August 28, 2020

Zacks Small-Cap Research

Sponsored – Impartial - Comprehensive

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

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

Windtree Therapeutics (WINT-NASDAQ)

WINT: Advancing Two Lead *Fast Track* Designated Drug Candidates Toward Approval & Commercialization

We are optimistic about the chances of istaroxime and AEROSURF receiving FDA approval and of the subsequent commercial demand of these treatment therapies. We estimate rapid growth for both once they are commercialized and believe WINT shares do not adequately reflect the prospects of the company's product pipeline.

Current Price (08/28/20)	$8.27
Valuation	**$12.00**

OUTLOOK

Windtree Therapeutics, Inc. is advancing drug candidate istaroxime and drug/device combination AEROSURF toward FDA approval. Following a recent merger and financing, the company is well-funded to advance these assets, with $31.5 million in cash at June 2020, committed financing from a partner and potential licensing revenue to support its development efforts of multiple late-stage assets and programs focused on important markets with high unmet needs.

SUMMARY DATA

52-Week High	**$14.97**
52-Week Low	**$6.00**
One-Year Return (%)	**-31.26**
Beta	**0.33**
Average Daily Volume (sh)	**79,463**
Shares Outstanding (mil)	**17**
Market Capitalization ($mil)	**$140**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**0**
Insider Ownership (%)	**15**
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 2020 Estimate	**N/A**
P/E using 2021 Estimate	**N/A**
Zacks Rank	**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)
2019	0.0A	0.2A	0.0A	0.0A	0.2 A
2020	0.0A	0.0A	0.0E	0.0E	0.0 E
2021					1.0 E
2022					5.2 E

Loss Per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2019	($0.61)A	($0.60)A	($0.66)A	($0.64)A	($2.51)A
2020	($0.48)A	($0.63)A	($0.49)E	($0.46)E	($2.06)
2022					($2.00)
2022					($1.72)

Quarters might not add to annual reflecting rounding

Disclosures on page 17

© Copyright 2020, Zacks Investment Research. All Rights Reserved.

KEY POINTS

- **We are initiating coverage of Windtree Therapeutics, Inc.,** a small-cap public company with multiple late-stage assets and programs focused on important markets with high unmet needs. With recent successful financings and an uplisting to Nasdaq, the company is executing on a number of clinical and business development activities that have the potential for important milestones and potential catalysts.

- **Istaroxime** is a first-in-class dual mechanism therapy designed to improve both systolic contraction and diastolic relaxation functions of the heart. Istaroxime produces these effects by inhibiting sodium-potassium ATPase and by activation of SERCA2a. Data from two Phase 2 studies in patients with **acute heart failure (AHF)** demonstrate that istaroxime infused intravenously significantly improves cardiac function and blood pressure without causing heart rate increases or rhythm disturbances. Given the observed significant improvements to blood pressure, istaroxime is also being studied in AHF patients suffering from **early cardiogenic shock** for which there is substantial unmet medical need. WINT believes that successful results of clinical studies could lead to the FDA granting Breakthrough Designation for istaroxime treatment of early cardiogenic shock.

- WINT's other primary asset is **AEROSURF**, a drug-device combination that incorporates synthetic KL4 surfactant with an innovative, proprietary aerosol delivery system to treat premature infants with **respiratory distress syndrome (RDS)**, a common complication with premature births due to insufficient endogenous surfactant. AEROSURF delivers surfactant non-invasively to avoid the complications associated with invasive administration. Data from the phase 2 program have demonstrated that AEROSURF can improve lung function and eliminate the need for intubation and mechanical ventilation in premature infants with RDS and also has the potential to impact bronchopulmonary dysplasia (BPD), a condition of chronic lung disease that has no approved therapies. WINT has also produced substantial pre-clinical data in a variety of lung injury models beyond RDS and intends to apply this knowledge and KL4 surfactant's potential to mitigate lung injury in a small study in **COVID-19** patients in 2H20.

- In addition to the Istaroxime and AEROSURF programs, Windtree has a phase 2 stage drug candidate for genetically associated hypertension, as well as a pipeline of heart failure and acute pulmonary assets and potential programs.

- We are optimistic about the chances of istaroxime and AEROSURF receiving FDA approval and of the subsequent commercial demand of these treatment therapies. We estimate rapid growth for both once they are commercialized and believe WINT could generate roughly $28 million in revenue in 2023, which translates into an implied near-term valuation of about $12.00/share on a fully diluted basis. We also believe several factors, including pre-approval partnerships, faster, or less-costly path to US approval and opportunities in other geographies (China, for one) imply potential upside to this valuation.

COMPANY DESCRIPTION

Two Lead Drug Candidates; Multiple Programs

Pennsylvania-based Windtree Therapeutics, Inc. (NASDAQ: WINT) is a biopharma and medical device company developing therapies for a range of acute cardiovascular and pulmonary conditions that necessitate critical care, including acute heart failure (AHF), cardiogenic shock due to heart failure, respiratory distress syndrome (RDS) in premature babies and other lung injuries. Following a December 2018 merger with privately held CVie Investments, the company has a diversified asset portfolio, with two lead drug candidates that are in advanced stages of development in multiple programs. Windtree contributed the AEROSURF / KL4 platform and CVIE was primarily developing Istaroxime. With successful fundraising in December of 2019 and, more recently a public raise in May 2020 that supported

a Nasdaq listing, Windtree is now executing multiple clinical programs that lay the groundwork for many potential milestones and catalysts.

