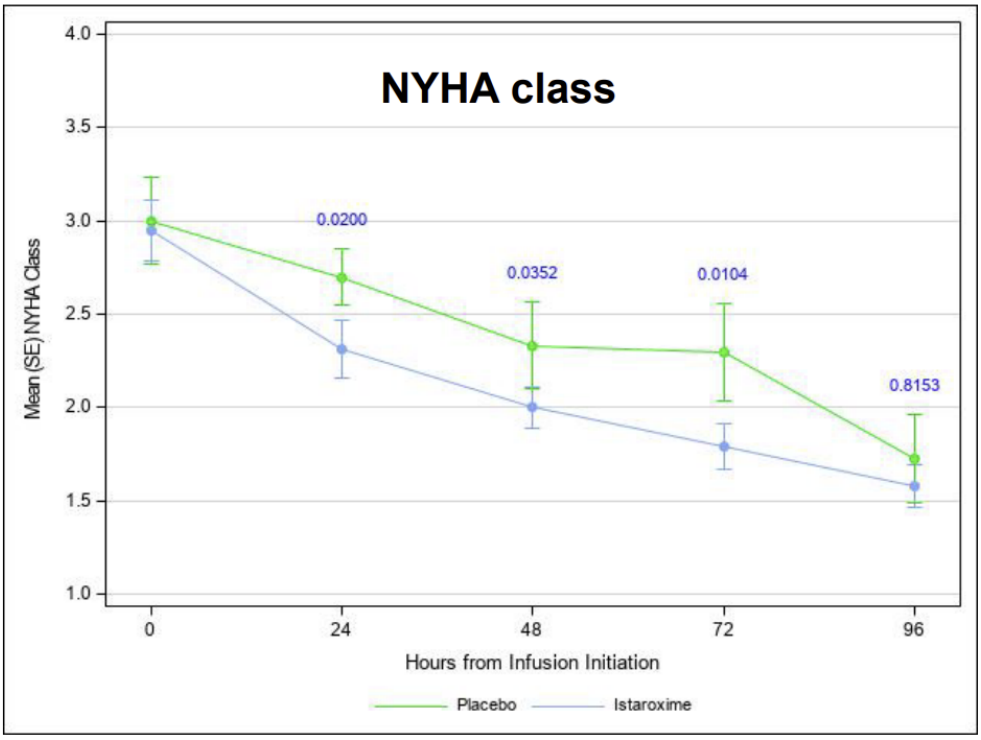
Study met its primary endpoint

- The study met its primary endpoint in significantly improving systolic blood pressure over six hours (SBP AUC), with the combined Part A and Part B SEISMiC istaroxime group performing significantly better compared to the placebo group (62.0±7 vs 36.4±7 mmHg*hr, p = 0.0070). Despite the smaller number of patients in SEISMiC Part B, the SBP AUC was also significantly improved by istaroxime compared to placebo (78.4±12 vs. 39.6±14 mmHg*hr, p=0.0429).
- The improvements in SBP AUC at 24 hours in the combined Part A and Part B analysis were also significantly increased by istaroxime (292.4±24 vs 190.9±26 mmHg*hr, p=0.0031). In Part B alone, the istaroxime group was significantly better compared to the placebo group (299.3±48 vs 139.0±56mmHg*hr, (p = 0.0377). With the longer istaroxime dosing in Part B, the SBP AUC was significantly improved at 48 hours (594.4±95 vs 271.7±110, p = 0.0352) and 60 hours (711.4±119 vs 320.4±138 mmHg*hr, p = 0.0408) as well.

SEISMiC Part B results:

• **Cardiac output was improved in the istaroxime group.** Over the treatment period, the amount of blood pumped by the heart per minute, or cardiac output[1], was improved during the infusion by about 15% in the istaroxime group. There was no statistically significant increase in heart rate versus placebo in the istaroxime group and heart rate tended to decrease. At 12 and 24 hours, patients in the istaroxime group experienced statistically significant reductions in heart rate (p = 0.0102 and p = 0.0218, respectively).
• **Istaroxime treatment reduced PCWP more than placebo.** This patient population generally has elevated pulmonary capillary wedge pressure (PCWP[2]) and the study participants were consistent with this at baseline. Istaroxime reduced PCWP significantly more than placebo within six hours (-6.6 vs -0.9 mmHg, p = 0.0001), with the effect lasting through 60 hours.
• **Organ perfusion, as assessed by mixed venous oxygen saturation (SVO2[3]), was significantly improved** by 12 hours (mean difference of the istaroxime group compared to placebo was approximately 9%, p=0.0071), and remained significant through 48 hours (p=0.0001) and generally persisted through a 60-hour assessment.
• **Renal function was improved.** Renal function measured by estimated glomerular filtration rate (eGFR) was improved in the istaroxime group compared to placebo at all time points, reaching statistical significance at 48 hours (p =0.0291).

The clinical symptoms of congestion and heart failure were improved in both istaroxime groups. Specifically, the NYHA (New York Heart Association) classification of heart failure severity was significantly lower in the istaroxime group at 24 hours (p=0.020), 48 hours (p=0.035), and 72 hours (p=0.010) and was similar to placebo at 96 hours. Importantly, worsening heart failure as a serious adverse event (AE) occurred with lower frequency in the istaroxime cohort compared to placebo (5.3% versus 18.2%, respectively).



