As filed with the Securities and Exchange Commission on April 30, 2019

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM S-1
REGISTRATION STATEMENT UNDER
THE SECURITIES ACT OF 1933

Windtree Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**2836**	**94-3171943**
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

2600 Kelly Road, Suite 100
Warrington, Pennsylvania 18976
(215) 488-9300
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Mary B. Templeton, Esq.
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Copies to:

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New York, New York 10020
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Approximate date of commencement of proposed sale to the public: From time to time after this registration statement is declared effective.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. ☒

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filter	☒	Smaller reporting company	☒
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act. ☐

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CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered[1]	Proposed Maximum Offering Price per Share[2]	Proposed Maximum Aggregate Offering Price[2]	Amount of Registration Fee[2]
Common Stock, $0.001 par value per share	37,308,973	$ 4.16	$ 155,205,327.68	$ 18,810.89
Total	37,308,973	$ 4.16	155,205,327.68	$ 18,810.89

(1) The Registrant is registering for resale by the selling stockholders identified in the prospectus contained herein up to 37,308,973 shares of common stock, which consists of: (i) 31,018,286 shares of common stock and (ii) 6,290,687 shares of common stock issuable upon exercise of common stock purchase warrants held by the selling stockholders. Pursuant to Rule 416 under the Securities Act of 1933, as amended, the shares of common stock registered hereby also include an indeterminate number of additional shares of common stock as may from time to time become issuable by reason of stock splits, stock dividends, recapitalizations or other similar transactions.

(2) Estimated solely for the purpose of calculating the amount of the registration fee pursuant to Rule 457(c) under the Securities Act of 1933, as amended, based on the average of the high and low price of the Registrant's common stock on April 24, 2019, as quoted on The OTCQB® Market on a day within five business days from the date of filings of this registration statement.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

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The information in this prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion, dated April 30, 2019

37,308,973 Shares

COMMON STOCK

This prospectus relates to the resale of up to 37,308,973 shares of our common stock, par value $0.001 per share (the Common Stock), which may be offered for sale from time to time by the selling stockholders identified in this prospectus (the selling stockholders). The shares of Common Stock covered by this prospectus consist of (i) 31,018,286 shares of Common Stock (the Common Shares), (ii) 135,417 of Common Stock (the Series C Warrant Shares) issuable upon exercise of our Series C Warrants to purchase Common Stock, (iii) 187,500 of Common Stock (the Series D Warrant Shares) issuable upon exercise of our Series D Warrants to purchase Common Stock, (iv) 75,000 of Common Stock (the Series E Warrant Shares) issuable upon exercise of our Series E Warrants to purchase Common Stock (v) 2,003,541 shares of Common Stock (the Series F Warrant Shares) issuable upon exercise of our Series F Warrants to purchase Common Stock (the Series F Warrants), and (vi) 3,889,229 shares of Common Stock (the Series G Warrant Shares, and together with the Series C Warrant Shares, Series D Warrant Shares, Series E Warrant Shares and Series F Warrant Shares, the Warrant Shares) issuable upon exercise of our Series G Warrants to purchase Common Stock (the Series G Warrants, and together with the Series C Warrants, Series D Warrants, Series E Warrants and Series F Warrants, the Warrants). The Common Shares and the Warrants were issued by us to the selling stockholders in offerings exempt from registration under the Securities Act of 1933, as amended (the Securities Act). We are hereby registering the offer and sale of the Common Shares and the Warrant Shares to satisfy registration rights that we have granted to the selling stockholders in connection with such offerings.

We are not selling any shares of our Common Stock and we will not receive any proceeds from the sale of shares of our Common Stock by the selling stockholders. However, upon a cash exercise of the Warrants by the selling stockholders, we will receive cash proceeds per share equal to the exercise price per share of the Warrants. The Series C Warrants, Series D Warrants, Series E Warrants, Series F Warrants and Series G Warrants have per share exercise prices of $5.52, $4.00, $6.50, $3.68, and $4.05, respectively. If the Warrants are exercised in a cashless exercise, we will not receive any proceeds from the exercise of the Warrants. We have agreed to pay certain registration expenses, other than underwriting discounts and commissions.

The selling stockholders may from time to time sell, transfer or otherwise dispose of any or all of their shares of Common Stock in a number of different ways and at varying prices. See “Plan of Distribution” for more information.

We may amend or supplement this prospectus from time to time by filing amendments or supplements as required. You should read this entire prospectus and any amendments or supplements carefully before you make your investment decision.

Our Common Stock is currently traded on The OTCQB® Market (OTCQB) under the symbol WINT. On April 24, 2019, the last reported sale price of our Common Stock on the OTCQB was $4.32 per share.

Investing in our Common Stock involves significant risks. See “Risk Factors” beginning on page 5 of this prospectus.

Neither the Securities and Exchange Commission (the SEC) nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is , 2019.

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This prospectus is part of a registration statement that we have filed with the SEC pursuant to which the selling stockholders named herein may, from time to time, offer and sell or otherwise dispose of the shares of our Common Stock covered by this prospectus. You should not assume that the information contained in this prospectus is accurate on any date subsequent to the date set forth on the front cover of this prospectus or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus is delivered or shares of Common Stock are sold or otherwise disposed of on a later date. It is important for you to read and consider all information contained in this prospectus, including the documents incorporated by reference herein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you under the caption "Where You Can Find More Information" in this prospectus.

We have not authorized any dealer, salesman or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus. This prospectus does not constitute an offer to sell or the solicitation of an offer to buy any of our shares of Common Stock other than the shares of our Common Stock covered hereby, nor does this prospectus constitute an offer to sell or the solicitation of an offer to buy any securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

This prospectus contains forward-looking statements that are subject to a number of risks and uncertainties, many of which are beyond our control. See "Risk Factors" and "Cautionary Note Regarding Forward-Looking Statements."

Unless the context otherwise requires, references in this prospectus to "Windtree," "Windtree Therapeutics," "the Company," "we," "our," and "us" refer to Windtree Therapeutics, Inc., a Delaware corporation, and its consolidated subsidiaries.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus, is not complete, and does not contain all of the information that you should consider before making your investment decision. You should carefully read the entire prospectus, including the information presented under the sections entitled "Risk Factors" and "Cautionary Note Regarding Forward-Looking Statements" and the consolidated financial statements and the notes thereto and other documents incorporated by reference in this prospectus before making an investment decision.

Company Overview

Windtree Therapeutics, Inc. (referred to as “we,” “us,” or “the Company”) is a Delaware corporation, with our principal offices located at 2600 Kelly Road, Suite 100, Warrington, Pennsylvania. We were incorporated as a Delaware corporation in 1992. Our telephone number is 215-488-9300 and our corporate website address is www.windtreetx.com. Our common stock is currently traded on The OTCQB® Venture Market (OTCQB) quotation system operated by The OTC Markets Group Inc., and our symbol is WINT.

We are a biotechnology and medical device company focused on developing drug product candidates and medical device technologies to address acute pulmonary and cardiovascular diseases. Historically, our focus has been on the development of our proprietary KL4 surfactant technology and aerosol delivery system (ADS) technology for the treatment and or prevention of respiratory distress syndrome (RDS) in premature infants. Following our acquisition of CVie Investments in December 2018 (discussed below), we are also focusing on therapies for acute heart failure and hypertension and associated organ dysfunction.

Our four lead development programs are (1) istaroxime for treatment of acute decompensated heart failure (ADHF), (2) AEROSURF® (lucinactant for inhalation) for non-invasive delivery of our lyophilized KL4 surfactant to treat RDS in premature infants, (3) lyophilized KL4 surfactant intratracheal suspension for RDS, and (4) rostafuroxin for genetically associated hypertension.

On December 21, 2018, we entered into an Agreement and Plan of Merger (the CVie Acquisition) with CVie Investments Limited (CVie Investments), an exempted company with limited liability incorporated under the laws of the Cayman Islands. Under the terms of the Acquisition Agreement, we issued shares of our common stock, par value $0.001 per share (common stock), to CVie Investments’ former shareholders, at an exchange ratio of 0.3512 share of common stock for each share of CVie Investments outstanding prior to the acquisition, resulting in the issuance of 16,265,060 shares of common stock in exchange for the outstanding shares of CVie Investments. The CVie Acquisition closed on December 21, 2018.

Since the CVie Acquisition we have operated CVie Investments, and its wholly-owned subsidiary, CVie Therapeutics Limited (CVie Therapeutics), a Taiwan corporation organized under the laws of the Republic of China, as a business division (the entities may be collectively referred to herein as CVie) focused on early development of drug product candidates for cardiovascular diseases. We undertook the acquisition as part of a strategic initiative to create stockholder value that resulted from a multi-year process focused on identifying strategic opportunities, including potential strategic alliances, collaborations (primarily outside the United States (US)), joint development opportunities, acquisitions, technology licensing arrangements, as well as potential combinations (including by merger or acquisition) or other corporate transactions.

Heart failure is a chronic, progressive condition in which patients often experience episodic periods of increased symptoms called ADHF, where the heart fails to adequately pump, resulting in worsening symptoms, including pulmonary and peripheral edema and other severe complications. In the US, nearly 6 million people (nearly two percent of the adult population) have heart failure and approximately half of these patients are expected to die within 5 years of diagnosis; and in the combined US, EU and Japan markets, there are over 14 million patients with heart failure. ADHF can be precipitated by many factors and puts patients at increased risk for morbidity, hospital readmission and mortality. Heart failure is the leading cause of hospitalization in patients age 65 years and older. There are more than 1.1 million hospital admissions for heart failure in the US each year and over 2.5 million hospital estimated admissions for ADHF in the combined US, EU and Japan markets. We estimate that ADHF may represent a potential addressable market of approximately $1.6 billion dollars annually (in the US, EU and Japan). Based on preclinical and clinical studies performed to date, we believe that istaroxime, if approved, may have the potential to address unmet medical needs of these patients by improving cardiac function and management of fluid accumulation that contributes to heart failure symptoms while potentially avoiding complications associated with current ADHF therapies. We are also focused on early development of oral and other intravenous therapies to potentially address both acute and chronic heart failure. In addition to the ADHF market, GlobalData has estimated that the sales market for chronic heart failure therapies in the base year (2016) totaled $3.6 billion within the seven major markets, with the US contributing just over 70% of these sales.

