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

FORM 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended **December 31, 2023**

Or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from _____ to _____

Commission **File Number**: 001-39290

WINDTREE THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**94-3171943**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
2600 Kelly Road, Suite 100 **Warrington, Pennsylvania**	**18976-3622**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: **(215) 488-9300**

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol(s)	Name of exchange on which registered
Common Stock, $0.001 par value	**WINT**	**The Nasdaq Capital Market**

Securities registered pursuant to Section 12(g) of the Act:
None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes ☐ No ☒

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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 filer ☒	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 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

On June 30, 2023 the aggregate market value of shares of voting and non-voting common equity held by non-affiliates of the registrant was approximately $6.2 million (based on the closing price on The Nasdaq Capital Market on that date). In determining this amount, the registrant has assumed solely for this purpose that all of its directors, executive officers and persons beneficially owning 10% or more of the outstanding shares of common stock of the registrant may be considered to be affiliates. This assumption shall not be deemed conclusive as to affiliate status for this or any other purpose.

As of April 16, 2024, there were 9,183,220 shares of the registrant's common stock outstanding.

Unless the context otherwise requires, all references to "we," "us," "our," and the "Company" include Windtree Therapeutics, Inc., and its consolidated subsidiaries.

RISK FACTOR SUMMARY

The risk factors summarized and detailed below could materially harm our business, operating results and/or financial condition, impair our future prospects and/or cause the price of our common stock to decline. These are not all of the risks we face, and other factors not presently known to us or that we currently believe are immaterial may also affect our business if they occur. The following is a summary of the material risks that may affect our business, operating results and financial condition include, but are not necessarily limited to, those relating to:

Risks Related to Our Financial Condition

- Our current cash position, losses, negative cash flows from operations, and accumulated deficit raise substantial doubt about our ability to continue as a going concern absent obtaining adequate new debt or equity financings;
- We have incurred significant operating losses since inception, we expect to incur operating losses in the future, and we may not be able to achieve or sustain profitability;
- We have incurred indebtedness, which could adversely affect our operating flexibility and financial condition; and
- If we fail to maintain proper and effective internal control over financial reporting, our ability to produce accurate and timely financial statements could be impaired, investors may lose confidence in our financial reporting and the trading price of our common stock may decline.

Risks Related to our Development Activities and Regulatory Approval of our Product Candidates

- We are substantially dependent on the success of our lead product candidate istaroxime. To the extent that our clinical development of istaroxime is not successful, our business, financial condition, and results of operations may be materially adversely affected and the price of our common stock may decline; and
- Although we have multiple product candidates or potential indications of those candidates in our clinical pipeline, we may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on other product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Risks Related to Our Reliance on Third Parties

- We rely on third parties, primarily outside of the U.S., to conduct many of our preclinical studies and clinical trials. Any failure by a third party to conduct the clinical trials according to good clinical practices, and other requirements and in a timely and quality manner may delay or prevent our ability to seek or obtain regulatory approval for or commercialize our product candidates; and
- We plan to rely on third parties, some of which are located outside the U.S., to manufacture our drug product candidates, which exposes us to risks that may affect our ability to maintain supplies of our clinical materials, and subject us to uncertainty associated with the international political climate, and could potentially delay or cease our research and development activities, as well as eventual regulatory approval and commercialization of our drug product candidates.

Risks Related to our Business and Operations

- Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or any guidance we may provide;
- We may seek to enter into licensing transactions, collaboration arrangements, and other similar transactions and strategic opportunities, and may not be successful in doing so, and even if we are, we may not realize the benefits of such relationships; and
- We could be adversely affected by any interruption, including from breaches in cybersecurity, in our ability to conduct business at our current location.

Risks Related to Government Regulation

- Our activities are subject to various and complex laws and regulations, and we are susceptible to a changing regulatory environment. Violations or allegations of violations of these laws may result in large civil and criminal penalties, debarment from participating in government programs, diversion of management time, attention and resources and may otherwise have a material adverse effect on our business, financial condition and results of operations;
- We face risks related to our collection and use of data, including personal information, which could result in investigations, inquiries, litigation, fines, legislative and regulatory action and negative press about our privacy and data protection practices;
- Healthcare reform measures in the U.S., as well as the general tightening of drug reimbursement pathways and levels of reimbursement globally, are expected to add additional pressure to achieve financial expectations for our product candidates, if approved; and

- Our international operations subject us to additional regulatory oversight in foreign jurisdictions, as well as economic, social, and political uncertainties, which could cause a material adverse effect on our business, financial position, and operating results.