Windtree Therapeutics – Multiple Advanced Clinical Programs

	Lead Products	Pre-	Phase I	Phase II	Phase III	Next Milestone
FDA Fast Track Designation	**Istaroxime** (Acute Heart Failure)			Phase 2b		• Initiate study start up in 2H 2020 for second phase 2b clinical trial in ~300 patients targeted to start in 1H 2021
Potential for Breakthrough designation	**Istaroxime** (Cardiogenic Shock)			Phase 2		• Q3 2020- Initiate ~60 patient study in early cardiogenic shock
FDA, EMA Orphan Drug for RDS	**KL4 Surfactant – COVID 19** (COVID 19 Pilot; Possible invasive Tx for RDS in neonates)			Phase 2		• Q3-2020 File IND; Initiate trial
FDA Fast Track Designation, Orphan Drug	**AEROSURF** (Non-Invasive Tx for RDS)			Phase 2b		• Active study in ~80 patient with new ADS supported by licensee resources
	Rostafuroxin (Genetically Associated HTN)			Phase 2b		• Out-licensing opportunity
	Oral SERCA2a Activators (Chronic HF; including HFpEF)					• High interest target for partnership • Chronic and Acute Heart Failure

Source: Windtree Therapeutics

Istaroxime, fast track designation

- First in class, dual mechanism clinical-stage therapeutic for heart failure, istaroxime can improve both systolic contractions of the heart, as well as its diastolic relaxation. The mechanism includes SERCA2a activation mediated control of heart relaxation that could be a key differentiator
- Acute Heart Failure - positive phase 2a & phase 2b results
- Cardiogenic heart shock – represents a second program that could potentially attain FDA breakthrough designation

AEROSURF and KL4 Surfactant, fast track designation & orphan designation for RDS in US & EU

- AEROSURF is a drug/device combination for the treatment of respiratory distress syndromes (RDS) in pre-term infants. The company has completed three phase 2 studies and is currently in an active small study, with a new delivery system device, bridging to phase 3
- KL4 Surfactant (the drug in AEROSURF) is also part of a planned study in COVID-19 patients to improve respiratory parameters and treat lung injury in patients that have progressed to respiratory failure and require the support of a mechanical ventilator

Prior to the merger, CVie was also developing rostafuroxin for genetically associated hypertension. Rostafuroxin targets resistant hypertensive patients with a specific genetic profile found in roughly 20% to 25% of the adult hypertensive population. The company has studied rostafuroxin in three phase 2 clinical trials. A phase 2 study showed the potential for rostafuroxin to successfully treat hypertension within certain niche genetic groups.

WINT does not plan to develop rostafuroxin internally and intends to engage in discussions with large pharmaceutical companies for potential licensing opportunities. Non-dilutive funds from a possible licensing agreement would be earmarked to support the development of istaroxime and AEROSURF programs.

WINT also intends to conduct research leveraging its Istaroxime and AEROSURF technologies and expertise for treatment extensions. The company plans to study:

- **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 platform addressing unmet needs for treatment of heart failure. Advancement might include potential partnership opportunities with large pharmaceutical companies.
- **KL4 surfactant** for the prevention of lung injury in COVID-19 respiratory failure patients and other lung injury patients, thereby leveraging preclinical studies in acute lung injury.

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.

WINT'S LEADING DRUG CANDIDATES FOCUS ON UNMET NEEDS
In Acute Heart Failure (AHF) and Cardiogenic Shock

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, acute 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.

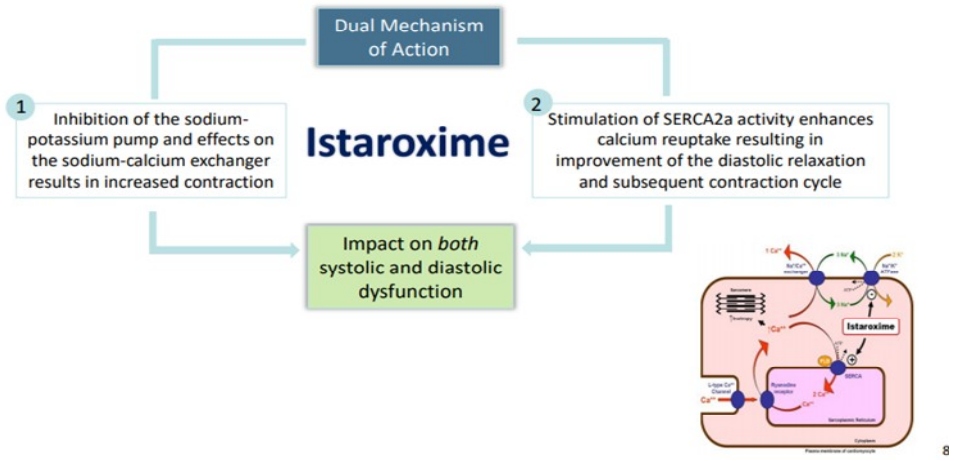
Istaroxime has been evaluated in six studies, including two Phase 2 clinical trials. Results suggest that istaroxime significantly improves cardiovascular physiology with minimal adverse effects. Istaroxime treatment has shown decreases in PCWP (pulmonary capillary wedge pressure) and heart rate and increases in blood pressure (which is a desired effect in those with normal to low blood pressure) without adverse events such as heart rhythm disturbances 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.

Positive phase 2b data supports WINT's confidence that istaroxime could be a better way to treat AHF patients – particularly those patients that can be the most challenging to manage and where many of the existing therapies have unwanted side effects in this population (as discussed below). Due to the positive observed effects on cardiac function and blood pressure, WINT also intends to study istaroxime for treatment of early cardiogenic shock due to heart failure – a potential second indication and another path to potential regulatory approval.

Istaroxime Has FDA Fast Track Designation and Innovative, First-in-Class Mechanism

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.

Designed to Improve Heart's Systolic Contraction & Diastolic Relaxation



Source: Windtree Therapeutics

Traditional treatments of patients with AHF include the use of diuretics, inhibitors of neurohumoral imbalances and beta blockers. There have been no recently approved novel treatments and there are multiple side effects associated with the use of other agents to address cardiac function, including hypotension, worsening renal function and even increased mortality in some cases. Istaroxime represents a novel treatment approach, with a dual mechanism of action to improve cardiovascular functions:

Improving cardiac function

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.