Surfactants are produced naturally in the lung and are essential for normal respiratory function and survival. RDS is a condition that occurs in premature infants who may not have fully-developed natural lung surfactant and may require surfactant therapy to sustain life. RDS is the most prevalent respiratory disease in the neonatal intensive care unit (NICU). RDS can result in long-term respiratory problems, developmental delays and death. We believe that the current surfactant market for RDS is estimated to be approximately $70 to $90 million annually in the US and approximately $400 to $425 million annually worldwide. We believe that this market has been constrained because surfactants are generally administered using intubation, frequently with mechanical ventilation, two invasive procedures that may result in serious respiratory and non-respiratory complications. By contrast, AEROSURF is a combination drug/device product that is designed to administer our KL4 surfactant noninvasively and, we believe, may avoid these invasive procedures and achieve a competitively advantageous position in an expanding RDS market. We also believe that AEROSURF may support an expansion of the RDS surfactant market by reducing the need for intubation and mechanical ventilation, reducing hospital costs, and enabling dosing and repeat dosing as needed using noninvasive delivery of AEROSURF via nasal continuous positive airway pressure (nCPAP). Moreover, while the current surfactant market represents drug-only revenues, we plan to capture revenues from the drug product and the ADS disposable cartridges, supported by anticipated pharmacoeconomic benefits associated with the successful use of nCPAP. As such, we believe that AEROSURF, if approved, may be administered in less specialized hospitals and birthing centers, potentially further expanding access to treatment and potentially achieving a higher price per patient in an addressable market that could be in excess of $1 billion annually. In addition, we are assessing a potential development plan potentially to gain regulatory approval for our lyophilized KL4 surfactant as an intratracheal suspension for RDS, which would allow us to make our KL4 surfactant available in an expanded market to treat the smallest infants and those who are unable to breathe on their own and may not be good candidates for AEROSURF.

Our fourth product candidate is rostafuroxin for the treatment of hypertension associated with certain patient genotypes. According to the Centers for Disease Control (CDC), patients with high blood pressure have a greater risk for heart disease and stroke, which are the leading causes of death in the US. Currently, an estimated 75 million adults, or approximately one third of the adult population in the US, have high blood pressure and the incidence is increasing. During 2014, high blood pressure was a primary or contributing cause of death for more than 410,000 adults in the US. The estimated annual cost of high blood pressure in the US, including for health care services, medications, and missed days of work, is approximately $48.6 billion. Unfortunately, hypertension is a heterogeneous disease in which a majority of treated patients (50-85% globally) do not reach their therapeutic target blood pressure and patients often have persistent hypertension despite being on multiple therapies. Ethnicity and genetic makeup are known to impact the response to anti-hypertensive treatments, and uncontrolled hypertension has been associated with certain genetic makeups. We believe, based on preclinical and clinical studies performed to date, that rostafuroxin may potentially reduce or normalize blood pressure and may address unmet medical needs in a genetically identified subset of patients that could represent approximately 20% - 25% of patients with hypertension. Given the size of the market and the prevalence of unmet medical needs, major pharmaceutical companies have maintained hypertension as a key area of focus and continue to seek new drugs to compete in markets they have established with previous anti-hypertensive therapies. We plan to develop rostafuroxin and potentially leverage the industry’s interest in licensing opportunities in this market.

ISTAROXIME

Overview

Our lead cardiovascular product is istaroxime, an investigational drug that we are developing to treat acute decompensated heart failure (ADHF). Heart failure can result from structural or functional cardiac abnormalities. Heart failure is a chronic, progressive disease that commonly but episodically worsens to a point of decompensation, where cardiac output fails to meet the body’s metabolic needs. The disease is characterized by inadequate pumping function of the heart that results in fluid accumulation manifesting as pulmonary congestion, peripheral edema and congestion in other parts of the body. Insufficient cardiac output can result in inadequate peripheral perfusion that increases the risk of other organ dysfunction such as renal failure. Chronic heart failure is commonly treated with multiple medications including diuretics, inhibitors of neurohumoral imbalances (angiotensin, renin, aldosterone, naturetic peptides) and beta blockers. Effective treatments for ADHF are lacking.

Intensification of heart failure therapy in the hospital typically includes intravenous diuretics and, if the blood pressure is low, supportive therapy with inotropes. Inotropes can be associated with adverse effects that include hypotension, arrhythmias and possibly increased mortality. These drugs are used only if needed to support blood pressure and cardiac function.

Istaroxime represents a novel approach to the treatment of ADHF. It has a dual mechanism of action referred to as luso-inotropic, to improve cardiovascular physiology. First, it activates the SERCA2a calcium pump on the sarcoplasmic reticulum (SR) leading to enhanced SR calcium uptake and a reduction in cytoplasmic calcium that allows for improved myocardial relaxation (lusitropic). Second, it inhibits the sodium-potassium ATPase activity leading to improved myocardial contractility (inotropic). We believe that this mechanism of action may result in improvement in cardiac function and perfusion to reduce congestion and edema and preserve other organ function while avoiding the side effects associated with other classes of heart failure therapies. Preclinical and clinical studies performed to date suggest that istaroxime may improve cardiovascular physiology as assessed by parameters of pump function, decreases in pulmonary capillary wedge pressure, decreases in heart rate, increases in blood pressure without adverse events such as arrhythmias, cardiac damage (as indicated by elevated troponin values) or adverse impact on kidney function. We believe that these features of istaroxime, if approved, could potentially result in clinical improvement of patients' heart failure symptoms and reduce both complications and length of hospital stays when compared to current therapeutic regimens for ADHF.

In 2007, CVie Therapeutics completed a phase 2a randomized, double-blind, placebo-controlled, dose-escalation clinical trial that was designed to evaluate 3 doses of istaroxime in a study of 120 hospitalized patients (~30 patients per cohort) with ADHF and reduced left ventricular ejection fraction with 3 doses of istaroxime administered over a 6-hour infusion period. The primary endpoint, lowering of pulmonary capillary wedge pressure (PCWP) was significantly improved in all 3 doses relative to placebo, and the certain secondary hemodynamic endpoints (increased systolic blood pressure and decreased heart rate) also improved. The main side effects were vomiting (7.9%) and pain at the infusion site (5.6%); one severe adverse event of ventricular tachycardia was observed. The favorable effects on PCWP, blood pressure and heart rate with potential luso-inotropic effects provided the basis for moving the program forward into a phase clinical 2b trial and for selecting the doses to study.

In January 2019, we announced topline results of a phase 2b randomized, double-blind, placebo-controlled, dose-escalation clinical trial, a multicenter, randomized, placebo-controlled study in 120 hospitalized patients in Europe and Asia with ADHF that was designed to evaluate two doses of istaroxime administered over a 24-hour infusion period (~ 40 patients per dose group). The primary endpoint, E/Ea, (reflecting change in PCWP or left ventricle filling pressure) measured by echocardiography utilizing a single, central core laboratory, was significantly ($p<0.05$) improved by both doses of istaroxime. Stroke volume was substantially increased as well. There were no signs of increased risk for arrhythmias or increased troponin levels (a marker of heart muscle damage) during or after istaroxime infusion. Additionally, blood pressure tended to increase, and heart rate decrease, during the infusion. The most common adverse events were vomiting (2.4% and 25%) and infusion site pain (32% and 30%) in the 0.5 and 1.0 µg/kg/min groups, respectively. This study confirmed the physiologic improvements seen in the phase 2a study and replicates the effects of istaroxime in ADHF.

Focus for 2019 – Regulatory meetings and Clinical Development Plan

In 2019, we plan to work with top heart failure experts to review the program and engage with the FDA and regulators in the EU to determine next steps in clinical development for this potential novel therapy for ADHF.

Other

Istaroxime is manufactured for us by Zhaoke Pharmaceutical (Guangzhou) Co., Ltd. and/or Sigma Tau S.pA. Secondary packaging by DEPO PACK s.n.c.

The API used in production of the drug product is manufactured by Farmabios S.p.A. and / or ScinoPharm Taiwan, Ltd.

AEROSURF

Overview

One of our lead development programs is AEROSURF (lucinactant for inhalation), an investigational combination drug/device product that we are developing to improve the management of RDS in premature infants who may not have fully developed natural lung surfactant and may require surfactant therapy to sustain life. Surfactant therapy can be a life-saving treatment for RDS and is the primary therapy to address an underlying surfactant deficiency. Unfortunately, surfactants currently available in the US are animal-derived and are generally administered using invasive endotracheal intubation, frequently with mechanical ventilation, procedures that may result in serious respiratory conditions and other complications. AEROSURF is designed to deliver aerosolized KL4 surfactant noninvasively using our proprietary ADS technology and potentially may meaningfully reduce the use of invasive endotracheal intubation and mechanical ventilation. We believe that AEROSURF, if approved, has the potential to reduce the number of premature infants who are subjected to invasive surfactant administration, and potentially provide transformative clinical and pharmacoeconomic benefits. The FDA has granted Fast Track designation for our KL4 surfactant (including AEROSURF) to treat RDS.

We have filed an investigational new drug application (IND) with the FDA for AEROSURF for the treatment of RDS in premature infants and have completed three AEROSURF phase 2 clinical trials. All three clinical trials assessed the safety and tolerability of AEROSURF and suggested evidence of a beneficial treatment effect when the treatment is delivered as intended.