Risks Related to Intellectual Property Matters

- If we cannot protect our intellectual property, others could use our technology in competitive products. Even if we obtain patents to protect our product candidates, those patents may not be sufficiently broad, or they may expire and others could then compete with us; and
- Litigation or other proceedings or third-party claims of intellectual property infringement could require us to spend significant time and money and could prevent us from selling our product candidates or affect our stock price.

Risks Related to the Ownership of our Securities

- Our common stock is listed on the Nasdaq Capital Market, or Nasdaq. We can provide no assurance that we will be able to comply with the continued listing requirements over time and that our common stock will continue to be listed on Nasdaq;
- We effected a reverse stock split on February 24, 2023, and will need to effect a future reverse stock split to regain compliance with the Nasdaq Capital Market listing rules, which may adversely impact the market price of our common stock;
- The market price of our common stock may be highly volatile, and investors may not be able to resell their shares at or above the price at which they purchase them;
- The Certificate of Designation for the Series B Preferred Stock and our 10% senior convertible notes, or the Notes, each contain anti-dilution provisions that may result in the reduction of the conversion price of the Series B Preferred Stock and the Notes. These features may increase the number of shares of our common stock being issuable upon conversion of the Series B Preferred Stock and the Notes;
- The Series B Preferred Stock have a liquidation preference senior to our common stock; and
- Under the terms of the Notes, we are subject to certain restrictive covenants that may make it difficult to procure additional financing.

FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These forward-looking statements provide our current expectations or forecasts of future events and financial performance and may be identified by the use of forward-looking terminology, including such terms as "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "will," "should," "could," "targets," "projects," "contemplates," "predicts," "potential" or "continues" or, in each case, their negative, or other variations or comparable terminology, though the absence of these words does not necessarily mean that a statement is not forward-looking.

We intend that all forward-looking statements be subject to the safe-harbor provisions of the Private Securities Litigation Reform Act of 1995. 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 estimates regarding future results of operations, financial position, research and development costs, capital requirements, and our needs for additional financing;
- how long we can continue to fund our operations with our existing cash and cash equivalents;
- our ability to meet and regain compliance with the listing requirements of the Nasdaq Stock Market LLC, or Nasdaq;
- changes in market conditions, general economic conditions, and the banking sector, and potential constraints in accessing capital or credit if and when needed with favorable terms, if at all;
- the potential impairment of our intangible assets on our consolidated balance sheet, which could lead to material impairment charges in the future;
- our ability to repay indebtedness;
- potential delays and uncertainties in our anticipated timelines and milestones and additional costs associated with the impact of the residual effects of the COVID-19 pandemic and the evolving events in Israel and Gaza on our clinical trial operations;

- the costs, timing, and results, of our preclinical studies and clinical trials, as well as the number of required trials for regulatory approval and the criteria for success in such trials;
- legal and regulatory developments in the United States, or U.S., and foreign countries, including any actions or advice that may affect the design, initiation, timing, continuation, progress or outcome of clinical trials or result in the need for additional clinical trials;
- the difficulties and expenses associated with obtaining and maintaining regulatory approval of our product candidates, and the indication and labeling under any such approval;
- risks related to manufacturing active pharmaceutical ingredients, drug product, and other materials we need;
- delays, interruptions or failures in the manufacture and supply of our product candidates;
- the plans of our AEROSURF and KL4 licensee, Lee's Pharmaceutical (HK) Ltd., and its affiliate, Zhaoke Pharmaceutical (Hefei) Co. Ltd., and their ability to successfully source materials, execute necessary clinical and business development activities in a timely manner, if at all, to support development and commercialization of the licensed product candidates;
- the performance of third parties, both foreign and domestic, upon which we depend, including contract research organizations, contract manufacturing organizations, contract laboratories, and independent contractors;
- the size and growth of the potential markets for our product candidates, the regulatory requirements in such markets, the rate and degree of market acceptance of our product candidates, and our ability to serve those markets;
- the success of competing therapies and products that are or may become available;
- our ability to limit our exposure under product liability lawsuits;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- recently enacted and future legislation, including but not limited to, the Inflation Reduction Act of 2022, regarding the healthcare system in the U.S. or the healthcare systems in foreign jurisdictions;
- our ability to recruit or retain key scientific, commercial or management personnel or to retain our executive officers;
- our ability to secure electronically stored work product, including clinical data, analyses, research, communications, and other materials necessary to gain regulatory approval of our product candidates, including those acquired from third parties, and assure the integrity, proper functionality, and security of our internal computer and information systems and prevent or avoid cyber-attacks, malicious intrusion, breakdown, destruction, security incidents, data privacy violations, or other significant disruption;
- economic uncertainty resulting from inflation and the rapid increase in interest rates, including concerns involving liquidity, defaults or other non-performance by financial institutions; and
- economic uncertainty resulting from geopolitical instability, including the ongoing military conflict between Russia and Ukraine, the People's Republic of China and the Republic of China (Taiwan), and the evolving events in Israel and Gaza.