Improvement comes in a novel profile that may offer greater utility

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.

Based on previous data, WINT is focusing on studying istaroxime in two heart failure patient populations with limited treatment options: 1) patients with low systolic blood pressure and 2) patients who are diuretic resistant. WINT believes both groups, which represent a combined roughly 35% of patients with AHF, could benefit particularly from istaroxime's dual mechanism potential to increase blood pressure and improve cardiac and renal function. These patients tend to be the most challenging; they generally require longer hospital stays and are more difficult to treat. Thus, management believes the benefits of istaroxime could be most pronounced in clinical studies of this group.

Istaroxime: Next Steps in AHF Development

WINT is advancing istaroxime for the treatment of AHF to a Phase 3-ready position. Istaroxime has a potentially differentiated safety profile versus existing AHF therapies, as noted. In the recently completed Phase 2b clinical trial of istaroxime, the primary endpoint of cardiac function, E/Ea ratio (echocardiographic assessment reflecting changes in pulmonary capillary wedge pressure (PCWP) was significantly improved.

The company plans to initiate start-up activities for the above-noted additional Phase 2b clinical trial in patients with low systolic blood pressure and those who are diuretic resistant in 1H20. The company also plans to extend dosing duration in this clinical trial beyond those studied in previous trials and include clinical outcome measures that management believes will support the further development of istaroxime and regulatory approval.

Istaroxime Program Has Expanded to Include Studying Efficacy Treating Early Cardiogenic Shock

The company has expanded its istaroxime development program to include a study in early cardiogenic shock (CS) in heart failure patients. Based on prior phase 2 clinical studies in AHF showing dose related increase in blood pressure, WINT believes that istaroxime might also fulfill an unmet need in severe heart failure patients with early CS and that it might be a candidate for a breakthrough designation in this program.

CS 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. CS can be caused by an acute myocardial infarction / heart attack (the most common reason), by severe heart failure (what WINT is focusing on for their study) or other causes which damage the heart and compromises function

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 30-50%. Because of the unmet need, there are potential opportunities for an accelerated regulatory pathway and review.

The FDA has approved a pharmacological treatment for shock based primarily on improving blood pressure. (The precedent for this is Giapreza®, approved in 2017 for increasing mean arterial pressure [MAP] in distributive shock). Importantly, previous FDA precedent and position also point to the potential opportunity for a breakthrough designation and a possible accelerated pathway of development and approval.

Istaroxime: Cardiogenic Shock Study

WINT plans a small 60 patient study of istaroxime for the treatment of early CS in patients with heart failure to evaluate the potential of istaroxime to improve blood pressure and organ perfusion. The study will also evaluate the safety and side effect profile of istaroxime in this patient population. The pivotal endpoint is blood pressure increase. The study is set to begin in 3Q20 and management expects to produce data by mid-2021.

Because of the unmet need to treat early CS, the company believes there may be an opportunity for istaroxime to be considered for breakthrough therapy designation that could expedite its development program by increasing the chances that a marketing application for istaroxime receives priority review.

Istaroxime Market Opportunity

The company believes that istaroxime could improve treatment of patients' heart failure symptoms and reduce length of hospital stays. Cardiac abnormalities can lead to heart failure in which, according to the American Heart Association, the heart cannot pump enough blood to meet the body's needs for blood and oxygen. Heart failure is a chronic, progressive condition in which patients often experience episodic periods of increased symptoms known as AHF, where the heart fails to adequately pump. This can lead to worsening symptoms, including pulmonary and peripheral edema (swelling) and other severe complications.

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. The company estimates this represents a potential addressable market of about $1.6 billion.

SERCA2a Activation for Chronic and Acute Heart Failure – Potential Partnerships and Deal Value

Istaroxime is the foundation of the heart failure program but there are follow-on compounds, with pure SERCA2a stimulatory activity, in preclinical stage of development. Windtree believes that these programs represent a heart failure platform that has already provided novel intellectual property and additional potential opportunities.

- **Selective SERCA2a Activators** The selective SERCA2a activators are devoid of Na^+/K^+ pump inhibitory activities.
- **Dual Mechanism Compounds** Like istaroxime, these compounds have a dual mechanism of action as SERCA2a activators with Na^+/K^+ pump inhibitory activity.

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.

ACUTE PULMONARY CARE

Improved Treatment of Respiratory Distress Syndrome (RDS) & Possibly Lung Injuries Due to COVID-19 and Other Causes

AEROSURF Also Has FDA Fast Track Designation

WINT's lead pulmonary product candidate is **AEROSURF**, a combined drug and innovative medical device to administer lucinactant (synthetic pulmonary KL4 surfactant) in a non-invasive treatment of RDS in premature babies. This drug delivery does not require intubation but instead uses an aerosolization of the lucinactant that, through a connection to nasal CPAP, is breathed in non-invasively. Pulmonary surfactant is a mixture of lipids and proteins that the lungs naturally produce. Its primary function is to reduce surface tension at the air/liquid interface in the alveoli of the lung to support breathing by aiding in oxygen transfer and keeping the lungs from collapsing during exhalation. As lungs are one of the last organs to fully develop, premature babies are often born with immature lungs and therefore are deficient in surfactant. AEROSURF's use of synthetic KL4 surfactant avoids potential risks of animal-derived surfactant preparations and with a novel drug delivery system, avoids the potential trauma and complications often associated with invasive administration of surfactant. The FDA has granted AEROSURF *Fast Track* designation for RDS.