In June 2017, we announced that we had completed enrollment in our AEROSURF phase 2b clinical trial, a multicenter, randomized, controlled study with masked treatment assignment in 221 premature infants that was designed to evaluate aerosolized KL4 surfactant administered to premature infants 26 to 32 week gestational age receiving nCPAP, in two dose groups (25 and 50 minutes) with up to two potential repeat doses, compared to infants receiving nCPAP alone. This trial was conducted in approximately 50 clinical sites in the US, Canada, Europe and Latin America.

In this phase 2b clinical trial, based on the planned top-line results, AEROSURF did not meet the primary endpoint of a reduction in nCPAP failure at 72 hours. We believe this result was attributable in large part to an unexpected rate of treatment interruptions, which occurred in about 24% of active enrollments, predominantly in the 50-minute dose group. These interruptions, we believe, were primarily related to specific lots of disposable cartridge filters with a higher tendency to clog. After excluding patients in the 50-minute dose group whose dose was interrupted, in accordance with the predesignated statistical plan, nCPAP failure rates were 44% in the control group (n=71) compared to 32% (n=44) in the AEROSURF 50-minute dose group, which is a 12% absolute reduction or a 27% relative reduction in nCPAP failure compared to control. These data suggest a meaningful treatment effect in line with our desired targeted outcome. The overall data suggest that the safety and tolerability profile of AEROSURF was generally comparable to the control group. Reported adverse events and serious adverse events were those that are common and expected among premature infants with RDS and comparable to the control group. As expected, some peridosing events occurred (e.g., changes in oxygen requirements and blood pressure in the time around dosing) more commonly in the AEROSURF groups, however, these were transient in nature and occurred less frequently than seen in intratracheal administration.

Bronchopulmonary Dysplasia (BPD) is a chronic lung disease of premature infants who have required intubation, mechanical ventilation and oxygen therapy. BPD is associated with ongoing pulmonary disease and neurodevelopmental impairment that contributes to substantial patient morbidity. This is associated with increased health care utilization and higher healthcare costs. Notwithstanding, effective prevention and treatment strategies for BPD have been elusive and there is no approved treatment. In the post hoc pooled analysis of the AEROSURF phase 2b clinical trial and phase 2a clinical trial in infants 26-28 weeks gestational age, AEROSURF treatment was associated with significantly lowered incidence and severity of BPD compared to infants on nCPAP alone. This effect was observed without excluding patients whose treatment was interrupted.

In 2018, we transitioned from our prototype 2 ADS used in the phase 2 clinical program (phase 2 ADS) to a newly-designed ADS for use in our phase 3 program (phase 3 ADS), which combines the same aerosolization technology used during the phase 2 clinical program, but with improved ergonomics, interface, controls, and dose monitoring in a modular design. We successfully concluded design verification activities through a detailed assessment of the phase 3 ADS design and implemented design changes to potentially mitigate the risks of device-related treatment interruptions experienced in the prototype phase 2 device used in the phase 2b clinical trial. We believe that the phase 3 ADS will be easier and faster to use and may support enhanced clinical outcomes by potentially allowing for reduced time to initial administration of our KL4 surfactant and reduced time intervals between doses, if required.

With respect to our ADS, we are currently engaged in a technology transfer of our device manufacturing process from Battelle Memorial Institute (Battelle) to Mack Molding Company (Mack), an FDA-registered medical device manufacturer that we have engaged to produce a new phase 3 ADS for use in our planned AEROSURF bridging study and potentially address the unexpected rate of treatment interruptions (we previously referred to this new version as the NextGen ADS). If AEROSURF is approved for marketing, we expect that the phase 3 ADS will also support our commercial market platform. We currently have a Memorandum of Understanding with Mack to cover this transfer.

Focus for 2019 – AEROSURF Bridging Study

We are planning to conduct an additional AEROSURF clinical bridging study that is designed among other things, to clinically evaluate the design and performance of our new phase 3 ADS. This trial will not be powered to establish statistical significance but will generate additional higher dose treatment data to augment the higher dose data obtained in the phase 2b clinical trial. Our plans include a multicenter, randomized, controlled study with masked treatment assignment in approximately 70 premature infants that is designed to assess safety and tolerability of administering aerosolized KL4 surfactant administered to premature infants 26 to 32 week gestational age receiving nCPAP in an extended initial dose (consisting of two 50 minute-doses) with up to 3 repeat doses (each 50-minutes, administered with a minimum of 20 minutes between doses) compared to infants receiving nCPAP alone. In addition to assessing safety and tolerability, the key objectives of this trial include assessing nCPAP failure rates at 72 hours and 28 days and the performance of the phase 3 ADS. We plan to conduct this trial in 15 to 25 of our previous phase 2b, higher-performing clinical sites. We anticipate that this trial will start late in the third quarter or early fourth quarter of 2019; however, we will require additional capital to be in a position to complete the trial in accordance with our development plan, (*see*, Item 1A – Risk Factors – Risks Related to Capital Resource Requirements).

Other

We have contracted with Clinical Supplies Management, Inc. for the receipt, labeling, packaging and distribution of drug and materials to support our planned AEROSURF bridging study.

Our lyophilized KL4 surfactant is manufactured for us by Pharma Services Group, Patheon, part of Thermo Fisher Scientific (Patheon), under a development agreement providing for development and manufacture of our drug product through completion of process validation which will be completed during the manufacture of drug product to complete the planned phase 3 clinical program.

In our Warrington laboratory we conduct certain analytical and quality control activities including release testing of all API's and release and stability testing of our lyophilized and aerosolized KL4 surfactant drug product. We also work with a number of third-party institutions and laboratories that perform various studies as well as quality control release and stability testing.

KL4 surfactant is comprised of four active pharmaceutical ingredients (API's). Our API suppliers are Bachem Americas, Inc., Corden Pharma and Avanti Polar Lipids, Inc. We have supply agreements for KL4 and POPG and source the other two under purchase orders. With respect to KL4, we received a notice of nonrenewal from Bachem in connection with an expiration date in June 2019. We are working to develop a new manufacturing process and will select a successor based on request-for-proposal submissions. To provide a sufficient supply of KL4 to support our AEROSURF development plan through the planned phase 3 clinical program, we are manufacturing an inventory of KL4 with Bachem.

Lyophilized KL4Surfactant – Other Studies

We are assessing potential development pathways to secure marketing approval for lyophilized KL4 surfactant as an intratracheal instillate for the treatment and/or prevention of RDS. Lyophilized KL4 surfactant is the drug product component of AEROSURF and a lyophilized (freeze-dried) dosage form of the liquid KL4 surfactant intratracheal instillate (SURFAXIN®) that was approved by the FDA in 2012. In April 2015, we voluntarily ceased commercializing SURFAXIN to focus our resources on the development of aerosolized KL4 surfactant for respiratory diseases, beginning with AEROSURF.

Our KL4 surfactant can be lyophilized (freeze-dried) and reconstituted to a liquid just prior to administration. We currently maintain continuous cold chain storage for this product. We plan to conduct studies to assess potential reduction of cold chain storage and refrigeration requirements in the hospital. We have demonstrated in laboratory experiments that our lyophilized KL4 surfactant retains many of the key attributes and characteristics of our liquid instillate. We previously discussed with the FDA a potential development plan, trial design and regulatory plan for approval and plan potentially to re-engage with the FDA in the second half of 2019. If we can define an acceptable development program that is achievable from a cost, timing and resource perspective, we may seek approval to treat premature infants who, because they are unable to breathe on their own or other reason, are not candidates for AEROSURF.

In addition, on March 12, 2018, we announced a collaboration with Eleison Pharmaceuticals, Inc., a specialty pharmaceutical company developing life-saving therapeutics for rare cancers, to assess the feasibility of using our ADS potentially to deliver Eleison's inhaled lipid cisplatin (ILC), potentially in combination with our KL4 surfactant. Eleison is developing ILC for non-small cell lung cancer (NSCLC) and completed a phase II study of ILC in patients with bone cancer (osteosarcoma) metastatic to the lung.

We believe our lyophilized KL4 surfactant and ADS technologies may potentially support a product pipeline to address a broad range of serious respiratory conditions in children and adults. We have received support, and plan to seek additional support, from the National Institutes of Health (NIH) and other government funding sources to explore the utility of our KL4 surfactant to address a variety of such respiratory conditions as acute lung injury (ALI), including acute radiation exposure to the lung (acute pneumonitis and delayed lung injury), chemical-induced ALI, and influenza-induced ALI; as well as chronic rhinosinusitis, complications of certain major surgeries, mechanical ventilator-induced lung injury (often referred to as VILI), pneumonia, and diseases involving mucociliary clearance disorders, such as chronic obstructive pulmonary disease (COPD) and cystic fibrosis (CF).

Rostafuroxin

Overview

Rostafuroxin is a novel investigational drug product candidate that is designed to be a selective antagonist of adducin polymorphisms and endogenous ouabain, both known triggers of hypertension, and creates functional effects by enhancing renal tubular sodium reabsorption and increasing vascular tone. Rostafuroxin targets resistant hypertensive patients with a specific genetic profile, which is found in approximately 20% – 25% of the adult hypertensive population. Based on the preclinical and clinical studies performed to date, we believe that rostafuroxin may reduce or normalize blood pressure in this genetically identified subset of patients and may reduce the risk of hypertension-related sequelae beyond the level normally associated with the absolute reduction of blood pressure, per se, because the molecular mechanism blocked by rostafuroxin may also be involved in organ damage.