We have based these forward-looking statements largely on our current expectations, estimates, forecasts, and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy, and financial needs. In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report on Form 10-K, we cannot guarantee that the future results, levels of activity, performance, or events and circumstances reflected in the forward-looking statements will be achieved or occur at all. You should refer to the section entitled "Risk Factors," set forth in Part I, Item 1A of this Annual Report on Form 10-K for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. Except as required by law, we undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results, performance or achievements may be materially different from what we expect. 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.

Trademark Notice
AEROSURF®, **AFECTAIR®**, **SURFAXIN®**, **SURFAXIN LS™**, **WINDTREE THERAPEUTICS® (logo)**, **WINDTREE THERAPEUTICS™**, and **WINDTREE™** are registered and common law trademarks of Windtree Therapeutics, Inc. (Warrington, PA).

WINDTREE THERAPEUTICS, INC.

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PART I

ITEM 1. BUSINESS.

Overview

We are a biotechnology company focused on advancing early and late-stage innovative therapies for critical conditions and diseases. Our portfolio of product candidates includes istaroxime, a Phase 2 candidate with sarco endoplasmic reticulum Ca2+ -ATPase 2a, or SERCA2a, activating properties for acute heart failure and associated cardiogenic shock, preclinical SERCA2a activators for heart failure, rostafuroxin for the treatment of hypertension in patients with a specific genetic profile, and a preclinical atypical protein kinase C iota, or aPKCi, inhibitor (topical and oral formulations), being developed for potential application in rare and broad oncology indications. We also have a licensing business model with partnership out-licenses currently in place.

Our lead product candidate, istaroxime, is a first-in-class, dual-acting agent being developed to increase blood pressure and improve cardiac function in patients with cardiogenic shock and to improve cardiac function in patients with acute heart failure, or AHF, and reverse the hypotension and hypoperfusion associated with heart failure that deteriorates to cardiogenic shock. Istaroxime demonstrated significant improvement in both systolic and diastolic aspects of cardiac function and was generally well tolerated in three Phase 2 clinical trials. Istaroxime has been granted Fast Track designation for the treatment of AHF by the U.S. Food and Drug Administration, or FDA. Based on the profile observed in our Phase 2 clinical studies in AHF, where istaroxime significantly improved cardiac function and systolic blood pressure, or SBP, in acute decompensated heart failure patients and had a favorable renal profile, we initiated a Phase 2 global clinical study, or the SEISMiC Study, to evaluate istaroxime for the treatment of early cardiogenic shock (Society for Cardiovascular Angiography and Interventions, or SCAI, Stage B shock), a severe form of AHF characterized by very low blood pressure and risk for hypoperfusion to critical organs and mortality. In April 2022, we announced our observations in the SEISMiC Study that istaroxime rapidly and significantly increased SBP while also improving cardiac function and preserving renal function. We believe that istaroxime has the potential to fulfill an unmet need in early and potentially more severe cardiogenic shock. We further believe that the data from the SEISMiC Study supports continued development in both cardiogenic shock and AHF. In the fourth quarter of 2023, we initiated an extension to the SEISMiC Study, or the SEISMiC Extension, to evaluate a longer dosing period and to continue to characterize the effects of istaroxime, including activation of SERCA2a. The SEISMiC Extension study is expected to enroll up to 30 subjects with SCAI Stage B cardiogenic shock with data anticipated in the second half of 2024. Additionally, we have recently initiated a small study in more severe SCAI Stage C cardiogenic shock, or SEISMiC C, to evaluate the safety and efficacy of istaroxime in cardiogenic shock patients who are also receiving standard of care rescue therapy for shock. The SEISMiC C study is expected to enroll up to 20 subjects with SCAI Stage C cardiogenic shock with enrollment anticipated to be completed in late 2024. Our ability to complete both of these studies with their intended sample size is dependent upon us securing adequate resourcing for the program through financing efforts or business development activities.

Our heart failure cardiovascular portfolio also includes SERCA2a activators. This research program is evaluating these preclinical product candidates, including oral and intravenous SERCA2a activator heart failure compounds. These candidates would potentially be developed for both acute decompensated and chronic out-patient heart failure. In addition, our cardiovascular drug product candidates include rostafuroxin, a novel product candidate for the treatment of hypertension in patients with a specific genetic profile. We are pursuing potential licensing arrangements and/or other strategic partnerships and do not intend to advance rostafuroxin without securing such an arrangement or partnership.