Source: Company presentation

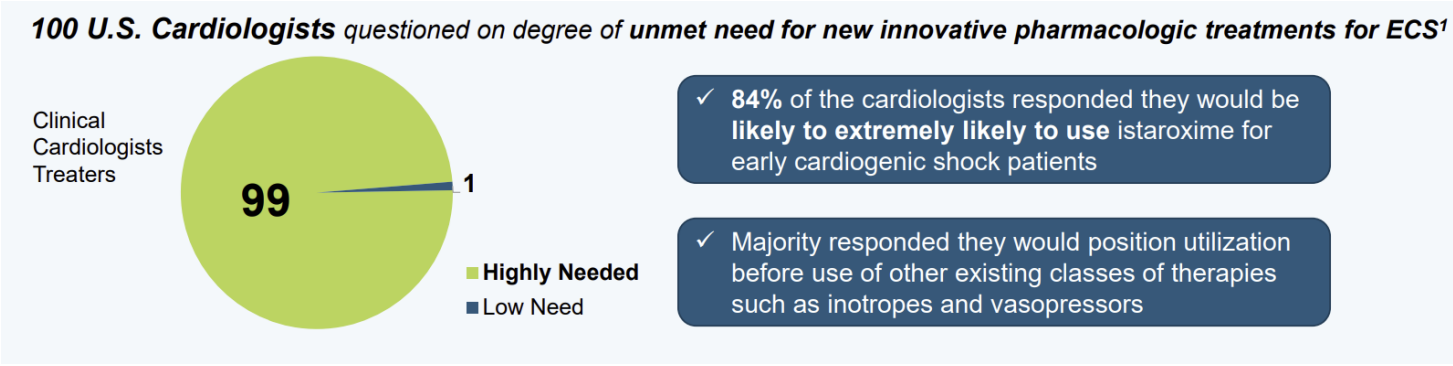
However, the istaroxime safety profile in Part B, although favorable, did record higher treatment related AEs, at 78.9% compared to 45.5% in the placebo group. This was largely related to nausea, vomiting, infusion site discomfort and headache, all side effects that had been observed with istaroxime in earlier studies. Nevertheless, serious adverse events were infrequent and occurred at a similar frequency in both the istaroxime and placebo groups (10.5% vs. 27.3%, respectively). Importantly, consistent with previous findings, istaroxime did not increase clinically significant arrythmias compared to the placebo group.

Serious Adverse Events in SEISMiC B

Event	Istaroxime (N=19)	Placebo (N=11)
All serious adverse events	**2 (11%)**	**3 (27%)**
Cardiac Failure (Worsening HF)	**1 (5%)**	**2 (18%)**
Cholecystitis	0	1 (9%)
Infection	2 (11%)	0
Arterial hemorrhage	0	1 (9%)

Source: Company presentation

KOLs, Cardiologists Support WINT's Optimism



Source: Company presentation

The results of this latest study augment the company's growing istaroxime database, which WINT believes support its confidence that istaroxime could be a better way to treat AHF and cardiac shock patients. Moreover, WINT's scientific board and numerous KOLs are optimistic about the prospects for istaroxime. Of 100 cardiologists surveyed, 84% indicated that they would be 'likely to extremely likely' to use istaroxime for early cardiogenic shock patients. Moreover, most indicated they would prioritize istaroxime before using other existing classes of therapies such as inotropes and vasopressors.

When asked what the ideal treatment for cardiogenic shock due to heart failure would look like, the responses indicated many of the attributes that characterize istaroxime, including that it:

▪ Improves systolic and diastolic cardiac function, which are the underlying cause of cardiogenic shock
▪ Improves blood pressure and organ perfusion
▪ Avoids harmful side-effects to kidney function and to the kidneys
▪ Does not increase heart rate or increase myocardial oxygen demand or energy requirements of the heart
▪ Does not increase or cause cardiac arrhythmias
▪ Contributes to effective diuresis and resolving fluid overload in lungs and body
▪ Rapid onset of action with a predictable effect that can be titrated to individual patients

POTENTIAL UPCOMING MILESTONES

Windtree expects multiple potential upcoming milestones

- Planned interim analysis of Istaroxime cardiogenic shock SCAI Stage C Phase 2 study for early 2Q25
- Potential type C meeting with the FDA for the back half of 2025
- The company's istaroxime regional licensing partner for greater China, Lee's Pharma, plans to begin an istaroxime acute heart failure Phase 3 program in its licensed territory
    - Lee's Pharma is responsible for the costs of the study
    - WINT is collaborating with its partner and has final say on the study protocol
- Potential business development partnership with cardiovascular portfolio
- Potential acquisitions of revenue ready FDA approved assets

Windtree asset portfolio includes both cardiovascular and oncology assets

SERCA2a A key property of istaroxime is that it also activates SERCA2a (sarco endoplasmic reticulum Ca2+ -ATPase 2a) to treat cardiogenic shock and acute heart failure . The company has next generation SERCA2a activators in the preclinical stage that it expects to move toward the clinic to evaluate oral and

intravenous administrations of these assets to potentially be utilized for inpatient acute decompensated and chronic out-patient heart failure.

Rostafuroxin The company's cardiovascular drug asset portfolio also includes rostafuroxin, a novel product candidate for the treatment of hypertension in patients with a specific genetic profile. Windtree does not plan to develop rostafuroxin independently and is pursuing potential licensing and / or strategic partnership opportunities to advance its development. We would expect Windtree to retain upside exposure to commercial opportunities if / when rostafuroxin is commercialized.