CVie Therapeutics conducted three phase 2 clinical trials assessing reduction in blood pressure when rostafuroxin is administered in a hypertensive population selected in accordance with a specified genetic profile. A phase 2b clinical trial was conducted as a two-part study with the first part conducted in Italy with Caucasian patients and the second part conducted in Taiwan with ethnic Chinese patients. The efficacy results in Italy were positive in both this trial and in an earlier phase 2a clinical trial; however, the blood pressure response in Chinese patients in the second part of the phase 2b study was minimal.

We are analyzing the results of these clinical trials potentially to identify the reasons for the limited response in Chinese patients, including with respect to potential differences between the populations in drug metabolism, bioavailability or drug interaction with traditional Chinese medicines that the patients may have been taking to manage their hypertension.

Focus for 2019

In 2019, we plan to focus on finalizing the drug formulation and defining drug product analytical methods supporting release and stability measures and assessments. Once we have developed a product profile, we plan to seek opportunities to out-license rostafuroxin to a larger company that has interest in and/or operates in the very large and broad antihypertension market.

Other

The drug product for rostafuroxin is manufactured by Doppel Farmaceutici S.r.l. The API used in the manufacture of rostafuroxin is manufactured by China Gateway Pharmaceutical Development Co., Ltd.

The Offerings

On December 21, 2018, we entered into an Agreement and Plan of Merger (CVie Acquisition) with, and thereby acquired, CVie Investments Limited (CVie Investments), an exempted company with limited liability incorporated under the laws of the Cayman Islands. Under the terms of the Acquisition Agreement, we issued shares of our common stock, par value $0.001 per share (common stock) to CVie Investments' former shareholders, at an exchange ratio of 0.3512 share of common stock for each share of CVie Investments outstanding prior to the merger, resulting in the issuance of 16,265,060 shares of common stock being issued in exchange for the shares of CVie Investments. The merger closed on December 21, 2018.

On December 21, 2018, we completed a private placement offering with institutional investors (Investors), for the purchase of an aggregate of 11,785,540 shares of common stock at a price per share of $3.3132, for an aggregate purchase price of approximately $39.0 million (the Private Placement Financing). Included in the purchase price, each of LPH II Investments Limited (LPH II), an affiliate of Lee's Pharmaceutical Holdings Ltd. (Lee's), and Battelle Memorial Institute converted $6.0 million and $1.0 million, respectively, of existing debt obligations at the same price per share of $3.3132. In connection with the Private Placement Financing, we issued (i) Series F Warrants to purchase an aggregate of 2,003,541 shares of common stock at an exercise price equal to $3.68 per share, which are exercisable through the 18-month anniversary of the date of issuance (the Series F Warrants), and (ii) Series G Warrants to purchase an aggregate of 3,889,229 shares of common stock at an exercise price equal to $4.05 per share, which are exercisable through the five-year anniversary of the date of issuance. The Warrants (i) may not be exercised to the extent that following such exercise, the holder would beneficially own more than 9.99% (or other percent as designated by each holder) of our outstanding shares of common stock, and (ii) contain customary provisions that adjust the exercise price and the number of shares of common stock into which the Warrants are exercisable in the event of a corporate transaction.

On December 21, 2018, we issued 114,415 shares of common stock to Rui Jin (HK) Consulting Management Company Limited, an affiliate of Panacea, for services rendered before Panacea and Mr. Huang became related parties to us.

In December 2018, we entered into a Payment Restructuring Agreement with Battelle Memorial Institute (Battelle). The Payment Restructuring Agreement restructures certain outstanding principal balance due to Battelle, which was approximately $4,342,300 as at October 18, 2017, under the Company's Services Agreement and Collaboration Agreement with Battelle. As part of the Payment Restructuring Agreement, the Company issued to Battelle 75,000 Series E Warrants to purchase 75,000 shares of common stock at an exercise price of $6.50 per share.

In July 2018, we executed and delivered to Panacea Venture Management Company Ltd, a Secured Convertible Promissory Note with respect to certain loans in the aggregate amount of up to $1.5 million. In connection with such loans, we issued to Panacea Venture Management Company Ltd. 187,500 Series D Warrants to purchase 187,500 shares of common stock at an exercise price of $4.00 per share.

In April 2018, we completed a private placement offering with LPH II Investments Limited, a Cayman Islands company organized and existing under the laws of Cayman Islands (LPH II) 541,667 shares of common stock and 135,417 Series C Warrants to purchase 135,417 shares of common stock at an exercise price of $5.52 per share (the Exercise Price). LPH II agreed to pay the Company a purchase price of $4.80 per Share for gross proceeds of $2.6 million, or approximately $2.5 million net proceeds (after deducting expenses).

In October 2017, we completed a private placement offering with LPH Investments Limited, a company incorporated in the Cayman Islands with limited liability and an affiliate of Lee's (LPH), for the purchase of $10.0 million of our common stock at a price of $4.326 per share, which represented a 15% premium over the average of the daily volume-weighted average price per share (VWAP) over the 10-day trading period ending on and including the date of the related agreement, and issued in 2,311,604 shares of our common stock. Following the transaction, Lee's beneficially owned 73% of our issued and outstanding shares of common stock. The investment included cancellation of $3.9 million in outstanding loans that we had borrowed from Lee's Pharmaceutical (HK) Ltd., a Hong Kong company organized and existing under the laws of Hong Kong (Lee's (HK)) under a Loan Agreement dated August 14, 2017, between ourselves and Lee's (HK).

Corporate Information

Our principal executive offices are located at 2600 Kelly Road, Suite 100, Warrington, Pennsylvania, 18976, our telephone number is 215-488-9300 and our corporate website address is www.windtreetx.com. Neither our website nor any information contained on our website is part of this prospectus. Our Common Stock is currently traded on the OTCQB, and our symbol is WINT.

THE OFFERING

Common stock offered by the selling stockholders	37,308,973 shares of Common Stock, which consists of: (i) 31,018,286 Common Shares and (ii) 6,290,687 Warrant Shares
Common stock outstanding	32,133,189 shares (as of April 9, 2019)
Use of proceeds	We will not receive any proceeds from the sale of shares of our Common Stock by the selling stockholders in this offering. See “Use of Proceeds.”
Risk factors	Investing in our Common Stock involves significant risks. See “Risk Factors” beginning on page 5 of this prospectus, which incorporates by reference the risk factors set forth in our most recent Annual Report on Form 10-K.
OTCQB ticker symbol	WINT

RISK FACTORS

An investment in our securities involves significant risks. You should carefully consider each of the risk factors set forth in our most recent Annual Report on Form 10-K, which was filed with the SEC on April 16, 2019, as amended on April 23, 2019, and as may be updated from time to time by our Quarterly Reports on Form 10-Q and other SEC filings filed after such annual report, and future filings with the SEC, which are incorporated by reference into this prospectus. Before making an investment decision, you should carefully consider these risks as well as other information we include or incorporate by reference in this prospectus and any prospectus supplement. Any of these risks and uncertainties could have a material adverse effect on our business, financial condition, cash flows and results of operations. If that occurs, the trading price of our Common Stock could decline materially and you could lose all or part of your investment.

The risks we have incorporated by reference into this prospectus are not the only risks we face. We may experience additional risks and uncertainties not currently known to us, or as a result of developments occurring in the future. Conditions that we currently deem to be immaterial may also materially and adversely affect our business, financial condition, cash flows, results of operations and prospects.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. The forward-looking statements provide our current expectations or forecasts of future events and financial performance and may be identified by the use of forward-looking terminology, including such terms as “believes,” “estimates,” “anticipates,” “expects,” “plans,” “intends,” “may,” “will” or “should” or, in each case, their negative, or other variations or comparable terminology, though the absence of these words does not necessarily mean that a statement is not forward-looking. Forward-looking statements include all matters that are not historical facts and include, without limitation, statements concerning our business strategy, outlook, future milestones, goals and objectives, and our financial plans and future financial condition, including the period of time during which our existing resources will enable us to fund our operations and continue as a going concern. Forward-looking statements also include our expectations about the timing and anticipated outcomes of submitting regulatory filings in the United States (US) and other markets for our products under development; our research and development programs, including planned development activities, anticipated timing of clinical trials and potential development milestones, for our KL4 surfactant product candidates, our aerosol delivery system (ADS), which we are designing to aerosolize our KL4 surfactant, our istaroxime product candidate, and our rostafuroxin product candidate; manufacturing plans for our drug products, active pharmaceutical ingredients (APIs), materials and ADS; and our plans regarding potential strategic alliances, collaboration agreements, including licensing opportunities, and other potential strategic transactions (including without limitation, by merger, acquisition or other corporate transaction).

We intend that all forward-looking statements be subject to the safe-harbor provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements are subject to many risks and uncertainties that could cause actual results to differ materially from any future results expressed or implied by the forward-looking statements. We caution you therefore against relying on any of these forward-looking statements. They are neither statements of historical fact nor guarantees or assurances of future performance. Examples of such risks and uncertainties, which potentially could have a material adverse effect on our development programs, business and/or operations, include, but are not limited to the following:

- our ongoing capital resource requirements and our ability to raise funds to meet such requirements
- our ability to successfully identify and enter into strategic and other non-dilutive transactions
- our ability to successfully execute development activities
- our ability to successfully integrate our company following our acquisition by merger of CVie Investments
- risks related to manufacturing active pharmaceutical ingredients, drug product, medical devices and other materials we need; and
- other risks and uncertainties detailed in “Risk Factors” and elsewhere in our most recent Annual Report on Form 10-K, which was filed with the SEC on April 16, 2019, as amended on April 23, 2019, and in the documents incorporated by reference therein.

Pharmaceutical, biotechnology and medical technology companies have suffered significant setbacks conducting clinical trials, even after obtaining promising earlier preclinical and clinical data. In addition, data obtained from clinical trials are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. After gaining approval of a drug product, medical device or combination drug/device product, pharmaceutical and biotechnology companies face considerable challenges in marketing and distributing their products and may never become profitable.