Our cardiovascular assets and programs are associated with a regional licensed partnership with Lee's Pharmaceutical (HK) Ltd., or Lee's (HK), for the development and commercialization of our product candidate, istaroxime, in Greater China. In addition to istaroxime, the agreement also licenses our preclinical next-generation SERCA2a activators, known as dual mechanism SERCA2a activators, and rostafuroxin, a Phase 2 product candidate for hypertension associated with specific genotypes. In addition, we are supporting the efforts of Lee's (HK) in starting a Phase 3 trial in AHF with istaroxime. Further, we are engaged in discussions regarding potential global licensing partnerships outside of Lee's (HK) territory.

On April 2, 2024, we entered into an Asset Purchase Agreement, or the Asset Purchase Agreement, with Varian Biopharmaceuticals, Inc., or Varian. Pursuant to the Asset Purchase Agreement, we purchased all of the assets of Varian's business associated with a Licence Agreement, dated as of July 5, 2019, by and between Varian and Cancer Research Technology Limited, or the Licence Agreement, including the Licence Agreement, all rights in molecules and compounds subject to the Licence Agreement, know-how and inventory of drug substance, or the Transferred Assets. The Transferred Assets include a novel, potential high-potency, specific, aPKCi with possible broad use in oncology as well as certain rare malignant diseases. The asset platform includes two formulations (topical and oral) of an aPKCi inhibitor. We plan to advance investigational new drug, or IND, enabling activities and are in the process of determining the expected clinical development plan for the platform.

Our ability to advance our development programs is dependent upon our ability to secure additional capital in both the near and long-term, through public or private securities offerings; convertible debt financings; and/or potential strategic opportunities, including licensing agreements, drug product development, and marketing collaboration arrangements, pharmaceutical research cooperation arrangements, and/or other similar transactions in geographic markets, including the U.S., and/or through potential grants and other funding commitments from U.S. government agencies, in each case, if available. We have engaged with potential counterparties in various markets and will continue to pursue non-dilutive sources of capital as well as potential private and public securities offerings. There can be no assurance, however, that we will be able to identify and enter into public or private securities offerings on acceptable terms and in amounts sufficient to meet our needs or qualify for non-dilutive funding opportunities under any grant programs sponsored by U.S. government agencies, private foundations, and/or leading academic institutions, or identify and enter into any strategic transactions that will provide the additional capital that we will require. If none of these alternatives is available, or if available and we are unable to raise sufficient capital through such transactions, we potentially could be forced to limit or cease our development activities, which would have a material adverse effect on our business, financial condition, and results of operations.

Our Development Programs

The table below summarizes the current status and anticipated milestones for our principal product development programs. However, due to the disruptive impact of the COVID-19 pandemic, in the U.S. and globally, and its effect on hospital resources, focus, availability of services, and professional staff, our clinical trials and the next expected milestones of our product candidates have previously been impacted, and it is possible that we may experience additional delays in anticipated timelines and milestones. These timelines are dependent on our ability to secure sufficient capital to continue development without interruption.

Product Candidate	Indication	Status	Next Expected Milestone
Cardiovascular Programs			
Istaroxime	Cardiogenic Shock	Phase 2	Completed clinical study in 60 patients; announced positive topline data results in April 2022. Initiated the SEISMiC Extension study during the third quarter of 2023, which is expected to enroll up to 30 subjects with SCAI Stage B cardiogenic shock. Initiated a study of istaroxime in more severe SCAI Stage C cardiogenic shock during the fourth quarter of 2023 with the initial data readout after 20 patients are enrolled.
Istaroxime	AHF	Phase 2	Plan to utilize cardiogenic shock Phase 2 data and experience, along with the positive Phase 2a and 2b AHF studies, to potentially proceed toward Phase 3 for acute decompensated heart failure in the normal to low SBP population.
Oral SERCA2a Activators	Chronic and AHF	Preclinical	Ongoing preclinical studies; pursuing potential licensing transactions, research partnership arrangements, or other strategic opportunities.
Rostafuroxin	Genetically Associated Treatment Resistant Hypertension	Phase 2	Pursuing licensing arrangements, other strategic partnerships, and/or grant funding.
Oncology Programs			
aPKCi Inhibitor (topical and oral)	Cutaneous Malignancies and Solid Tumors	Preclinical	IND-enabling preclinical studies to support the development options under evaluation. Target diseases are to be determined after a detail multidisciplinary review of the options.