RDS is a clinical condition in which preterm infant's lungs are not yet fully developed and lack naturally occurring surfactant, which keeps the lungs open between breaths and aids proper gas exchange. Without surfactant, lungs collapse, making it difficult for the infant to breathe. RDS is a critical factor in mortality rates of preterm infants, according to NCBI and if it is not properly treated, RDS can lead to significant, lasting comorbidities. Current treatment is generally animal-derived surfactant replacement therapy, which has shown a significant reduction in mortality, but which relies on invasive intubation to administer commonly followed by mechanical ventilation. The invasive administration to these small, fragile infants causes trauma and is associated with many known side effects (some of which can be severe). In an attempt to avoid these well-documented complications, an alternative that has also

emerged is to try to treat the baby with nCPAP (positive airway pressure) to hold the lungs open. However, without addressing the underlying cause of RDS - lack of surfactant - nCPAP alone fails about half the time, which in turn often leads back to delayed, invasive surfactant administration. Because of this, most preterm infants with RDS are intubated. WINT's AEROSURF program seeks to change this treatment by offering rapid surfactant delivery without invasive administration. This has the added benefit of also avoiding most of the downside of other treatment options, including nCPAP failure and/or complications associated with invasive administration of surfactant.

WINT has completed three AEROSURF phase 2 clinical trials demonstrating improved respiratory parameters, decreased nCPAP failures and reduction in the rates of intubation. While the data across the patients dosed / treated demonstrated positive results, the data in the last phase 2 trial was impacted by a previous prototype device that stopped treatment to be delivered in a portion of patients and thus negatively impacted the top line results that included all of these patients (versus those that were dosed as intended and received the full dose). Importantly, the program is now operating with a new, improved design ADS delivery technology that uses the same aerosolization technology as WINT used in Phase 2 clinical programs, but has improved ergonomics, controls, and dose monitoring. The upgrades are intended to help mitigate the risks of device-related treatment interruptions that occurred previously.

One of the most significant complications of invasive administration and accompanying respiratory support with a ventilator is increased incidence of a condition called bronchopulmonary dysplasia (BPD). This occurs due to damage to the lungs and impaired development. There are no approved treatments for BPD. This complication of RDS can result in long-term respiratory problems that persist even as the baby gets older. Study results indicate the potential of AEROSURF to impact the clinical course of RDS and potentially the longer-term respiratory health of preterm infants, which can be seen with significantly lower rates and severity of BPD with AEROSURF treatment compared to those recorded with traditional therapies.

Bridge Study to Transition AEROSURF To Phase 3-Ready Development

The company has commenced a bridge study designed to transition AEROSURF to Phase 3-ready development. In 2Q20, the company enrolled the first patient and began a small (approximately 80 patients) Phase 2b bridging study in premature infants with RDS as it prepares to transition to phase 3 clinical programs by demonstrating the revised ADS performance in the NICU and also demonstrating a more intensive dosing regimen to supplement data previously generated in the Phase 2 clinical program. WINT's China license partner has agreed to fund this global bridging study to minimize the cost to the company. Complicated by well-documented air pollution, China / Hong Kong is the largest RDS and surfactant market (about 5x larger than the U.S.), according to WINT, and WINT's license partner hopes to market KL4 surfactant and AEROSURF to the region following successful clinical trials and regulatory approvals.

AEROSURF MARKET OPPORTUNITY

RDS is the most common respiratory disease in the neonatal intensive care unit. Current treatment, as noted, relies on surfactant replacement therapy using animal-derived surfactants administered using invasive intubation where the infant is often placed on mechanical ventilation and the treatment itself can often lead to severe and often persistent respiratory conditions and complications. WINT expects that the AEROSURF combined drug/delivery treatment has the potential to displace a significant portion of care using standard surfactant replacement therapy. AEROSURF would be added to nCPAP use to make it more efficacious and reduce the need for intubation.

According to the National Institutes of Health (NIH), roughly 7% of all preterm infants develop RDS and incidence is negatively correlated to gestational age, reaching as high as 93% in extremely preterm infants (which NIH defines as a gestational age <28 weeks.) One of the most significant therapeutic interventions has been replacement of natural surfactant with purified surfactant from the lungs of other

species. WINT's surfactant is chemically produced. Because WINT's KL4 surfactant is synthetic, there are no immunological concerns associated with its use, according to management.

According to the NIH, the expected cost of treating premature babies with RDS can exceed $100,000 per case, with ~135,000 affected by RDS in the U.S. each year, accounting for 20% of neonatal deaths. Moreover, WINT believes it can capture revenues from both the drug therapy and the ADS disposable cartridges and that AEROSURF could be administered in less specialized hospitals and birthing centers. In turn, this could expand the access to treatment. WINT estimates the addressable market could be north of $1 billion annually. Beyond this, given the simplified non-invasive delivery by non-specialized staff, unlike the complex invasive delivery, AEROSURF also holds the potential to enable surfactant therapy at smaller hospitals and ambulatory centers globally, thereby broadening the treatment market.