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

Product Candidates	Indication	Phase	Development Status / Plans
Istaroxime (SERCA2a activator/ Na/K ATPase inhibitor)	**Cardiogenic Shock**	**Phase 2b**	• **Positive Phase 2b studies** • **Executing small follow-on studies intended to transition to Phase 3**
Istaroxime	Acute Heart Failure	Phase 2b	• Positive Phase 2a and 2b data • Greater China regional license with **Lee's Pharma who is advancing and paying for Phase 3 AHF program in territory**
SERCA2a Activators (oral)	Chronic Heart Failure, including potentially HFpEF	Preclinical	• Chronic and Acute Heart Failure • Target for collaboration/partnership
aPKCi inhibitor (topical and oral)	**Cutaneous and systemic treatment in broad and/or rare malignant diseases**	Preclinical	• **IND enabling studies**
Rostafuroxin	Treatment Resistant Hypertension – Genotypically identified patients	Phase 2b	• Phase 2 data in hypertension • Company holding development to out-license and reposition 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 in place** • Partner responsible for all costs of development

Source: Company reports

Oncology assets: aPKCi inhibitor In addition to istaroxime for treatments of cardiac conditions, through a recent acquisition, WINT has added a first in class, novel, protein kinase C iota inhibitor oncology platform to its portfolio with both topical and oral formulations for potential application in rare and broad oncology indications. Specifically, Windtree purchased the aPKCi inhibitor assets of Varian Biopharmaceuticals, Inc. in April 2024. The drug candidates are in the preclinical stage and have potential for broad application in oncology and certain rare malignant cancer, as well. The platform includes two formulations of an aPKCi inhibitor, both topical and oral.

The company is optimistic about this platform and intends to move these assets forward in 2025. We would anticipate an update on the clinical development plan for this platform in the future. WINT has leveraged strategic M&A to expand its asset portfolio before. Notably, the company acquired its lead asset istaroxime through M&A.

To support its licensing opportunities and protect its IP, Windtree continues to expand its patent position domestically and globally. Windtree was issued an istaroxime patent for Hong Kong that is set to expire in 2039. A patent for mainland China and for Japan were granted earlier. Overall, the company has completed filings of patent applications in various market, including the U.S., Germany, France, Italy, Japan and China. Earlier this quarter, the company was issued a patent in Japan for "Inhibitors of atypical protein kinase C (aPKCi) and their use in treating hedgehog pathway-dependent cancers." The patent is expected to support and protect the company's oncology platform. Most recently, the U.S. Patent and Trademark Office issued a Notice of Allowance for istaroxime for intravenous treatment of AHF.

Potential partnerships to enhance potential returns

In addition to the new corporate strategy noted above and to further augment its R&D spending, WINT intends to enter into licensing and / or strategic partnerships to advance development of various assets, as noted. The company has a regional licensing and research partnership with Lee's Pharmaceutical for greater China and intends to engage in discussions with other large pharma companies for additional potential licensing opportunities. Lee's Pharma will finance a Phase 3 AHF program in Greater China.

WINT has indicated that it is currently engaged in discussions with pharmaceutical companies for out-licensing and partnership opportunities in its cardiovascular portfolio. WINT seeks to leverage the positive early cardiogenic shock and acute heart failure results, including the recent positive Phase 2b in early CS to secure potentially non-dilutive funding via a partnership for istaroxime, as well as the next generation, oral SERCA2a activators for all global territory ex-Greater China. The company expects a licensing partnership would provide non-dilutive funds and provide the funding for development of istaroxime and other cardiovascular assets.

Potential for Additional Licensing Deals from Big Pharma

As noted, the istaroxime lead indication is cardiogenic shock and a second indication is acute heart failure. Istaroxime has been evaluated in multiple studies, including four positive Phase 2 clinical trials. Results suggest that istaroxime significantly improves cardiovascular physiology with minimal adverse effects. Istaroxime treatment has shown improvement in cardiac function, decreases in PCWP (pulmonary capillary wedge pressure), maintains or reduces heart rate and increases systolic blood pressure (which is a desired effect in those with normal to low blood pressure) without adverse events such as heart rhythm disturbances – arrhythmia – or heart muscle damage. The most common adverse complaint associated with istaroxime treatment is nausea, particularly at the highest dose, and discomfort at the infusion site.

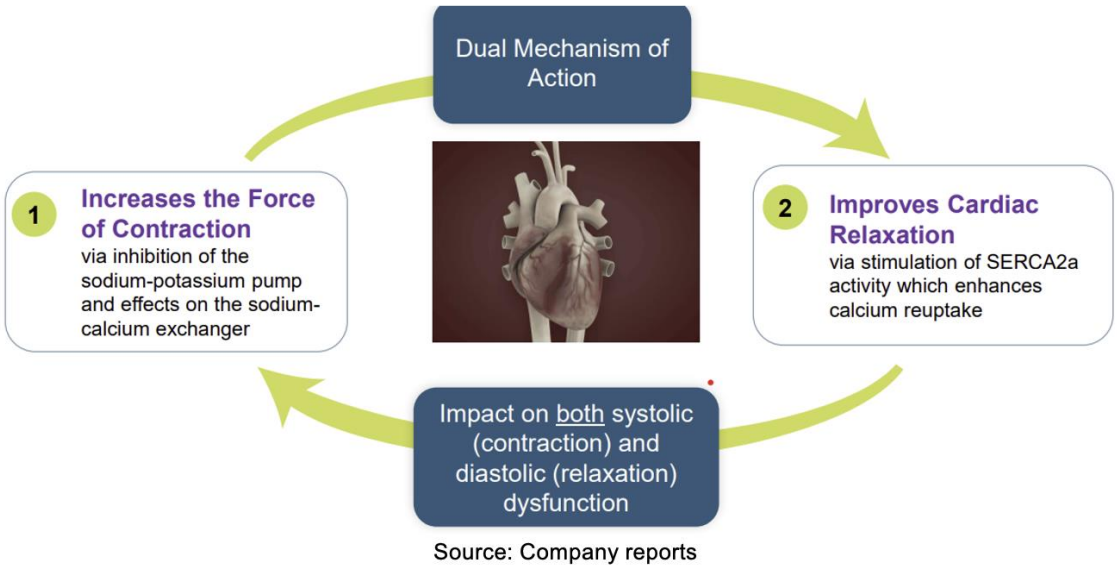
Due to the positive effects observed in earlier istaroxime studies on cardiac function, blood pressure and renal function, WINT is studying istaroxime for treatment of early cardiogenic shock due to heart failure. The company believes it might have an attractive regulatory pathway for cardiac shock. Moreover, given the unfortunate incidence of cardiac shock, the potential commercial market is large, at an estimated $1.25 billion worldwide. Overall, WINT is prioritizing its cardiac shock program reflect several factors, including that the company believes:

- Market research and KOL feedback indicate that there are no other suitable drug therapies on the market currently
- The company also believes there are no other drugs in development for cardiogenic shock other than istaroxime
- Cardiogenic shock represents an estimated $1.25 billion global market
- The company believes that istaroxime could have a favorable regulatory pathway of significantly increasing blood pressure as a pivotal endpoint

It also has next generation SERCA2a activator preclinical stage drug candidates. One family of SERCA2a activators are called the dual mechanism SERCA2a activators and are envisioned as a fast follow-on to istaroxime in acute heart failure – these can utilize intravenous administration inpatient and upon the patients discharge from the hospital be continued on an oral formulation as chronic therapy. A second family of SERCA2a activators is called the pure SERCA2a activators and are envisioned for heart failure with preserved ejection fraction as outpatient chronic therapy with an oral formulation. Specifically,

Why has Istaroxime been shown effective? Better squeeze pumps more blood from the heart; relaxation allows heart to fill more effectively

Istaroxime's innovative dual mechanisms of action impact both systolic and diastolic dysfunction. By inhibiting the sodium-potassium ATPase, istaroxime creates a stronger contraction. By stimulating SERCA2a activity, istaroxime also aids the heart in relaxing between contractions, allowing it to fill with blood more effectively. This dual effect on both contraction and relaxation creates a stronger pumping action with a greater amount of blood ejected with each heartbeat. This dual mechanism of action is a key differentiator for istaroxime.



Source: Company reports

In simple terms, unlike many other commercially available agents, istaroxime improves cardiac systolic and diastolic function with an increase (rather than decrease) in systolic blood pressure and has a generally positive profile on renal function. Moreover, there has not been a negative effect on heart rhythm / arrythmias profile, a lower heart rate (which is generally desired) and no measure of cardiac muscle injury, which is another important differentiator from many other agents.

Istaroxime inhibits the sodium-potassium ATPase activity, which makes more calcium available to improve myocardial contractility (inotropic). Istaroxime also activates the SERCA2a, which acts to decrease intracellular calcium by pumping it into sarcoplasmic reticulum (SR) after a contraction. This relaxes the heart muscle, which in turn allows the ventricle to fill more effectively for the next contraction. In combination, these mechanisms produce a stronger contraction and improved cardiac function.

MARKET OPPORTUNITIES

Istaroxime Cardiogenic Shock Market Opportunity

Cardiogenic shock is an area of extreme unmet need with no satisfactory pharmacologic interventions to reverse the condition. Thus, it has a high associated mortality and morbidity of approximately 20-30%%. Because of the unmet need, there are potential opportunities for an accelerated regulatory pathway and review. The company estimates that the combined U.S. and EU markets represent a market opportunity of roughly $1.25 billion, given the high unmet need and prevalence of patients suffering from various cardiovascular diseases, including CS. CS is caused by severe impairment of myocardial performance that leads to reduced cardiac output, organ hypoperfusion, and hypoxia, according to JAHA. It is a severe presentation of heart failure characterized by extremely low blood pressure and hypo-perfusion to critical

organs. CS is most commonly caused by heart failure – the company utilized US hospital claims data and epi data outside the US to confirm this.

According to the Journal of the American Heart Association (JAHA), cardiovascular diseases are the leading cause of death and disability in many global markets. In the U.S., these diseases represent a large portion of the economic cost of overall healthcare expense.

According to the National Institute of Health (NIH), globally at least 26 million people are affected with heart failure where the heart cannot pump blood at the rate the body needs. The most critical presentation of heart failure, AHF, requires immediate treatment in a hospital to stabilize the patient. Stabilization is usually achieved using strong intravenous diuretics and often requires that the patient be placed in an intensive care unit with treatment that can take many days. The clinical goal is to get the patient out of crisis, resolve the fluid overload and improve the patient's condition so that the patient can be discharged in a condition to begin out-patient chronic therapies and lower the risk of being readmitted to the hospital. There have been no significant advances in effective cardiac therapies to aid this process in decades, which management believes implies that this is a niche that istaroxime could fill.

According to the CDC, roughly 6.5 million adults in the U.S. have heart failure. Of these, about 50% are expected to die within five years of diagnosis; AHF and low cardiac output also increase the risk of other organ dysfunction such as renal failure. The disease costs the country more than $30 billion per annum in medical treatment and hospital stays and work days missed. In the U.S., EU and Japan combined, more than 18 million patients suffer from heart failure.