Cardiovascular Programs

Heart failure is a chronic, progressive condition in which patients often experience episodic periods of increased symptoms known as AHF, where the heart fails to adequately pump, resulting in worsening symptoms, including pulmonary and peripheral edema and other severe complications. In the U.S., approximately 6 million people (nearly 2% of the adult population) have heart failure and approximately half of these patients are expected to die within five years of diagnosis; and in the combined U.S., EU and Japan markets, there are more than 18 million patients suffering from heart failure. Heart failure is the leading cause of hospitalization in patients age 65 years and older. AHF can be precipitated by many factors and puts patients at increased risk for morbidity, hospital readmission and mortality. There are more than 1.3 million hospital admissions for heart failure in the U.S. each year and over 2.5 million hospital estimated admissions for AHF in the combined U.S., the European Union, or EU, and Japan markets. We estimate that AHF may represent a potential combined annual addressable market (U.S., EU and Japan) of approximately two million patients with multi-billion-dollar annual market value.

Our lead product candidate in heart failure is istaroxime, a first-in-class, dual action investigational drug that we are developing to treat cardiogenic shock and AHF with a potentially differentiated safety profile from current therapies.

Istaroxime (Early Cardiogenic Shock)

We are evaluating istaroxime for the treatment of early cardiogenic shock, a severe presentation of heart failure characterized by very low blood pressure and risk for hypoperfusion to critical organs which is associated with high mortality and morbidity and is not well treated with current therapies.

In September 2020, we initiated a Phase 2 clinical study of istaroxime for the acute treatment of cardiogenic shock in more severe heart failure patients than previously studied to evaluate the potential to improve blood pressure (primary measure) and cardiac function (secondary measure). The study also evaluated the safety and side effect profile of istaroxime in this patient population. In April 2022, we announced positive topline results with istaroxime in rapidly and significantly raising SBP. In May 2022, we presented data from our positive Phase 2 study of istaroxime in early cardiogenic shock in a late-breaker presentation at the European Society of Cardiology Heart Failure Meeting in Madrid, Spain and, in September 2022, the results were published in the European Journal of Heart Failure. There is a significant unmet medical need in the area of early cardiogenic shock and severe heart failure. Istaroxime demonstrated a meaningful increase in blood pressure while simultaneously increasing cardiac output and preserving renal function in clinical trials of this condition.

In order to continue our development of istaroxime for the acute treatment of cardiogenic shock, during the third quarter of 2023, we initiated the SEISMiC Extension study, which is expected to enroll up to 30 subjects with SCAI Stage B cardiogenic shock. We believe that this extension will advance the characterization of the physiology associated with longer dosing as well as enhancing dose optimization. Additionally, in the fourth quarter of 2023, we commenced with study start up activities for the SEISMiC C study, which is expected to enroll up to 20 subjects with SCAI Stage C cardiogenic shock. We also believe that the SEISMiC Extension and SEISMiC C studies will further characterize the effects associated with SERCA2a activation and will support our clinical and regulatory strategy for istaroxime. We currently do not have sufficient capital to fully complete these clinical trials.

Using cardiogenic shock patient U.S. hospital claims and worldwide prevalence data, we estimate the worldwide total market value of cardiogenic shock to be $1.25 billion. This estimate is calculated by multiplying the patient numbers from the largest markets, by the assumed various regional prices of drug treatment in the acute care market. The addressable market for istaroxime will be a subset of the total market value of $1.25 billion.

Istaroxime (AHF)

In 2019, we announced topline results of a successful Phase 2b clinical trial of istaroxime in which the primary endpoint of cardiac function, E/e' ratio (echocardiographic assessment reflecting changes in pulmonary capillary wedge pressure, or PCWP, or left ventricular filing pressure) as well as other important parameters were significantly improved. Istaroxime has been granted Fast Track designation by the FDA for the treatment of AHF. In April 2020, at the American College of Cardiology 2020 meeting, a new subset analysis from a Phase 2b study of istaroxime in patients hospitalized with AHF was presented. This post-hoc analysis characterized the responses to istaroxime between Caucasian and Asian patients. The analysis demonstrated that the dose of 0.5 µg/kg/min produced a similar response on E/e' and stroke volume index in the two regions studied.

Istaroxime represents a novel approach to the treatment of AHF. It has a dual mechanism of action to improve cardiovascular physiology. Current therapy for heart failure in the hospital typically includes intravenous diuretics and, if the blood pressure is low, supportive therapy with inotropes. Inotropes are often associated with adverse effects such as hypotension, arrhythmias and, in some cases, increased mortality. These drugs are used only if needed to support blood pressure and cardiac function. 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 with a potentially differentiated safety profile from current AHF therapies, including a potential reduction in complications and improvement of other clinical outcomes.