WINT Expanding to Study Treatment of COVID-19/ Other Conditions

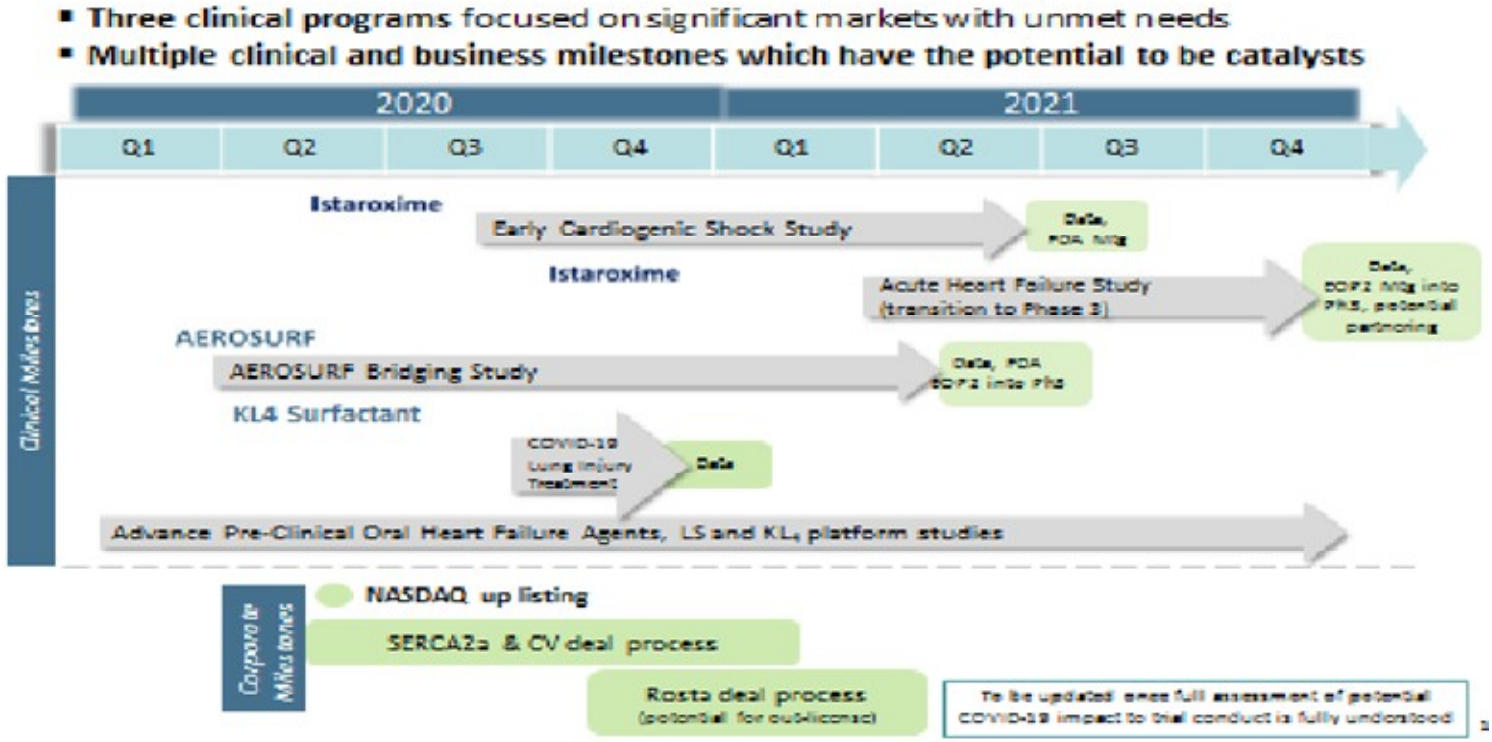
COVID-19 Study Could Lead to New Application for KL4 surfactant and potentially AEROSURF

The company has produced substantial pre-clinical data in a variety of lung injury models. In 2H20, WINT plans to leverage its findings and expertise and the potential of its KL4 surfactants to mitigate lung injury in a small study in COVID-19 patients. Against the backdrop of the COVID-19 pandemic and with many studies demonstrating a positive impact to reducing acute lung injury including in highly-pathogenic viral pneumonia, the company also plans to study KL4 surfactant for the prevention and treatment of lung injury resulting from severe COVID-19 that frequently leads to respiratory failure and ventilator use. The virus that causes COVID-19 infections can also destroy surfactant-producing cells within the lungs. There are parallels to the patient condition in these cases with those of prenatal infants prior to the advent of surfactant replacement therapy. WINT is working through the investigational new drug (IND) application process with the FDA for an initial pilot clinical trial in the U.S. to assess the impact of non-aerosolized KL4 surfactant on key respiratory parameters in ventilated COVID-19 patients to show the physiologic improvements that occur when KL4 surfactant is administered. The primary outcome measure will be an assessment of oxygenation. The company anticipates initiating the trial as early as 2H20 following appropriate regulatory clearance.

If successful, the company would then move to stage 2, which would be a larger, randomized and controlled trial with clinical endpoints as the primary assessment. WINT would also expect to leverage its ADS delivery technology in trial work with step 2, as well. The company believes it can apply the AEROSURF technology to COVID-19, as many patients progress to acute respiratory distress syndrome (ARDS) and require mechanical ventilation. Studies suggest that surfactant replacement therapy could improve lung function and decrease pulmonary inflammation, often reducing or even eliminating the need for mechanical ventilation. This has the dual benefit of helping patients breathe on their own earlier and freeing ventilators up for other patients. Treatment of COVID-19 could provide additional data on AEROSURF's efficacy for treatment of lung injury generally.

CLINICAL DEVELOPMENT SUMMARY

WINT's Strategy for Value Creation & Planned Milestones



Source: Windtree Therapeutics

FINANCIAL HISTORY

In December 2018, Windtree merged with privately-held CVie Investments Limited. The two companies had been developing drug candidates that complement one another. Windtree was focused on developing AEROSURF and CVie was developing istaroxime and rostafuroxin, as noted. In tandem with the merger, WINT raised $39.0 million through a private placement. In December 2019, WINT also raised $26.4 million through a private placement.

In March 2020, WINT entered into an agreement with Lee's Pharmaceutical (HK), a major pharma company based in China. Lee's agreed to provide up to $2.8 million in project financing for WINT to continue to develop AEROSURF for RDS treatment of premature babies in a phase 2b bridge study intended to transition AEROSURF into phase 3-ready clinical product development. In August 2020, WINT and Lee's (HK) entered into a project financing agreement. Lee's agreed to pay additional amounts as the development budget is updated. With the Lee's funding subsidizing AEROSURF, WINT has been able to use cash on hand to advance istaroxime, including the cardiogenic shock clinical study and AHF phase 2b trial. WINT will repay Lee's the principle plus 25% of that amount if it commercializes AEROSURF. The company believes Lee's could also be a strong partner to help WINT enroll patients in its clinical trials and ultimately to help commercialize AEROSURF in the Chinese market.

In April 2020, WINT implemented a 1-for-3 reverse stock split and uplisted its shares to NASDAQ in May, following an issuance of 3.2 million shares plus warrants to purchase up to 3.2 million shares that

raised $23 million in an over-subscribed issuance. The company has cash of $31.5 million as of June 30, 2020. Management expects that it can continue to advance its candidates and maintain operations for at least the next twelve months with this cash on hand.