The forward-looking statements contained herein or in the documents incorporated by reference herein speak only as of their respective dates. Factors or events that could cause our actual results to differ may emerge from time to time and it is not possible for us to predict them all. Except to the extent required by applicable laws, rules or regulations, we do not undertake any obligation to publicly update any forward-looking statements or to publicly announce revisions to any of the forward-looking statements, whether as a result of new information, future events or otherwise.

USE OF PROCEEDS

The shares of our Common Stock being offered by this prospectus are solely for the account of the selling stockholders. We will not receive any proceeds from the sale of these shares by the selling stockholders. However, upon a cash exercise of the Series F Warrants by the selling stockholders, we will receive a per share exercise price of $3.68, upon a cash exercise of the Series G Warrants by the selling stockholders, we will receive a per share exercise price of $4.05, upon a cash exercise of the Series E Warrants by the selling stockholders, we will receive a per share exercise price of $6.50, upon exercise of the Series D Warrants by the selling stockholders, we will receive a per share exercise price of $4.00, and upon exercise of the Series C Warrants by the selling stockholders, we will receive a per share exercise price of $5.52. If the Warrants are exercised in a cashless exercise, we will not receive any proceeds from the exercise of the Warrants.

SELLING STOCKHOLDERS

This prospectus relates to the resale by the selling stockholders of Common Shares and Warrant Shares. The Common Shares and the Warrant Shares were issued by us to the selling stockholders on December 21, 2018 in the exempt offerings. For additional information regarding the issuance of these securities, see “Prospectus Summary - The Exempt Offerings” above. We are filing the registration statement of which this prospectus is a part pursuant to (i) the provisions of the registration rights agreement and (ii) the Merger Agreement, which granted the selling stockholders registration rights in connection with the Private Placement Financing and the Merger, respectively. Except as otherwise disclosed below in the footnotes to the selling stockholders table below, the selling security holders have not had any material relationship with us within the past three years.

The selling stockholders may from time to time offer and sell pursuant to this prospectus any or all of the Common Shares or the Warrant Shares that they acquire upon exercise of the Warrants.

The following table presents information regarding the selling stockholders and the shares that any of the selling stockholders may offer and sell from time to time under this prospectus. This table reflects holdings as of April 9, 2019 to the best of our knowledge. As used in this prospectus, the term “selling stockholders” includes the selling stockholders and any donees, pledges, transferees or other successors in interest of the selling stockholders. The number of shares in the column “Maximum Number of Shares of Common Stock to be Sold Pursuant to this Prospectus” represents all of the shares that the selling stockholders may offer under this prospectus. The selling stockholders may sell some, all or none of its shares. We do not know how long the selling stockholders will hold the shares before selling them, and we currently have no agreements, arrangements or understandings with the selling stockholders regarding the sale of any of the shares.

The Warrants contain limitations that prevent the holder from acquiring shares upon exercise of a Warrant that would result in the number of shares beneficially owned by it and its affiliates exceeding 9.99% (or such lesser percent as designated by each selling stockholder) of the total number of shares of our common stock then issued and outstanding. The beneficial ownership percentage in the third and sixth columns for certain selling stockholders reflect these limitations, which are further described in footnotes relating to each selling stockholder. The selling stockholders may sell all, some or none of their shares in this offering. See “Plan of Distribution.”

Beneficial ownership is determined in accordance with Rule 13d-3(d) promulgated by the SEC under the Exchange Act, as amended, and includes shares of Common Stock with respect to which the selling stockholders have voting and investment power. The offering is based on 32,133,189 shares of our Common Stock actually outstanding on April 9, 2019.

Name of Selling Stockholder	Number of Shares of Common Stock Beneficially Owned Prior to Offering[1]	% of Shares of Common Stock Beneficially Owned Prior to Offering[1]	Maximum Number of Shares of Common Stock to be Sold Pursuant to this Prospectus	Number of Shares of Common Stock Beneficially Owned After Offering[1] [2]	% of Shares of Common Stock Beneficially Owned After Offering[1] [2]
Kingsbridge Capital Limited	107,158	*	74,701	32,457	*
Battelle Memorial Institute	708,126	2.18%	527,735	180,391	*
Bioengine Capital Inc.	4,683,586	14.08%	4,683,586[3]	-	*
Misland Capital Limited Acting as a Nominee to Green Bermuda Limited	452,735	1.40%	452,735	-	*
Tyrus-DA Global Healthcare No. 1	3,795,205	9.99%	3,795,205	-	*
LPH II Investments Limited	3,809,761	9.99%	3,393,491	416,270	1.24%
Panacea Venture Healthcare Fund I L.P.	7,093,793	9.99%	6,978,518	115,275	*
China Cardiovascular Focus Limited	8,063,861	9.99%	8,063,861	-	*
Ivy Blue Holdings Limited (KPCB China II)	4,336,790	9.99%	4,336,790	-	*
Lilly Asia Ventures	1,337,741	4.16%	1,337,741	-	*
Yuanta Asia Investment Limited	644,039	2.00%	644,039	-	*
CDIB Venture Capital Corp.	594,552	1.85%	594,552	-	*
LPH Investments Limited	3,732,778	9.99%	2,311,604	1,421,174	4.24%
Rui Jin (HK) Consulting Management Company(4)	114,415	*	114,415	-	*

(1) We have determined beneficial ownership in accordance with Rule 13d-3(d) promulgated by the SEC under the Exchange Act, as amended. Certain shares of Common Stock issuable upon exercise of warrants are subject to beneficial ownership limitation provisions and/or exercise restrictions, as further described in the footnotes below.

(2) Assumes that all of the shares of Common Stock represented by this prospectus have been sold.

(3) The Warrants held by Bioengine Capital Inc. provide for a beneficial ownership cap of 19.99%. The Warrants held by LPH II Investments, China Cardiovascular Focus Limited and LPH Investments Limited provide for a beneficial ownership cap of 9.99% in the aggregate.

(4) Rui Jin (HK) Consulting Management Company Limited is an entity of which James Huang, our Chairman of the Board, is a director.

(*) Less than 1%

PLAN OF DISTRIBUTION

We are registering 37,308,973 shares of Common Stock under this prospectus on behalf of the selling stockholders. The selling stockholders will pay any brokerage commissions and similar selling expenses attributable to the sale of the shares. We will not receive any of the proceeds from the sale of the shares by the selling stockholders. However, upon a cash exercise of the Series C Warrants, Series D Warrants, Series E Warrants, Series F Warrants and Series G Warrants by the selling stockholders, we will receive a per share exercise price of $5.52, $4.00, $6.50, $3.68, and $4.05, respectively. If the Warrants are exercised in a cashless exercise, we will not receive any proceeds from the exercise of the Warrants.

These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices. To the extent any of the selling stockholders gift, pledge or otherwise transfer the shares offered hereby, such transferees may offer and sell the shares from time to time under this prospectus, provided that this prospectus has been amended under Rule 424(b)(3) or other applicable provision of the Securities Act to include the name of such transferee in the list of selling stockholders under this prospectus.

The selling stockholders may use any one or more of the following methods when disposing of shares or interests therein: ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers; block trades in which the broker-dealer will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction; purchases by a broker-dealer as principal and resale by the broker-dealer for its account; an exchange distribution in accordance with the rules of the applicable exchange; privately negotiated transactions; short sales; through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise; broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share; a combination of any such methods of sale; and any other method permitted pursuant to applicable law.

The selling stockholders may, from time to time, pledge or grant a security interest in some or all of the shares of Common Stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of Common Stock, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus.

In connection with the sale of our Common Stock or interests therein, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the Common Stock in the course of hedging the positions they assume. The selling stockholders may also sell shares of our Common Stock short and deliver these securities to close out their short positions, or loan or pledge the Common Stock to broker-dealers that in turn may sell these securities. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The aggregate proceeds to the selling stockholders from the sale of the Common Stock offered by them will be the purchase price of the Common Stock less discounts or commissions, if any. Each of the selling stockholders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of Common Stock to be made directly or through agents. We will not receive any of the proceeds from this offering. Upon any exercise of the Warrants by payment of cash, however, we will receive the exercise price of the Warrants.

To the extent required, the shares of our Common Stock to be sold, the names of the selling stockholders, the respective purchase prices and public offering prices, the names of any agents, dealer or underwriter, any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the Common Stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the Common Stock may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

The anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of shares in the market and to the activities of the selling stockholders and their affiliates. In addition, we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling stockholders for the purpose of satisfying any applicable prospectus delivery requirements of the Securities Act.

We have agreed to indemnify the selling stockholders against certain liabilities, including liabilities under the Securities Act and state securities laws, relating to the registration of the shares offered by this prospectus.

The selling stockholders and any broker-dealers that act in connection with the sale of the shares may be deemed to be “underwriters” as the term is defined in Section 2(11) of the Securities Act. Consequently, any commissions received by these broker-dealers and any profit on the resale of the shares sold by them while acting as principals might be deemed to be underwriting discounts or commissions under the Securities Act.

The selling stockholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act of 1933, provided that they meet the criteria and conform to the requirements of that rule.