There is substantial potential synergy between our clinical trial program in early cardiogenic shock and our development program in acute decompensated heart failure. Both programs are focused on treating heart failure patients with acute congestion and low blood pressure requiring hospitalization. We believe that this category of heart failure patients (whether they are in shock or not) could particularly benefit from the unique profile and potential ability of istaroxime to improve cardiac function and increase blood pressure while maintaining or improving renal function. Our strategy is to advance istaroxime in cardiogenic shock as the lead indication and utilize this data and experience, along with the positive Phase 2a and 2b AHF studies, already completed, to potentially enter Phase 3 for acute decompensated heart failure in the normal to low SBP population. We currently do not have sufficient capital to execute our clinical trial in AHF and are seeking partnership opportunities to advance the program. We believe the Phase 3 AHF program being planned by our licensing partner in China may provide supportive data for potential AHF programs initiated in the future.

Rostafuroxin

Rostafuroxin is a novel investigational drug product candidate being developed for the treatment of hypertension in patients with a specific genetic profile, which is found in approximately 20% to 25% of the adult hypertensive population. Rostafuroxin has been studied in three Phase 2 clinical trials assessing reduction in blood pressure in a hypertensive population selected in accordance with the specified genetic profile. After positive Phase 2a results, a Phase 2b study was initiated. In this most recent Phase 2b clinical trial, rostafuroxin demonstrated efficacy in Caucasian patients in treatment naïve hypertension. As part of our annual quantitative impairment assessment of indefinite-lived in-process research and development, or IPR&D, intangible assets as of December 1, 2022, we reassessed certain assumptions related to our rostafuroxin drug candidate due to the continued difficulties in current macroeconomic conditions which have continued to make it more challenging to secure the funding needed to conduct the additional Phase 2 clinical trial and have therefore further delayed our intended development of rostafuroxin. As a result, we recorded an impairment of the related intangible asset during the year ended December 31, 2022. We are continuing to pursue licensing arrangements and/or other strategic partnerships for rostafuroxin. We do not intend to conduct the additional Phase 2 clinical trial without securing such an arrangement or partnership.

According to the Centers for Disease Control and Prevention, or the CDC, patients with high blood pressure have a greater risk for heart disease and stroke, which are leading causes of death in the U.S. Nearly half of adults in the U.S. (116 million, or 47%) have hypertension defined as a SBP ≥ 130 mm Hg or a diastolic blood pressure ≥ 80 mm Hg or are taking medication for hypertension. In 2020, more than half a million deaths in the U.S. included hypertension as a primary or contributing cause. Only about 1 in 4 adults (24%) with hypertension have their condition under control. 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. 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.

SERCA2a Activators – Preclinical Oral, Chronic and AHF Product Candidates

We are conducting early exploratory research to assess potential product candidates, including oral and intravenous SERCA2a activator heart failure compounds, and believe that we can add value to our cardiovascular portfolio by advancing these SERCA2a

activator candidates through preclinical studies. These preclinical programs build upon our expertise in the SERCA2a mechanism, that led to the development of istaroxime, the first-in-class dual mechanism agent that acts by: (i) partially inhibiting the Na+/K+ pump resulting in an inotropic effect and (ii) stimulating the SERCA2a pump activity on sarcoplasmic reticulum strengthening contraction but importantly improving relaxation and diastolic function.

Istaroxime is the first example of a dual acting agent with SERCA2a activation. We also have two families of follow-on compounds in early development. The first are those endowed with the same dual-acting mechanism of action as istaroxime, which may include potential oral bioavailability for chronic use, and the second family are those with only SERCA2a stimulatory activity. We believe that these programs represent a heart failure platform that has already provided new, novel intellectual property and additional potential opportunities that may extend into the out-patient, chronic heart failure market.

To further advance these product candidates, we are actively exploring potential licensing transactions, research partnership arrangements, or other strategic opportunities.

Oncology Programs

Protein kinase inhibitors are a class of anti-cancer therapeutics that has made a significant impact on the treatment of cancers. Among the kinase targets for further development are the Protein Kinase C, or PKC, family, which are key components of many signaling pathways that drive the formation of cancer. Recently, numerous publications in the scientific literature have identified one member of the PKC family, aPKCi, as important in a number of oncogenic signaling pathways. Numerous scientific publications have identified aPKCi as an oncogene, whose presence and activation has been implicated in the development and growth of multiple forms of human cancer including basal cell carcinoma, or BCC, cutaneous T-cell lymphoma, pancreatic, non-small cell lung cancer, or NSCLC, acute myeloid leukemia, and several others. We are planning to advance aPKCi inhibitory compounds that, based on the literature and preclinical studies to date, we believe may be able to target important signaling pathways that are validated in scientific literature, including the Hedgehog (Hh) pathway, the RAS-RAF-MEK pathway, the TGFbeta pathway and the P13K-AKT-mTOR pathway. These signaling pathways are essential to the formation and growth of many tumor types, including BCC, lung, pancreatic, ovarian and colorectal cancers. GLI1 is a transcription factor at the terminal end of the Hh signaling pathway. In certain cancers, activation of GLI1 has been linked to the promotion of cancer properties such as proliferation, metastasis, chemotherapeutic resistance and others, and there has been observed correlation between GLI1 expression and disease severity. Preclinical data showed dose dependent modulation of BCC cell viability and GLI-1 pathway modulation (downstream from systemic pathway smoothened inhibitors) in vitro, as well as dose dependent anti-tumor activity in xenograft mouse models of non-small cell lung cancer and pancreatic ductal carcinoma.