Istaroxime Market Opportunity for Cardiogenic Shock is an estimated $1.25B globally

There have been no significant advances in effective cardiac therapies in decades, implying that istaroxime could become the standard of care in cardiogenic shock. Moreover, the company believes there is no other potentially competitive therapies in active development. Cardiogenic shock is caused by severe impairment of myocardial performance that leads to reduced cardiac output, organ hypoperfusion, and hypoxia, according to the Journal of the American Heart Association (JAHA). It is a severe presentation of heart failure characterized by extremely low blood pressure and hypo-perfusion to critical organs and generally damages the heart and compromises organ function, including renal activity.

Based on data from multiple sources, cardiogenic shock represents an estimated $1.25 billion global market, as noted, of which the US + EU represent a combined roughly $1.0 billion. The company believes this patient segment represents a significant opportunity for istaroxime because the drugs that are available currently generally have negative side effects and can result in poor outcomes. Even following stabilization treatments, the risk of mortality remains high, with associated mortality of approximately 20-30%.

Istaroxime Market Opportunity for acute heart failure

2nd Istaroxime Program – AHF: Discussions regarding potential partnerships in AHF and cardiogenic shock

WINT has indicated that it is engaged in discussions with pharmaceutical companies regarding potential partnership opportunities in both AHF and cardiogenic shock. The company believes that a partnership with pharma would be the ideal way to maximize the opportunity for istaroxime in AHF. Windtree is currently in discussions with multiple pharmaceutical companies about partnership.

Partner, Lee's Pharmaceutical, also Conducting Clinical Activities for its licensed territory of greater China

WINT's licensing partner, Lee's Pharmaceutical, is preparing to embark on a Phase 3 AHF study, following two Phase 2 global studies in which istaroxime consistently demonstrated significant

improvement in cardiac function of a failing heart plus significant improvement in blood pressure. Windtree anticipates receiving milestone payments of up to $120 million and subsequent low double digit royalties if / when istaroxime is commercialized in Lee Pharma's licensed territory.

RECENT AND PLANNED UPCOMING CLINICAL ACTIVITIES

Following positive results in earlier SEISMiC A and B in SCAI Stage B cardiogenic shock trials (see below), Windtree recently began enrolling participants in the SEISMiC C trial in SCAI Stage C CS. In the earlier trials, istaroxime demonstrated improved systolic blood pressure, cardiac function and renal function with no increased risk for cardiac arrhythmias. This profile differentiates istaroxime from current standard of care treatments of shock.

As noted, SCAI Stage C cardiogenic shock is a more severely ill population than was previously studied with istaroxime. In SCAI Stage C patients, CS and heart failure have progressed to the point of tissue and vital organ hypoperfusion (lack of blood flow and oxygen). Thes, e patients generally need inotropic or vasopressor drugs, which have deleterious side effects. Based on results in earlier studies, WINT believes istaroxime might be able to avoid these negative side effects.

The SEISMiC C study is a global trial including sites in the U.S,. Europe and Latin America. It is a placebo-controlled, double-blinded study with istaroxime being added to current standard of care, inotropes or vasopressors. The effect of istaroxime in addition to these therapies will be assessed for six hours and withdrawing other therapies if the patient's condition supports it. The primary endpoint of the study is assessment of systolic blood pressure (SBP) profile over the first 6 hours of treatment. Other key study measurements include various measures of cardiac function, SBP changes at specified timepoints, the vasopressor-inotrope score, avoidance of progression to SCAI Stage D or E cardiogenic shock and need for mechanical cardiac support, time to treatment failure, arrhythmia assessments, days alive and out of the hospital through day 30, physiologic measures (e.g., cardiac index) and length of stay in the intensive care unit and hospital.

Extension programs; SERCA2a Activation for Chronic and Acute Heart Failure

Istaroxime forms the core of the company's heart failure programs, but there are also next generation follow-on compounds, with SERCA2a stimulatory activity that WINT has in preclinical stages of development. WINT hopes to develop these compounds to be potential oral (with potential intravenous administration) therapies for AHF and/or chronic HF (CHF). The company is in discussions with pharmaceutical companies for potential partnering and/or licensing opportunities with SERCA2a activators.

The company believes that each of its clinical programs addresses a large unmet need and provides another avenue of potential regulatory approval from the FDA. For example, the company is studying oral SERCA2a compounds, which is the unique mechanism of istaroxime, for chronic heart failure and possibly for AHF. Together with Istaroxime, these drug candidates create a heart failure platform that WINT intends to advance and also believes can be attractive to potential licensing and/or R&D partners in Big Pharma, while also enabling WINT to retain exposure to upside commercialization potential.

As discussed above, Windtree is executing multiple clinical programs that lay the groundwork for many potential milestones and catalysts. Among various upcoming milestones, the company expects to report results from its small Phase 2 cardiogenic shock SCAI Stage C study in early 2Q25 and prepare for Phase 3 readiness later in 2025.

The company also expects its license partner Lee's Pharma, working closely with Windtree, to launch a Phase 3 Acute Heart Failure study in Asia/PAC.

In terms of the SCAI Stage C study, once about 20 participants with SCAI Stage C CS due to acute decompensated heart failure have been enrolled, the company plans to review the data and expects this will occur 2Q25. Once it has reviewed the early data, WINT expects to issue guidance on the number of additional patients and timing to complete the study and planned Phase 2 completion.

Windtree is optimistic that data from SEISMiC C trial will support the potential advantages of istaroxime compared to current standard of care therapies and prepare the therapy for Phase 3 readiness in CS, as well as to be used for discussions with regulatory agencies to design the planned Phase 3 program.