LEGAL MATTERS

The validity of our Common Stock offered by this prospectus will be passed upon for us by Dentons US LLP, New York, New York.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2018 as set forth in their report (which contains an explanatory paragraph describing conditions that raise substantial doubt about the Company's ability to continue as a going concern as described in Note 4 to the consolidated financial statements) which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 (including the exhibits, schedules and amendments thereto) under the Securities Act with respect to our Common Stock offered hereby by the selling stockholders. This prospectus does not contain all of the information set forth in the registration statement and the exhibits and schedules thereto. For further information with respect to us and the Common Stock offered hereby by the selling stockholders, we refer you to the registration statement and the exhibits and schedules filed therewith. Statements contained in this prospectus as to the contents of any contract, agreement or any other document are summaries of the material terms of this contract, agreement or other document and are not necessarily complete. With respect to each of these contracts, agreements or other documents filed as an exhibit to the registration statement, reference is made to the exhibits for a more complete description of the matter involved. A copy of the registration statement, and the exhibits and schedules thereto, may be inspected without charge at the public reference facilities maintained by the SEC at 100 F Street NE, Washington, D.C. 20549. Copies of these materials may be obtained, upon payment of a duplicating fee, from the Public Reference Section of the SEC at 100 F Street NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facility. The SEC maintains a website that contains reports, proxy and information statements and other information regarding registrants that file electronically with the SEC. The address of the SEC's website is www.sec.gov.

We also make available free of charge on our website at www.windtreetx.com our Annual Reports on Form 10-K, our Quarterly Reports on Form 10-Q, our Current Reports on Form 8-K and any amendments to those reports, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information contained on our website is not incorporated by reference into this prospectus and you should not consider information contained on our website as part of this prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" the information we have filed with the SEC. This means we can disclose important information to you without actually including the specific information in this prospectus by referring to those documents. The information incorporated by reference is an important part of this prospectus.

If information in incorporated documents conflicts with information in this prospectus, you should rely on the most recent information. If information in an incorporated document conflicts with information in another incorporated document, you should rely on the most recent incorporated document. We incorporate by reference the documents listed below:

- our Annual Report on Form 10-K for the year ended December 31, 2018, filed with the SEC on April 16, 2019;
- our Amendment to our Annual Report on Form 10-K for the year ended December 31, 2018, filed with the SEC on April 23, 2019; and
- the description of our Common Stock contained in our registration statement on Form 8-A filed with the SEC on July 13, 1995 and February 6, 2004.

All documents subsequently filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, other than the information furnished pursuant to Item 2.02 or Item 7.01 of Form 8-K, prior to the filing of a post-effective amendment to this Registration Statement which indicates that all securities covered by this Registration Statement have been sold or which deregisters all of the securities then remaining unsold, shall be deemed to be incorporated by reference in this Registration Statement and to be part of this document from the date of filing of such documents. Any statement contained in a document incorporated or deemed to be incorporated by reference in this document, will be deemed to be modified or superseded for purposes of this Registration Statement to the extent that a statement contained in this document or in any other subsequently filed document which also is or is deemed to be incorporated by reference in this document modifies or supersedes such statement. Any such statement so modified or suspended will not be deemed, except as so modified or superseded, to constitute a part of this Registration Statement. We will provide a copy of these filings (including certain exhibits that are specifically incorporated by reference therein) to each person, including any beneficial owner, to whom a prospectus is delivered. You may request a copy of any or all of these filings at no cost, by writing or calling us at:

Windtree Therapeutics, Inc.
2600 Kelly Road, Suite 100
Warrington, Pennsylvania 18976
(215) 488-9300
Attention: Mary B. Templeton, Esq.

Copies of certain information filed by us with the SEC, including our annual report and quarterly reports, are also available on our website at www.windtreetx.com. Information contained on our website or that can be accessed through our website is not incorporated by reference herein.

You should read the information relating to us in this prospectus together with the information in the documents incorporated by reference. Nothing contained herein shall be deemed to incorporate information furnished to, but not filed with, the SEC.

37,308,973 Shares

Common Stock

Prospectus

, 2019

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth the expenses payable by the Registrant expected to be incurred in connection with the issuance and distribution of Common Stock being registered hereby (other than underwriting discounts and commissions). All of such expenses are estimates, except for the Securities and Exchange Commission (SEC) registration fee.

SEC registration fee	$	18,811
Legal fees and expenses		50,000
Accounting fees and expenses		25,000
Total	$	93,811

Item 14. Indemnification of Directors and Officers.

Article Eight of our Amended and Restated Certificate of Incorporation, as amended (Certificate of Incorporation), limits the liability of directors to the maximum extent permitted by Delaware law. Delaware law provides that directors of a corporation will not be personally liable for monetary damages for breach of their fiduciary duties as directors, except for liability for (i) any breach of their duty of loyalty to the corporation or its stockholders, (ii) acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law, (iii) unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the General Corporation Law of the State of Delaware or (iv) any transaction from which the director derives an improper personal benefit.

Our Amended and Restated By-Laws (By-Laws) provide that we shall indemnify our directors and officers, the directors and officers of any of our subsidiaries and any other individuals acting as directors or officers of any other corporation at our request, to the fullest extent permitted by law.

We have entered into indemnification agreements with our executive officers and directors containing provisions that may require us, among other things, to indemnify them against liabilities that may arise by reason of their status or service as officers or directors, as applicable, other than liabilities arising from willful misconduct of a culpable nature and to advance certain expenses incurred as a result of any proceeding against them as to which they could be indemnified. We have obtained limited directors' and officers' liability insurance.

These provisions in our Certificate of Incorporation and our By-Laws do not eliminate the officers' and directors' fiduciary duty, and in appropriate circumstances, equitable remedies such as injunctive or other forms of non-monetary relief will remain available under Delaware law. In addition, each officer and director will continue to be subject to liability for breach of their duty of loyalty to us for acts or omissions not in good faith or involving intentional misconduct, for knowing violations of law, for actions leading to improper personal benefit to the officer or director and for payment of dividends or approval of stock repurchases or redemptions that are unlawful under Delaware law. The provisions also do not affect an officer's or director's responsibilities under any other law, such as the federal securities laws or state or federal environmental laws.

Item 15. Recent Sales of Unregistered Securities.

In addition to the securities described above in "Prospectus Summary - The Exempt Offerings," we have sold the securities described below within the past three years which were not registered under the Securities Act. All of the sales listed below were made pursuant to an exemption from registration afforded by Section 4(a)(2) of the Securities Act and Regulation D thereunder, as the securities were issued to accredited investors, without a view to distribution, and were not issued through any general solicitation or advertisement.

Securities Purchase Agreement

On February 15, 2017, we completed a private placement offering of 7,049 Series A Convertible Preferred Stock units at a price per unit of $1,495, for an aggregate purchase price of approximately $10.5 million, including $1.6 million of non-cash consideration representing a reduction in amounts due and accrued as of December 31, 2016 for current development services that otherwise would have become payable in cash in the first and second quarters of 2017. Each unit consists of: (i) one share of Series A Convertible Preferred Stock, par value $0.001 per share (Preferred Shares); and (ii) 1,000 Series A-1 Warrants (Warrants) to purchase one share of common stock at an exercise price equal to $1.37 per share. Each Preferred Share may be converted at the holder's option at any time into 1,000 shares of common stock at a conversion price of $1.37 per share. The Warrants may be exercised beginning August 15, 2017 and through February 15, 2024. The Preferred Shares and the Warrants may not be converted or exercised to the extent that the holder would, following such exercise or conversion, beneficially own more than 9.99% (or other lesser percent as designated by each holder) of our outstanding shares of common stock. In the event of a liquidation, including without limitation, the sale of substantially all of our assets and certain mergers and other corporate transactions (as defined in the Certificate of Designation of Preferences, Rights and Limitations relating to the Preferred Shares), the holder of Preferred Shares will have a liquidation preference that could result in the holder receiving a return of its initial investment before any payments are made to holders of common stock, and then participating with other equity holders until it has received in the aggregate up to three times its original investment. In addition to the offering, the securities purchase agreement also provides that, until February 13, 2018, the investors are entitled to participate in subsequent bona fide capital raising transactions that we may conduct

Collaboration Agreement with Battelle

We entered into a Collaboration Agreement with Battelle Memorial Institute (Battelle) in October 2014, which was amended on August 2015 and March 2016, for the development of a new version (NextGen) of our aerosol delivery system.

In December 2018, we and Battelle entered into a Payment Restructuring Agreement (the Battelle Payment Restructuring), which reflected the terms of an October 2017 nonbinding memorandum of understanding, in which we outlined terms to restructure approximately $4.3 million then due to Battelle, under a Research and Development Services Agreement dated as of June 22, 2012 and the Collaboration Agreement. In connection with the Battelle Payment Restructuring, on December 11, 2018, we issued to Battelle warrants to purchase 75,000 shares of common stock, exercisable at a price of $6.50 per share, which expire on the fifth anniversary of the Effective Date.

AEROSURF Warrants

In connection with the CVie Acquisition, our Board of Directors declared a dividend to the holders of record of our outstanding shares of Common Stock, and holders of certain warrants to purchase Common Stock, that were outstanding on December 20, 2018 of 0.6148 Series H (AEROSURF) Warrant, for each share of Common Stock held by a shareholder or each warrant held by a warrant holder, as applicable, on the record date (the AEROSURF Warrants). The Company expects to distribute AEROSURF Warrants that are exercisable for an aggregate of 2,963,167 shares of Common Stock. Each AEROSURF Warrant has a term of five years and provides for automatic exercise into one share of Common Stock, without any exercise price, upon the Company's public announcement of the dosing of the first human subject enrolled in the Company's Phase 3 clinical trial for AEROSURF.

Deerfield

In October 2017, we entered into an Exchange and Termination Agreement (the Exchange and Termination Agreement) with affiliates of Deerfield Management Company, L.P. (Deerfield). Under the Exchange and Termination Agreement, (i) promissory notes evidencing an aggregate principal amount of $25,000,000 owed to Deerfield under that certain Facility Agreement dated as of February 13, 2013 (the Facility Agreement), as amended from time to time, and (ii) warrants to purchase up to 25,000 shares of the Company's Common Stock at an exercise price of $786.80 per share held by Deerfield (the Deerfield Warrants) were cancelled in consideration for (i) a cash payment in the aggregate amount of $2,500,000, (ii) an aggregate of 71,111 shares of Common Stock and (iii) the right to receive certain milestone payments (Milestone Payments) based on achievement of specified development and commercial milestones related to the Company's AEROSURF® development program, which, if achieved, could potentially total up to $15,000,000.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits.