Securities	Common Equivalents
Common Stock	16,868,732
Options (WAEP $17.41)	1,761,949
RSUs	35,000
Warrants (WAEP $16.38)	7,913,900
Fully Diluted	26,579,581

Source: Company reports

IP Position

WINT holds patents on its lyophilized KL4 surfactant portfolio that extend to 2033 and on its ADS portfolio through 2031.

VALUATION

We are optimistic about the chances of istaroxime and AEROSURF receiving FDA approval and of the subsequent commercial demand of these treatment therapies. Particularly telling of the difficulty in developing effective novel cardiac therapeutic advances, the FDA has issued new heart failure guidance to provide greater development flexibility that the FDA itself describes as designed "to spark" development of novel heart failure drugs.

And in terms of the potential commercial appeal for both programs, the dearth of effective therapies that have the limited side effects of istaroxime or AEROSURF and high related healthcare costs of alternate existing treatments plus frustration from medical professionals about the lack of better options could translate, we believe, into high demand for WINT's more effective therapies following clinical studies.

Once WINT's assets are commercialized, we estimate rapid growth for both commencing in approximately 2023 – 2024. We forecast $5.2 million and $28.1 million in revenue in 2023 and 2024 respectively. While it is difficult to know the revenue arc for WINT at this stage, these forecasts are supported, we believe, by the large unmet need each addresses and the current cost of standard care.

In our view, Windtree's differentiated products and programs imply that there are no direct publically traded peers. Moreover, we would also expect WINT to have a higher growth rate in the early years of commercializing its drug candidates. Nevertheless, we believe the average price-to-sales and EV/sales multiples of companies in our comparison, 14x and 13x respectively, provide valuation benchmarks.

Applying a 14x multiple to our $28.1 million 2023E revenue forecast and discounting back to the present at 11%/year results in a present value of nearly $320 million for WINT, or about $12.00/share on a fully diluted basis. We believe our forecast could be conservative particularly as the company expands the number of programs leveraging its therapies and expertise. For example, we believe that the incremental

value of the company's COVID-19 studies could be understated. While it is still early, the in-hospital cost of treating COVID-19 has been estimated at roughly $14,000 per patient.

We think the current share price of about $8.00 does not reflect the fundamental value of the company's pipeline and prospects. As the company continues to advance its candidates, we would anticipate multiple expansion. We also believe there are several factors that imply potential upside to our valuation, including: pre-approval partnerships that provide milestones and/or R&D cost sharing; a faster, or less-costly path to US approval; and the opportunities in other geographies (such as China).

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.

Examples of Valuation Multiples

		8/26/2020	Price / Revenue			EV / Revenue		
	Ticker	Price	2018A	2019E	2020E	2018A	2019E	2020E
Acceleron Pharma	XLRN	92.48	74.9x	54.5x	38.9x	69.9x	50.9x	36.3x
Akcea Therapeutics	AKCA	12.07	2.5x	11.3x	7.6x	1.7x	7.6x	5.1x
Amneal Pharmaceuticals	AMRX	4.01	0.7x	0.6x	0.6x	2.3x	2.0x	1.9x
Bellerophon Therapeutics	BLPH	11.82	NM	38.2x	11.2x	NM	18.3x	5.4x
BioCardia	BCDA	2.31	402.8x	286.0x	114.4x	266.3x	189.1x	75.6x
La Jolla Pharmaceutical	LJPC	4.22	5.0x	3.0x	1.8x	3.1x	1.9x	1.1x
MyoKardia, Inc.	MYOK	108.18	NM	NM	258.1x	NM	NM	219.1x
Milestone	MLSS	1.58	12.6x	30.6x	14.3x	10.7x	26.1x	12.2x
Portola Pharmaceuticals	PTLA	18.03	12.1x	10.5x	6.1x	10.2x	8.9x	5.2x
Sage Therapeutics	SAGE	50.11	379.0x	280.0x	125.6x	273.5x	202.0x	90.6x
United Therapeutics	UTHR	105.05	3.2x	3.3x	3.3x	2.2x	2.3x	2.3x
Average			99x	72x	53x	71x	51x	41x
Average ex outliers			21x	22x	14x	19x	19x	13x

Source: Company reports, Yahoo Finance, Thomson Reuters, Zacks

MANAGEMENT

The Windtree team management continues to manage the post-merger combined company. WINT executives have substantial industry experience.

CEO Craig Fraser
CEO Craig Fraser has extensive capital markets and drug development and commercialization experience in the biotech and life sciences sector, including at big pharma. He joined the company in February of 2016. Before that, he was a senior executive at several biopharmaceutical companies, including Novelion, where he was COO, Pfizer, Wyeth, Johnson & Johnson and Centocor.

Chief Medical Officer Dr. Steve Simonson
Dr. Steve Simonson has been WINT's Chief Medical Officer since October 2014, having joined the company in May of 2014 as VP of Clinical Development. Before WINT, he was Executive Director in the Molecular Development Group at Covance and VP of Clinical Development at Agennix, Inc. Earlier in his career, he spent 15 years in medical and clinical leadership at AstraZeneca.

CFO John Hamill
CFO John Hamill joined Windtree in July 2020. He has significant capital markets experience in the life sciences space. Prior to Windtree, he provided consulting services to several life science companies. His prior experience includes spearheading finance at Trevena, Inc., where he oversaw a successful equity

issuance, and NephroGenex during its IPO and financial restructuring and sale, Savient Pharmaceuticals during its $120 million sale and PharmaNet during its sale for approximately $250 million. He directed financial and administrative operations for the company once it became PharmaNet Development Group.

COO Eric Curtis
Eric Curtis joined the company in March of this year, bringing extensive prior industry experience. Before joining Windtree, he was CEO and president of Centurion Biopharma Corp. and COO of CytRx Corporation prior to that, among various executive positions, before joining the company.