In addition, WINT expects to secure additional licenses for istaroxime and SERCA2a activators to enhance its financial flexibility to advance its assets. In addition, Windtree intends to provide a business update for the preclinical oncology aPKCi inhibitors to progress toward IND enablement later this year.

MANAGEMENT

CEO

Jed Latkin was appointed CEO of Windtree Therapeutics on December 1, 2024. He has been a member of the Windtree board of directors since October 2024 and will continue to serve on the board. He has nearly three decades of financial and biotech experience, including as CEO of a public biotech company. At Navidea Biopharmaceuticals, he held the positions of CEO and CFO. For the past two years, he was both the Chief Operating Officer and Head of Finance at ProPhase Labs. Prior to that , he served as a CEO of Black Elk Energy Offshore in 2014 as part of Nagel Avenue Capital, which he joined after working for more than ten years with several financial services organizations, including ING, Morgan Stanley and Citigroup Securities.

President and Chief Operating Officer

Eric Curtis joined Windtree in March 2020. Prior to joining Windtree, he most recently served as CEO and President of Centurion Biopharma Corp., an oncology research and development company. Before Centurion, he was President and Chief Operating Officer of CytRX Corporation, a biopharmaceutical company and Centurion's parent company. Earlier in his career, he President, U.S. Commercial at Aegerion Pharmaceuticals (now Novelion Therapeutics), and was VP/GM of the Cardiopulmonary BU at Bayer, Global Commercial Leader and VP of Marketing at GlaxoSmithKline earlier. Mr. Curtis has also held senior marketing and sales roles at Johnson & Johnson.

Senior Vice President and Chief Medical Officer

Steve Simonson, M.D. was named Vice President of Clinical Development for Windtree in May of 2014 and has served as its SVP and Chief Medical Officer since October 2014. He has an extensive background in pulmonary critical care, with more than 25 years of medical practice and pharmaceutical industry clinical trial expertise including all phases of drug development.

His prior roles include executive positions with several firms, including Executive Director in the Molecular Development Group at Covance, Vice President of Clinical Development at Agennix, Inc., and various positions at AstraZeneca, where he spent 15 years in medical and clinical leadership.

Senior Vice President and Chief Financial Officer

Jamie McAndrew was appointed Windtree's Senior Vice President and Chief Financial Officer in September 2024. She joined Windtree in November 2013 and has held various positions, including Director of Accounting and Reporting, Controller, and Executive Director and Corporate Controller. Prior

to joining Windtree, she worked in public accounting at KPMG LLP from January 2008 to October 2013, holding positions of increasing responsibility.

RECENT RESULTS

R&D costs in partner territories covered by partner

Windtree is pre-revenue at this stage, as the company continues to advance its lead product, istaroxime, through a Phase 2 clinical trial. The company plans to enter into a licensing partnership which would provide non-dilutive capital, shift development costs to the licensee and provide royalty payments if launched in commercial markets.

The company's R&D in the first nine months of 2024 was approximately $14.1 million compared to $5.3 million during the same period of 2023. However, the annual increase primary reflected the acquisition of oncology assets from Varian, which accounted for about $7.5 million of non-cash R&D expense included in the increase. This, combined with higher costs on development programs as WINT completed its recent Phase 2 study of istaroxime and began an additional Phase 2 study, are primary factors behind the increase. Excluding the asset purchase, the pro forma R&D costs in the first nine months of 2024 would have been an estimated $6.6 million, compared to $5.3 million in the comparable period of 2023, representing a pro forma roughly 25% year-over-year increase as WINT moves istaroxime forward. This increase was partially offset by lower general and administrative (G&A) expenses. G&A expenses were approximately $6.5 million, down from $7.3 million, primarily related to lower personnel, severance and stock-based comp expense.

After potentially exploring strategic alternatives early this year, WINT is focused on finding non-dilutive ways to fund its development efforts, as noted, including entering into licensing partnerships. The company's partnership with Lee's Pharma is an example of shifting the cost of funding development activities to a better capitalized partner, while retaining upside exposure to revenue if / when the asset is commercialized. We would also expect the company to simplify its balance sheet going forward if it attains access to non-dilutive funding sources.

At September 30, 2024, the company had $2.3 million of cash to advance its strategy following two private placements during the quarter, and an $8.6 million warrant liability. With these funds and some $0.7 million in receivables, WINT anticipates that it has sufficient funds in the near-term. Management plans to raise additional funds, likely through a combination of adding revenue ready assets, dilutive and non-dilutive sources, potentially including licensing arrangements and other alliances (as noted, licensing partner Lee Pharma's is responsible to cover the cost of clinical trials in its licensed territory).

In June 2024, WINT entered into an ELOC purchase agreement to sell shares to an investor in exchange for an equity line of credit. This transaction established an equity line of credit for WINT for up to $35 million. In 3Q24, the company sold 1.4 million shares under the ELOC agreement, raising net proceeds of $3.1 million. Subsequently, WINT issued 4.3 million shares under the ELOC purchase agreement, raising net proceeds of $2.4 million.

The company added a new independent director to its board. Leanne Kelly, who has substantial public company experience and will chair WINT's audit committee. She has served as CFO of publicly-traded GRI Bio since April 2023 and was CFO of Vallon Pharmaceuticals from May 2021 until April 2023.

After receiving approval in a proxy with its shareholders, the company implemented a reverse 1-for-50 stock split which was effective on February 20, 2025. This brought WINT shares into compliance with Nasdaq share price requirements.