We intend to create and execute a comprehensive clinical, regulatory and CMC development plan that leverages the assets unique characteristics and mechanisms of action on the highest unmet disease needs. We expect that some of the CMC work in process for our active pharmaceutical ingredient, or API, in aPKCi inhibitor (topical) will be applicable to the development efforts and future regulatory submissions for aPKCi inhibitor (oral). We plan to identify and assess the various opportunities across tumor types where there are preclinical data and the mechanism of drug action is appropriate for the disease. We will utilize the input of the Scientific Advisory Committee to create and evaluate this plan. The topical formulation brings options for some unique development opportunities such as BCC with the potential for more limited risk of side effects from therapy, therefore continuing to advance the topical formulation development as well as including this route in our toxicology studies will be an initial priority.

Given the early stage of these product candidates, however, there can be no assurances that we will be able to address this need and we are unable to ascertain with any certainty whether the required preclinical testing can be completed, or completed in a timely fashion, nor whether the preclinical data generated will be sufficient to get regulatory approval or allowance to initiate a human clinical trial.

<u>aPKCi inhibitor (topical formulation previously designated as VAR-101)</u>

The topical (cutaneous) formulation is a small molecule that may have potential for the treatment of BCC. The API in aPKCi inhibitor (topical) has demonstrated dose dependent anti-tumor activity in murine and human BCC cell lines, in studies performed at Cancer Research UK, or CRUK, a charity registered in England and Scotland, and based in London, United Kingdom. CRUK collaborators, including Stanford University under a sponsored research agreement with CRUK, completed the preclinical tumor cell line data and the BCC cell line data that formed the basis for additional “method of use” patents that are included in the License Agreement. These types of in vitro studies in tumor cell lines are typical early-stage models of activity or efficacy when testing a new chemical compound, the data from which is used in regulatory filings for first-in-man clinical trials. These mouse models of BCC and lung cancer were performed by CRUK and their collaborators.

<u>aPKCi inhibitor (oral formulation previously designated as VAR-102)</u>

The oral formulation is a small molecule that may have potential for the treatment of solid tumors. The API in the aPKCi inhibitor (oral)is the same as the API in aPKCi inhibitor (topical). In the scientific literature, the presence and activation of aPKCi has been implicated in the growth of multiple human cancers including NSCLC, pancreatic, and ovarian cancer. The API in aPKCi inhibitor (oral) has demonstrated dose dependent anti-tumor activity in a mouse model of NSCLC (squamous cell lung carcinoma), in studies performed at CRUK and with its collaborators. Preclinical experiments of the API in aPKCi inhibitor (oral), appears to show dose dependent anti-tumor activity in a xenograft non-small cell lung cancer model.

Our Strategy

We intend to maximize the value of our product candidates and proprietary technologies. Our strategy to achieve this goal includes plans to:

- **Continue to study istaroxime for cardiogenic shock and, if the drug demonstrates adequate potential to raise blood pressure and improve cardiac function with an acceptable safety profile, obtain further partnerships to support the late-stage development of an indication in cardiogenic shock.** In March 2022, we completed a 60-patient Phase 2 clinical trial in early cardiogenic shock. In April 2022, we announced positive topline results with istaroxime in raising SBP. We are executing an extension study in cardiogenic shock to advance the characterization of the physiology associated with longer dosing as well as additional dose optimization. We have also initiated a small study in more severe SCAI Stage C cardiogenic shock to provide valuable information on the effects of istaroxime administration in more severe cardiogenic shock patients and istaroxime dosing information when given in addition to currently used rescue medications for shock;

- **Advance istaroxime for the treatment of AHF via our licensed partner regionally and potential future partnerships globally.** We plan to utilize cardiogenic shock Phase 2 data and experience, along with the positive Phase 2a and 2b AHF studies, to potentially proceed toward Phase 3 for acute decompensated heart failure in the normal to low SBP population subject to obtaining adequate funding;