See the Exhibit Index immediately following the signature page hereto, which is incorporated by reference as if fully set forth herein.

(b) Financial Statement Schedules.

None.

Item 17. Undertakings.

(a) The undersigned Registrant hereby undertakes:

(1) to file, during any period in which offers or sales are being made, a post-effective amendment to this Registration Statement:

(i) to include any prospectus required by Section 10(a)(3) of the Securities Act;

(ii) to reflect in the prospectus any facts or events arising after the effective date of the Registration Statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the Registration Statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the Calculation of Registration Fee" table in the effective Registration Statement; and

(iii) to include any material information with respect to the plan of distribution not previously disclosed in the Registration Statement or any material change to such information in the Registration Statement;

provided, however, that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the SEC by the Registrant pursuant to Section 13 or Section 15(d) of the Exchange Act that are incorporated by reference in the Registration Statement.

(2) that, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) to remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) that, for the purpose of determining liability under the Securities Act to any purchaser: each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A, shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness; provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such first use, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such date of first use.

(b) The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the Registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in the Registration Statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(c) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized on this 30th day of April, 2019.

Windtree Therapeutics, Inc.

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

POWER OF ATTORNEY

We, the undersigned officers and directors of Windtree Therapeutics, Inc., and each of us, do hereby constitute and appoint each of Craig E. Fraser, Mary B. Templeton, Esq., and John A. Tattory, or any of them, each acting alone, his true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, to do any and all acts and things in our name, place and stead, in any and all capacities, in connection with this registration statement on Form S-1 under the Securities Act, or any registration statement for the same offering that is to be effective upon filing under the Securities Act, including, without limitation, to sign for us or any of us in our names in the capacities indicated below any and all amendments or supplements to this registration statement, including any and all post-effective amendments to the registration statement, and to sign any and all additional registration statements relating to the same offering of securities as this registration statement that are filed pursuant to Rule 462(b) under the Securities Act, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the U.S. Securities and Exchange Commission and any applicable securities exchange or securities self-regulatory body, granting unto said attorneys-in-fact and agents, each acting alone, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or their substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities held on the dates indicated.

Signature	Name & Title	Date
/s/ Craig E. Fraser	Craig E. Fraser Director, President, and Chief Executive Officer (Principal Executive Officer)	April 30, 2019
/s/ John A. Tattory	John A. Tattory Senior Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	April 30, 2019
/s/ James Huang	James Huang Director (Chairman of the Board)	April 30, 2019
/s/ John R. Leone	John R. Leone Director	April 30, 2019
/s/ Joseph M. Mahady	Joseph M. Mahady Director	April 30, 2019
/s/ Bruce A. Peacock	Bruce A. Peacock Director	April 30, 2019
/s/ Brian D. Schreiber	Brian D. Schreiber, M.D. Director	April 30, 2019

EXHIBIT INDEX

The following exhibits are included with this Annual Report on Form 10-K.

Exhibit No.	Description	Method of Filing
3.1	Amended and Restated Certificate of Incorporation	Incorporated by reference to Exhibit 3.1 to Windtree's Annual Report on Form 10-K, as filed with the SEC on April 17, 2018
3.2	Amended and Restated By-Laws	Incorporated by reference to Exhibit 3.2 to Windtree's Current Report on Form 8-K, as filed with the SEC on April 18, 2016
4.1	Form of Warrant dated October 10, 2014	Incorporated by reference to Exhibit 4.11 to Windtree's Quarterly Report on Form 10-Q, as filed with the SEC on November 7, 2014
4.2	Form of Series A Warrant dated July 22, 2015	Incorporated by reference to Exhibit 4.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on July 17, 2015
4.3	Form of Series B Warrant dated July 22, 2015	Incorporated by reference to Exhibit 4.3 to Windtree's Current Report on Form 8-K, as filed with the SEC on July 17, 2015
4.4	Form of Series A-1 Warrant dated February 13, 2017	Incorporated by reference to Exhibit 4.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on February 15, 2017
4.5	Form of Series C Warrant dated April 4, 2018	Incorporated by reference to Exhibit 4.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on April 4, 2018
4.6	Form of Series D Warrant dated July 2, 2018	Incorporated by reference to Exhibit 4.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on July 6, 2018
4.7	Form of Series E Warrant dated December 11, 2018	Incorporated by reference to Exhibit 4.7 to Windtree's Annual Report on Form 10-K, as filed with the SEC on April 16, 2019
4.8	Form of Series F Warrant dated December 24, 2018	Incorporated by reference to Exhibit 4.2 to Windtree's Current Report on Form 8-K, as filed with the SEC on December 21, 2018
4.9	Form of Series G Warrant dated December 24, 2018	Incorporated by reference to Exhibit 4.3 to Windtree's Current Report on Form 8-K, as filed with the SEC on December 21, 2018
4.10	Form of Series H Warrant dated February 14, 2019	Incorporated by reference to Exhibit 4.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on December 21, 2018
5.1	Opinion of Dentons US LLP	Filed herewith
10.1+	Sublicense Agreement dated October 28, 1996, between Johnson & Johnson, Ortho Pharmaceutical Corporation and Acute Therapeutics, Inc.	Incorporated by reference to Exhibit 10.6 to Windtree's Registration Statement on Form SB-2/A, as filed with the SEC on April 18, 1997 (Commission File Number 333-19375)

10.2+	Amended and Restated License Agreement dated March 28, 2008, between Windtree and Philip Morris USA Inc.,	Incorporated by reference to Exhibit 10.4 to Windtree's Quarterly Report on Form 10-Q for the quarter ended March 31, 2008, as filed with the SEC on May 9, 2008
10.3+	License Agreement dated March 28, 2008, between Windtree and Philip Morris Products S.A.	Incorporated by reference to Exhibit 10.5 to Windtree's Quarterly Report on Form 10-Q for the quarter ended March 31, 2008, as filed with the SEC on May 9, 2008
10.4+	Amended and Restated Sublicense and Collaboration Agreement dated December 3, 2004, between Windtree and Laboratorios del Dr. Esteve, S.A.	Incorporated by reference to Exhibit 10.28 to Windtree's Annual Report on Form 10-K for the year ended December 31, 2004, as filed with the SEC on March 16, 2005
10.5+	Amended and Restated Supply Agreement dated December 3, 2004, between Windtree and Laboratorios del Dr. Esteve, S.A.	Incorporated by reference to Exhibit 10.29 to Windtree's Annual Report on Form 10-K for the year ended December 31, 2004, as filed with the SEC on March 16, 2005
10.6+	License, Development and Commercialization Agreement dated June 12, 2017, between Windtree and Lee's Pharmaceutical (HK) Ltd.	Incorporated by reference to Exhibit 10.1 to Windtree's Quarterly Report on Form 10-Q for the quarter ended June 30, 2017, as filed with the SEC on August 21, 2017
10.7+	Amendment No. 1 dated August 14, 2017 to the License Development and Commercialization Agreement between Windtree and Lee's Pharmaceutical (HK) Ltd. dated June 12, 2017	Incorporated by reference to Exhibit 10.1 to Windtree's Quarterly Report on Form 10-Q for the quarter ended September 30, 2017, as filed with the SEC on November 14, 2017
10.8*	Windtree's 2011 Long-Term Incentive Plan, as amended	Incorporated by reference to Exhibit 10.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on December 31, 2018
10.9*	Form of Employee Option Agreement under Windtree's 2011 Long-Term Incentive Plan	Incorporated by reference to Exhibit 10.2 to Windtree's Quarterly Report on Form 10-Q for the quarter ended March 31, 2012, as filed with the SEC on May 15, 2012
10.10*	Form of Non-Employee Director Option Agreement under Windtree's 2011 Long-Term Incentive Plan	Incorporated by reference to Exhibit 10.3 to Windtree's Quarterly Report on Form 10-Q for the quarter ended March 31, 2012, as filed with the SEC on May 15, 2012
10.11*	Form of Restricted Stock Unit Award Agreement for Non-Employee Directors under Windtree's 2011 Long-Term Incentive Plan	Incorporated by reference to Exhibit 10.11 to Windtree's Annual Report on Form 10-K for the year ended December 31, 2014, as filed with the SEC on March 16, 2015
10.12*	Form of Restricted Stock Unit Award Agreement for Employees under Windtree's 2011 Long-Term Incentive Plan	Incorporated by reference to Exhibit 10.14 to Windtree's Annual Report on Form 10-K for the year ended December 31, 2017, as filed with the SEC on April 17, 2018
10.13*	Employment Agreement dated February 1, 2016, between Windtree and Craig Fraser	Incorporated by reference to Exhibit 10.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on February 3, 2016
10.14*	Inducement Stock Option Award Agreement dated February 1, 2016, between Windtree and Craig Fraser	Incorporated by reference to Exhibit 10.3 to Windtree's Current Report on Form 8-K, as filed with the SEC on February 3, 2016