RECENT NEWS

- Windtree announced Istaroxime Notice of Allowance from the U.S. Patent and Trademark Office for Acute Heart Failure on March 4, 2025.
- On February 27, 2025, WINT filed Istaroxime Cardiogenic Shock and Prevention of Arrythmias Patent for India.
- On February 18, 2025, Windtree announced a 1-for-50 reverse stock split.
- On January 24, 2025, Windtree notified series C convertible preferred stockholders that it had decided to offer to reduce the conversion price.
- Windtree added a new patent from Japan on Jan 15, 2025.
- Windtree WINT added Leanne Kelly to its board on January 13, 2025.
- On January 8, 2025, WINT unveiled its new strategy to acquire small biotechs with FDA-approved revenue generating assets.
- Windtree announced a new istaroxime patent filing for preventing or reducing the risk of acute myocardial arrhythmia on December 9, 2024.
- On December 4, 2024, Windtree announced a partnership with New Growth Advisors to leverage the positive data from its recent Phase 2 Istaroxime CS study for a potential strategic transaction.
- Jed Latkin was named President and CEO of Windtree effective on December 1, 2024.
- On November 27, 2024 Windtree reported 3Q24 results and provided a business update.
- On November 14, 2024, Windtree announced a leadership transition.
- On November 4, 2024 Windtree announced it had been issued an istaroxime patent for Hong Kong in support of Lee's Pharma's upcoming Phase 3 activities in AHF.
- On October 23, 2024, Windtree Announces Istaroxime Cardiogenic Shock Patent Filings In Countries Around the World.
- On October 21, 2024, Windtree Announces Expansion of Patents with Issuance of Istaroxime Patent for Japan.
- On October 17, 2024, Windtree Therapeutics announced the issuance of an istaroxime patent.
- On October 9, 2024, WINT announced publication of positive istaroxime Phase 2b trial design.
- On September 30, 2024, WINT announced positive Phase 2b topline clinical results in early CS.

RISKS

Risks include that the competitive landscape could change, although management believes that istaroxime is the only therapy of its kind in development for the indications discussed above. In addition, the company's plans could incur higher costs than currently anticipated and WINT might have to raise funds that could be dilutive to existing shareholders, among other risks:

- WINT might need to raise additional capital earlier than or at higher costs than expected.
- The company might encounter delays in its clinical and commercialization timelines.
- Istaroxime might experience clinical failure.
- Istaroxime or other assets might not receive FDA and / or other regulatory approvals.
- The company might not find strategic partners or a licensee for programs that it does not plan to develop internally.
- The company's new M&A strategy might not be successful.

VALUATION

We are optimistic about the chances of istaroxime receiving regulatory approval and of the subsequent commercial demand, reflecting the dearth of effective therapies that have the limited side effects of istaroxime and high related healthcare costs of alternate existing treatments. While it is difficult to know the revenue arc for WINT at this stage, istaroxime addresses indications with significant unmet need and the current cost of standard care can be substantial. Moreover, the company is also optimistic that it can shorten the timeline to revenue through its newly launched strategic M&A strategy. With these factors, it is not unreasonable to expect that the company could generate revenue of $8 million to $10 million in the 2028-29 timeframe.

Although not directly comparable to WINT, which we would expect would exhibit higher growth in early years of commercialization, we believe the average price-to-sales multiples of other public companies could provide a valuation benchmark. Applying a multiple under 2x to our lower end of the range $8 million revenue forecast, discounting back to the present at 12%/year and applying a 50% risk adjustment factor results in a present value of about $4.00/share.

We also believe there are several factors that imply potential upside to our valuation, including: pre-approval partnerships that provide milestone payments and/or R&D cost sharing; a faster, or less-costly path to regulatory approval and the opportunities of adding new revenue producing small biotech companies and deriving synergies among them.

Any delay or failure in clinical development or regulatory approval could cause the share price to decline and represent a potential risk to our valuation but we believe the risk / reward ratio could be attractive for investors who have a higher than average risk tolerance and longer time horizon.

PROJECTED INCOME STATEMENT

Windtree Therapeutics, Inc. ($000s except per share data)