Insiders hold an aggregate of approximately 14.7% of WINT shares. In WINT's December 2019 private placement, Panacea Venture purchased 551,876 shares for $5.0 million and became a >5% shareholder. Panacea Venture also participated in the May 2020 financing and purchased 275,862 units for approximately $2.0 million. WINT Board Chairman and Director James Huang is also a director of Panacea Venture.

RECENT NEWS

- The company reported 2Q20 results on August 13, 2020 and provided a business update.
- On July 21, 2020, WINT expanded its team with the appointment of three industry veterans.
- The company appointed a new CFO, John Hamill, on July 20, 2020.
- On May 20, 2020, WINT shares began trading on the Nasdaq concurrent with a public financing of $23 million.
- On April 29, 2020, WINT implemented a 1-for-3 reverse split stock, which reduced the outstanding share count from 41.1 million to 13.7 million shares.
- In April 2020, the company presented at the American College of Cardiology 2020 virtual meeting a new subset analysis from a phase 2b study of istaroxime in patients hospitalized with AHF.
- In April of 2020, WINT received a Small Business Administration Paycheck Protection Program loan of roughly $0.5 million and subsequently announced that it was repaying the loan.

RISKS

Risks to Windtree achieving its objectives, and to our valuation, include the following.

- WINT might need to raise additional capital earlier than expected.
- COVID-19 might delay the company's clinical and commercialization timelines.
- Despite their *Fast Track* designations, istaroxime and AEROSURF might experience clinical failure and/or might not receive FDA approval.
- The company might not find strategic partners or a licensee for rostafuroxin.
- Production of istaroxime, which is manufactured in China, could be disrupted.

PROJECTED INCOME STATEMENT

Windtree Therapeutics Income Statement & Projections ($M)

	2019	1Q20	2Q20A	3Q20E	4Q20E	2020E	2021E	2022E	2023E
Total revenues	$0.2	$0.0	$0.0	$0.0	$0.0	$0.0	$1.0	$5.2	$28.1
Expenses:									
R&D	12.7	3.5	4.5	4.3	3.8	16.1	16.3	16.5	16.8
General & administrative	12.4	3.2	3.5	3.4	3.5	13.6	13.8	14.0	14.2
Total operating expenses	25.1	6.7	7.9	7.7	7.3	29.6	30.1	30.5	31.0
Operating loss	(24.9)	(6.7)	(7.9)	(7.7)	(7.3)	(29.6)	(29.1)	(25.3)	(2.9)
Other income (expense):									
Interest income	0.2	0.1	0.0	0.0	0.0	0.1	0.1	0.1	0.1
Interest expense	(0.5)	(0.0)	(0.0)	(0.0)	(0.0)	(0.1)	(0.1)	(0.1)	(0.1)
Other (expense) income, net	(0.4)	0.1	(1.6)	0.3	0.3	(1.0)	(1.0)	(1.0)	(1.0)
Total other (expense) income, net	(2.6)	0.2	(1.6)	0.2	0.2	(1.0)	(1.0)	(1.0)	(1.0)
Net loss	(27.5)	(6.5)	(9.6)	(7.5)	(7.1)	(30.6)	(30.1)	(26.4)	(4.0)
Per share data:									
Net loss per common share	($2.51)	($0.48)	($0.63)	($0.49)	($0.46)	($2.06)	($2.00)	($1.72)	($0.25)
Average shares outstanding*	10.9	13.7	15.1	15.2	15.4	14.9	15.1	15.3	15.5

*Adjusted for April 2020 1:3 reverse stock split

Source: Company reports, Zacks estimates

© Copyright 2020, Zacks Investment Research. All Rights Reserved.

APPENDIX: CLINICAL TRIAL SUMMARY

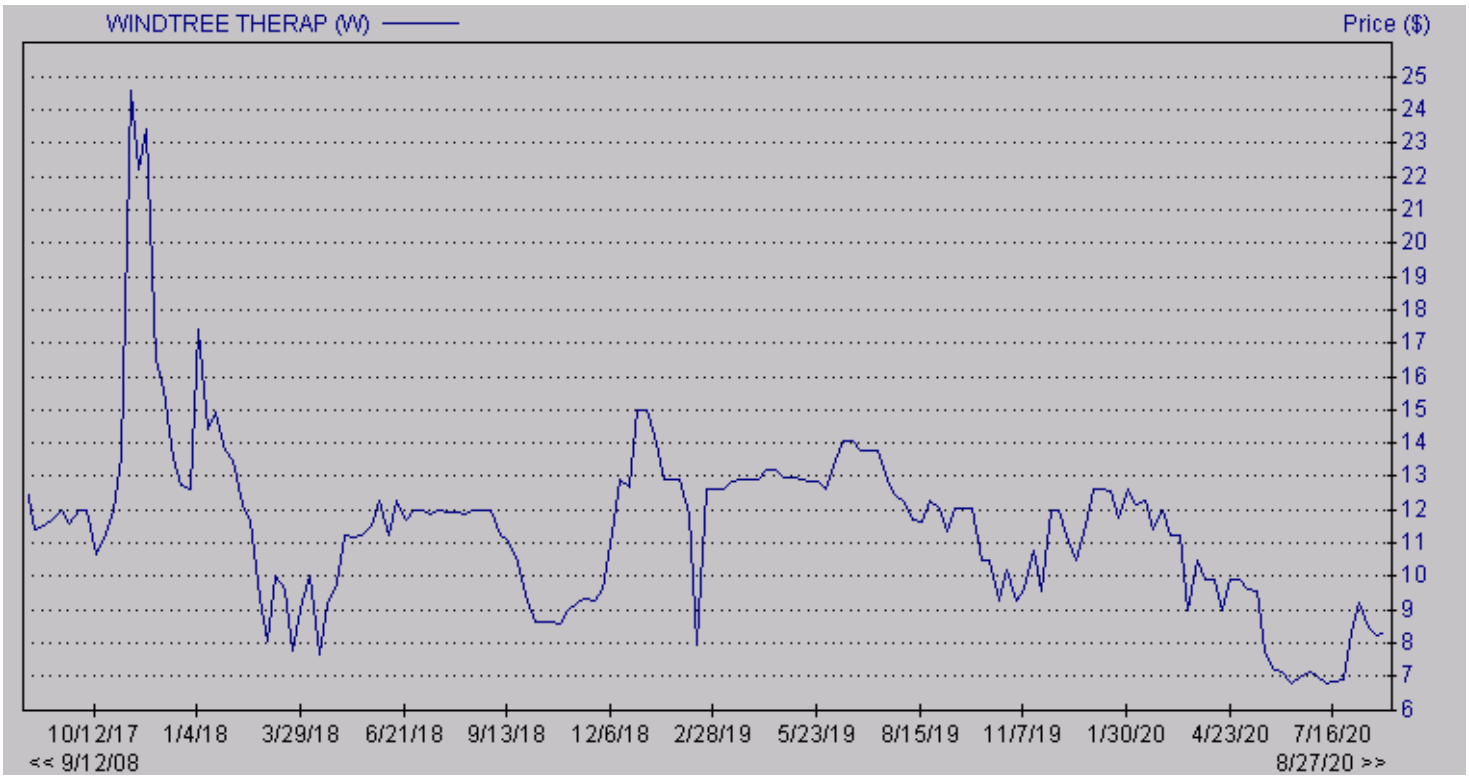
Summary of Recent Clinical Studies in Various Indications