10.15*	Amendment dated March 13, 2018, to Employment Agreement dated February 1, 2016, between Windtree and Craig Fraser	Incorporated by reference to Exhibit 10.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on March 16, 2018
10.16*	Employment Agreement dated December 19, 2014, between Windtree and Steven G. Simonson, M.D.	Incorporated by reference to Exhibit 10.4 to Windtree's Quarterly Report on Form 10-Q, as filed with the SEC on May 11, 2015
10.17*	Amendment dated December 29, 2014 to Employment Agreement dated December 19, 2014, effective as of April 1, 2015, between Windtree and Steven G. Simonson, M.D.	Incorporated by reference to Exhibit 10.5 to Windtree's Quarterly Report on Form 10-Q, as filed with the SEC on May 11, 2015
10.18*	Amendment dated March 13, 2018, to Employment Agreement dated December 19, 2014 between Windtree and Steven G. Simonson, M.D.	Incorporated by reference to Exhibit 10.3 to Windtree's Current Report on Form 8-K, as filed with the SEC on March 16, 2018
10.19*	Employment Agreement dated March 21, 2014, between Windtree and John A. Tattory	Incorporated by reference to Exhibit 10.1 to Windtree's Quarterly Report on Form 10-Q, as filed with the SEC on May 12, 2014
10.20*	Amendment dated December 29, 2014 to Employment Agreement dated March 21, 2014, effective as of April 1, 2015, between Windtree and John A. Tattory	Incorporated by reference to Exhibit 10.19 to Windtree's Annual Report on Form 10-K for the year ended December 31, 2014, as filed with the SEC on March 16, 2015
10.21*	Amendment dated March 13, 2018 to Employment Agreement dated March 21, 2014 between John A. Tattory	Incorporated by reference to Exhibit 10.2 to Windtree's Current Report on Form 8-K, as filed with the SEC on March 16, 2018
10.22*	Form of Indemnification Agreement between Windtree and certain named executive officers and directors	Incorporated by reference to Exhibit 10.4 to Windtree's Current Report on Form 8-K, as filed with the SEC on February 3, 2016
10.23*	Form of Indemnification Agreement between Windtree and certain named directors	Incorporated by reference to Exhibit 10.23 to Windtree's Annual Report on Form 10-K, as filed with the SEC on April 16, 2019
10.24	Lease Agreement dated May 26, 2004, and First Amendment to Lease Agreement, dated April 2, 2007, between TR Stone Manor Corp. and Windtree	Incorporated by reference to Exhibits 10.1 and 10.2 to Windtree's Current Report on Form 8-K, as filed with the SEC on April 6, 2007
10.25	Second Amendment to Lease Agreement dated January 3, 2013 between TR Stone Manor Corp. and Windtree	Incorporated by reference to Exhibits 10.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on January 8, 2013
10.26	Fourth Amendment to Lease Agreement dated April 29, 2016, between PH Stone Manor LP and Windtree	Incorporated by reference to Exhibits 10.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on May 31, 2016
10.27	Fifth Amendment to Lease Agreement dated February 23, 2018, between PH Stone Manor LP and Windtree	Incorporated by reference to Exhibit 10.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on March 1, 2018
10.28+	Master Services Agreement dated October 24, 2013 between Windtree and DSM Pharmaceuticals, Inc. (now known as Patheon Manufacturing Services LLC)	Incorporated by reference to Exhibit 10.3 to Windtree's Quarterly Report on Form 10-Q, as filed with the SEC on November 12, 2013

10.29+	Supply Agreement dated December 22, 2010 between Corden Pharma (formerly Genzyme Pharmaceuticals LLC, now known as Corden Pharma) and Windtree	Incorporated by reference to Exhibit 10.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on December 29, 2010
10.30	Exchange and Termination Agreement dated October 27, 2017, between Windtree and Deerfield	Incorporated by reference to Exhibit 10.2 to Windtree's Current Report on Form 8-K, as filed with the SEC on November 1, 2017
10.31	Registration Rights Agreement dated October 27, 2017, between Windtree and LPH Investments Limited	Incorporated by reference to Exhibit 99.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on November 1, 2017
10.32	Registration Rights Agreement dated March 30, 2018, between Windtree and LPH II Investments Limited	Incorporated by reference to Exhibit 10.2 to Windtree's Current Report on Form 8-K, as filed with the SEC on April 4, 2018
10.33	Payment Restructuring Agreement effective December 7, 2018, between Windtree and Battelle Memorial Institute	Incorporated by reference to Exhibit 10.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on December 7, 2018
10.34	Loan Agreement dated October 25, 2018, between CVie Therapeutics, Lee's Pharmaceutical Holdings Limited, and O-Bank Co., Ltd.	Incorporated by reference to Exhibit 10.34 to Windtree's Annual Report on Form 10-K, as filed with the SEC on April 16, 2019
10.35	Shareholder Loan Agreement dated April 24, 2018, between Lee's Pharmaceutical International Limited and CVie Therapeutics	Incorporated by reference to Exhibit 10.35 to Windtree's Annual Report on Form 10-K, as filed with the SEC on April 16, 2019
10.36	Shareholder Loan Agreement dated September 20, 2018, between Lee's Pharmaceutical International Limited and CVie Therapeutics	Incorporated by reference to Exhibit 10.36 to Windtree's Annual Report on Form 10-K, as filed with the SEC on April 16, 2019
10.37	Shareholder Loan Agreement dated October 26, 2018, between Lee's Pharmaceutical International Limited and CVie Therapeutics	Incorporated by reference to Exhibit 10.37 to Windtree's Annual Report on Form 10-K, as filed with the SEC on April 16, 2019
10.38	Shareholder Loan Agreement dated November 16, 2018, between Lee's Pharmaceutical International Limited and CVie Therapeutics	Incorporated by reference to Exhibit 10.38 to Windtree's Annual Report on Form 10-K, as filed with the SEC on April 16, 2019
10.39	Merger Agreement dated December 21, 2018, between Windtree, WT Acquisition Corp., and CVie Investments Limited	Incorporated by reference to Exhibit 10.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on December 21, 2018
10.40	Indemnification Letter Agreement dated December 21, 2018, between Windtree and Lee's Pharmaceutical Holdings Limited	Incorporated by reference to Exhibit 10.2 to Windtree's Current Report on Form 8-K, as filed with the SEC on December 21, 2018
10.41	Securities Purchase Agreement dated December 21, 2018 between Windtree and certain purchasers party thereto	Incorporated by reference to Exhibit 10.3 to Windtree's Current Report on Form 8-K, as filed with the SEC on December 21, 2018
10.42	Registration Rights Agreement dated December 21, 2018 between Windtree and certain purchasers party thereto	Incorporated by reference to Exhibit 10.4 to Windtree's Current Report on Form 8-K, as filed with the SEC on December 21, 2018
21.1	Subsidiaries of Windtree	Incorporated by reference to Exhibit 21.1 to the Windtree's Annual Report on Form 10-K, as filed with the SEC on April 16, 2019

23.1	Consent of Ernst & Young LLP, independent registered public accounting firm	Filed herewith

+Confidential treatment requested as to certain portions of these exhibits. Such portions have been redacted and filed separately with the Commission.

*A management contract or compensatory plan or arrangement required to be filed as an exhibit to this annual report pursuant to Item 15(b) of Form 10-K.

Exhibit 5.1

大成 DENTONS

April 30, 2019

Board of Directors
Windtree Therapeutics, Inc.
2600 Kelly Road, Suite 100
Warrington, Pennsylvania 18976

Re: Windtree Therapeutics, Inc.-- Registration Statement on Form S-1

Ladies and Gentlemen:

You have requested our opinion with respect to certain matters in connection with the filing by Windtree Therapeutics, Inc., a Delaware corporation (the "**Company**"), of a Registration Statement on Form S-1 (the "**Registration Statement**") with the Securities and Exchange Commission on April 30, 2019, including a related prospectus filed with the Registration Statement (the "**Prospectus**"), covering the sale of an aggregate of 37,308,973 shares of the Company's common stock, $0.001 par value per share, (the "**Shares**") issued and outstanding, or issuable upon the exercise of certain of the Company's warrants (the "**Warrants**").

We are delivering this opinion to you at your request in accordance with the requirements of Item 601(b)(5) of Regulation S-K under the Act.

In connection with rendering this opinion, we have examined and are familiar with (i) the Company's Amended and Restated Certificate of Incorporation, (ii) the Company's By-Laws, (iii) the Registration Statement, including the Prospectus, (iv) corporate proceedings of the Company relating to the issuance of the Shares and the Warrants (v) the certificates evidencing the Warrants and (vi) such other instruments and documents as we have deemed relevant under the circumstances.

In making the aforesaid examinations, we have assumed the genuineness of all signatures and the conformity to original documents of all copies furnished to us as original or photostatic copies. We have also assumed that the corporate records furnished to us by the Company include all corporate proceedings taken by the Company to date. As to certain factual matters, we have relied upon a certificate of officers of the Company and have not sought to independently verify such matters.

Based upon the foregoing, and in reliance thereon, and subject to the qualifications, limitations and exceptions stated herein, we are of the opinion, having due regard for such legal considerations as we deem relevant, that the Shares have been duly authorized by the Company and, when issued in accordance with the terms set forth in the Registration Statement and the Prospectus, and when issued in accordance with the terms of the Warrants, as applicable, will be validly issued, fully paid and nonassessable.

The foregoing opinion is limited to laws of the State of New York and Delaware corporate law (which includes the Delaware General Corporation Law and applicable provisions of the Delaware constitution, as well as reported judicial opinions interpreting same), and we do not purport to express any opinion on the laws of any other jurisdiction.

We hereby consent to the use of our opinion as an exhibit to the Registration Statement and to the reference to this firm and this opinion under the heading "Legal Matters" in the Registration Statement. In giving such consent, we do not hereby admit that we come within the category of persons whose consent is required under Section 7 of the Act, or the rules and regulations of the Commission thereunder.

Very truly yours,

/s/ Dentons US LLP

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption "Experts" and to the use of our report dated April 16, 2019, in the Registration Statement (Form S-1) and related Prospectus of Windtree Therapeutics, Inc. and subsidiaries for the registration of 37,308,973 shares of its common stock.

/s/ Ernst & Young LLP

Philadelphia, Pennsylvania
April 30, 2019