	2022	1Q23	2Q23	3Q23	4Q23	2023	1Q24	2Q24	3Q24	4Q24E	2024E	2025E
Product revenue	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
R&D	11,099	1,415	1,763	2,110	3,053	8,341	2,253	9,863	1,968	1,970	16,054	7,900
General & administrative	10,790	2,292	2,420	2,580	1,906	9,198	2,152	1,589	2,773	2,776	9,290	11,131
Loss on goodwill impairment	12,624	484	2,574	-	-	3,058			-	-	-	-
Loss on other impairments	6,820	-	-	-	-	-	-	-	-	-	-	-
Total operating expenses	41,333	4,191	6,757	4,690	4,959	20,597	4,405	11,452	4,741	4,746	25,344	19,030
Operating loss	(41,333)	(4,191)	(6,757)	(4,690)	(4,959)	(20,597)	(4,405)	(11,452)	(4,741)	(4,746)	(25,344)	(19,030)
Other income (expense)												
Gain on debt extinguishment	-	-	-	-	-	-	14,520		71		14,591	-
Chg in fair value warrant liability	-	-	-	-	-	-	-	-	2,166	50	2,216	50
Interest income	109	44	108	112	61	325	30	20	12	12	74	47
Interest expense	(53)	(12)	(13)	(13)	(12)	(50)	(13)	(110)	(51)	(54)	(228)	(217)
Other income (expense)	702	48	61	166	(244)	31	201	(285)	(446)	(473)	(1,003)	(300)
Total other	758	80	156	265	(195)	306	14,738	(375)	1,752	(465)	15,650	(420)
Pretax income (loss)	(40,575)	(4,111)	(6,601)	(4,425)	(5,154)	(20,291)	10,333	(11,827)	(2,989)	(5,211)	(9,694)	(19,451)
Income (tax) benefit	1,367	-	-	-	-		(114)	(197)	240	-	(71)	-
Net income (loss)	(39,208)	(4,111)	(6,601)	(4,425)	(5,154)	(20,291)	10,219	(12,024)	(2,749)	(5,211)	(9,765)	(19,451)
Extinguishment series B preferred	-	-	-	-	-	-	-	-	572	-	572	-
Deemed dividend series C preferred	-	-	-	-	-	-	-	-	(1,573)	(522)	(2,095)	-
Net loss to common stockholders	(39,208)	(4,111)	(6,601)	(4,425)	(5,154)	(20,291)	10,219	(12,024)	(3,750)	(5,733)	(11,288)	(19,451)
EPS (LPS)	($62.23)	($85.65)	($29.47)	($15.47)	($0.95)	($5.24)	$21.98	($20.91)	($4.23)	($0.64)	($3.80)	($2.16)
EPS (LPS) PF	($4.36)	($0.46)	($0.73)	($0.49)	($0.57)	($2.26)	$1.14	($1.34)	($0.42)	($0.64)	($1.26)	($2.16)
Avg shrs out	630	48	224	286	5,399	3,876	465	575	887	8,990	2,729	9,000

Source: Company reports, Zacks estimates

2Q24 R&D includes purchase of oncology assets

PF EPS / (LPS) based on Nov. 2024 share count

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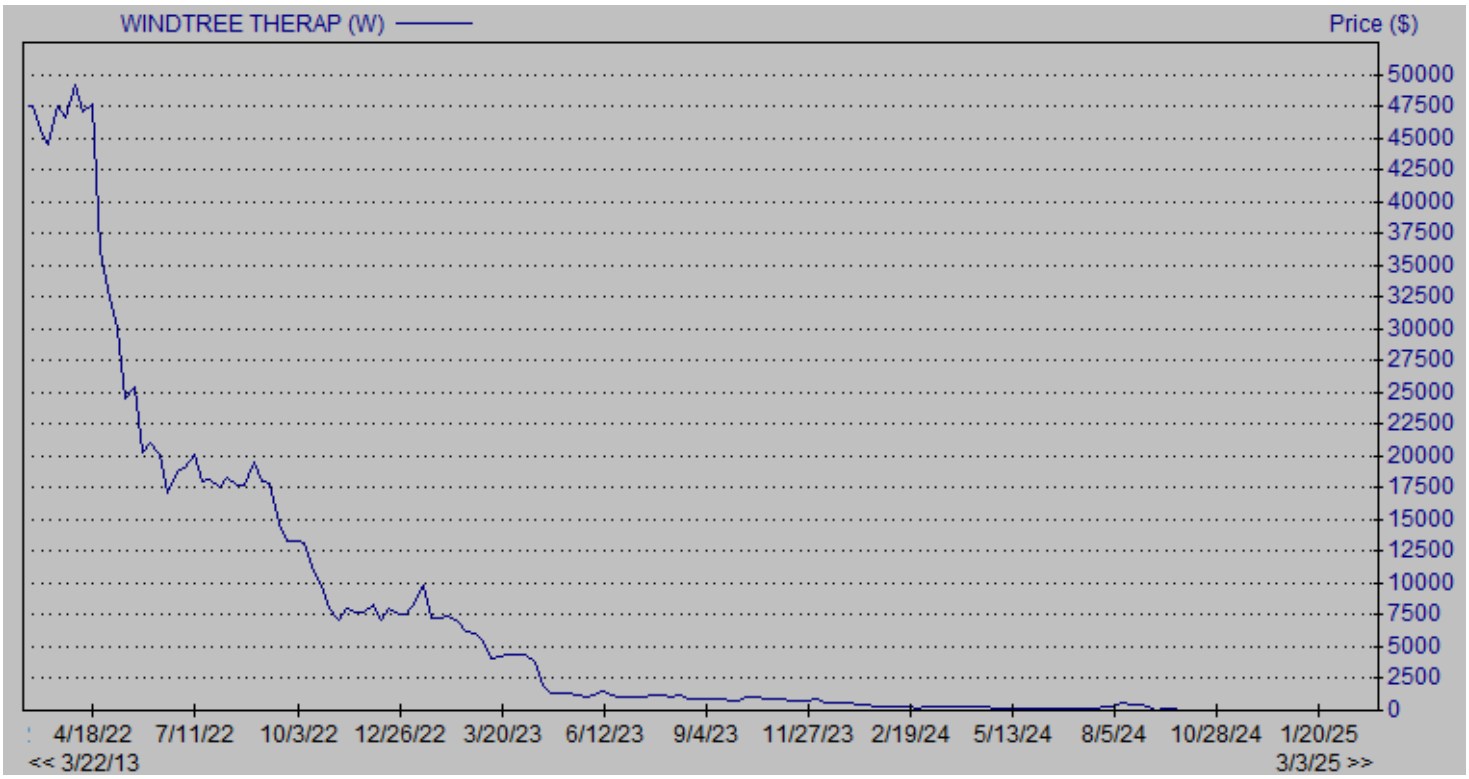
HISTORICAL STOCK PRICE



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