Product Candidate	Indication	Status	Next Expected Milestone
Istaroxime	AHF	Phase 2b	Initiate start-up activities for second phase 2b clinical trial in ~300 patients in second half of 2020.
Istaroxime	Early Cardiogenic Shock	Phase 2a	Initiate phase 2a clinical trial in ~60 patients mid-year 2020.
AEROSURF (aerosolized KL4 surfactant)	RDS	Phase 2b	Initiate in second quarter of 2020 a ~90-patient bridging study with new ADS (developed for use in our phase 3 program), relying on licensee resources.
Rostafuroxin	Genetically Associated Hypertension	Phase 2b	Out-licensing.
Lyophilized KL4 Surfactant	Lung Injury resulting from COVID-19	Pilot	Program planning; targeted start mid-year 2020, subject to securing the additional capital resources required for the program.

Source: Company reports

© Copyright 2020, Zacks Investment Research. All Rights Reserved.

HISTORICAL STOCK PRICE



DISCLOSURES

The following disclosures relate to relationships between Zacks Small-Cap Research ("Zacks SCR"), a division of Zacks Investment Research ("ZIR"), and the issuers covered by the Zacks SCR Analysts in the Small-Cap Universe.

ANALYST DISCLOSURES

I, M. Marin, hereby certify that the view expressed in this research report accurately reflect my personal views about the subject securities and issuers. I also certify that no part of my compensation was, is, or will be, directly or indirectly, related to the recommendations or views expressed in this research report. I believe the information used for the creation of this report has been obtained from sources I considered to be reliable, but I can neither guarantee nor represent the completeness or accuracy of the information herewith. Such information and the opinions expressed are subject to change without notice.

INVESTMENT BANKING AND FEES FOR SERVICES

Zacks SCR does not provide investment banking services nor has it received compensation for investment banking services from the issuers of the securities covered in this report or article.
Zacks SCR has received compensation from the issuer directly, from an investment manager, or from an investor relations consulting firm engaged by the issuer for providing non-investment banking services to this issuer and expects to receive additional compensation for such non-investment banking services provided to this issuer. The non-investment banking services provided to the issuer includes the preparation of this report, investor relations services, investment software, financial database analysis, organization of non-deal road shows, and attendance fees for conferences sponsored or co-sponsored by Zacks SCR. The fees for these services vary on a per-client basis and are subject to the number and types of services contracted. Fees typically range between ten thousand and fifty thousand dollars per annum. Details of fees paid by this issuer are available upon request.

POLICY DISCLOSURES

This report provides an objective valuation of the issuer today and expected valuations of the issuer at various future dates based on applying standard investment valuation methodologies to the revenue and EPS forecasts made by the SCR Analyst of the issuer's business.
SCR Analysts are restricted from holding or trading securities in the issuers that they cover. ZIR and Zacks SCR do not make a market in any security followed by SCR nor do they act as dealers in these securities. Each Zacks SCR Analyst has full discretion over the valuation of the issuer included in this report based on his or her own due diligence. SCR Analysts are paid based on the number of companies they cover. SCR Analyst compensation is not, was not, nor will be, directly or indirectly, related to the specific valuations or views expressed in any report or article.

ADDITIONAL INFORMATION

Additional information is available upon request. Zacks SCR reports and articles are based on data obtained from sources that it believes to be reliable, but are not guaranteed to be accurate nor do they purport to be complete. Because of individual financial or investment objectives and/or financial circumstances, this report or article should not be construed as advice designed to meet the particular investment needs of any investor. Investing involves risk. Any opinions expressed by Zacks SCR Analysts are subject to change without notice. Reports or articles or tweets are not to be construed as an offer or solicitation of an offer to buy or sell the securities herein mentioned.

CANADIAN COVERAGE

This research report is a product of Zacks SCR and prepared by a research analyst who is employed by or is a consultant to Zacks SCR. The research analyst preparing the research report is resident outside of Canada, and is not an associated person of any Canadian registered adviser and/or dealer. Therefore, the analyst is not subject to supervision by a Canadian registered adviser and/or dealer, and is not required to satisfy the regulatory licensing requirements of any Canadian provincial securities regulators, the Investment Industry Regulatory Organization of Canada and is not required to otherwise comply with Canadian rules or regulations.