- **Advance development of chronic and acute preclinical heart failure programs**. In an effort to create added value for our cardiovascular portfolio, we plan to advance oral (chronic) and intravenous (acute) SERCA2a activator product candidates through selected preclinical studies to progress toward submission of an investigational new drug application, or IND, subject to the receipt of adequate resourcing through potential licensing transactions, research partnership arrangements, or other strategic opportunities;

- **Advance development of our aPKCi platform through IND-enablement and into human testing. Our initial focus is on the topical formulation being developed for cutaneous malignancies.** We intend to further refine the full development strategy and plan in the second half of 2024 by matching preclinical data, key product candidate attributes, scientific rationale and market opportunities to help determine what we would believe to be the optimal development path and tumor type program focus; and

- **Enhance our product portfolio and leverage our depth of experience in clinical development and commercialization, we plan to pursue a focused business development agenda directed towards enhancing our current offerings and identifying additional product candidates that enhance our portfolio and provide more opportunity to grow value and diversify risk.** The strategic focus is on areas that fit our market focus (specialty critical, acute care and/or orphan designation), fit our scale for development and cost structure and leverage our therapeutic area and other competencies such as clinical-stage development.

Our Product Candidates

Istaroxime

Our lead cardiovascular product candidate is istaroxime, a novel, first-in-class, dual action investigational drug that we are developing to treat early cardiogenic shock and AHF. Istaroxime has been evaluated in a Phase 2 clinical study for the acute treatment of cardiogenic shock in more severe heart failure patients than previously studied in the Phase 2 AHF program. This study demonstrated the potential of istaroxime to improve blood pressure (primary measure) and cardiac function (secondary measure) while simultaneously increasing cardiac output and preserving renal function. Istaroxime has also been evaluated in two Phase 2 clinical trials in AHF. The results of these studies indicate that istaroxime may improve cardiovascular physiological function as assessed by cardiac output/stroke volume, heart rate, blood pressure and renal function (as measured by glomerular filtration rate) without adverse events such as increased incidence of arrhythmias or cardiac damage (as indicated by elevated troponin values). In August 2019, the FDA granted us Fast Track designation for istaroxime for the treatment of AHF.

AHF and Early Cardiogenic Shock Overview

Early cardiogenic shock is a severe presentation of heart failure characterized by very low blood pressure and risk for hypoperfusion to critical organs. It is associated with high mortality and morbidity and is not well treated with current therapies.

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 critical 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 AHF in a hospital setting are lacking.

Clinical objectives for AHF patient management include: (i) relieve pulmonary congestion and general edema with intravenous diuretics, (ii) improve cardiac function and peripheral / organ perfusion, (iii) achieve a stable, fully compensated clinical state, and (iv) transition to oral, outpatient medicines (for chronic management of their heart failure).

Current approaches to acutely improve cardiac function are associated with unwanted effects including heart rhythm disturbances, increased heart rate and myocardial oxygen demand, decreased blood pressure, potential damage to the heart muscle, worsening renal function, and even increases in mortality have been observed. In particular, patients with low SBP and peripheral hypoperfusion are high risk, challenging patients and are also generally resistant to diuretic therapy and often discharged in a sub-optimal state.

Method of Action

Istaroxime represents a novel approach to the treatment of AHF. It has a dual mechanism of action to improve cardiovascular physiology. First, it inhibits the sodium-potassium ATPase activity leading to improved myocardial contractility. Second, it activates the SERCA2a calcium pump on the sarcoplasmic reticulum, or SR, leading to enhanced SR calcium uptake and a reduction in cytoplasmic calcium that is thought to improve myocardial relaxation and provide for increased calcium release for the subsequent contraction.

We believe that these mechanisms 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. Data from preclinical, Phase 2a and Phase 2b clinical studies performed to date suggest that istaroxime may improve cardiovascular physiology without an increase in 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, reduce complications, and improve other clinical outcomes when compared to current therapeutic regimens for AHF.

Clinical Development

Early Cardiogenic Shock

After assessing the regulatory landscape and data from the istaroxime Phase 2 clinical program in AHF and discussions with our scientific advisors, we added to our istaroxime development program a study in early cardiogenic shock due to heart failure. We believe that istaroxime may fulfill an unmet medical need in early cardiogenic shock based on the profile observed in prior Phase 2 clinical studies in AHF, in which istaroxime improved cardiac stroke volume and increased SBP, suggesting that istaroxime could potentially contribute to the clinical improvement of select patients in cardiogenic shock due to heart failure.

In the second half of 2020, we initiated a study of istaroxime for the acute treatment of early cardiogenic shock in patients with more severe cases of heart failure, to evaluate the potential to improve blood pressure. This study was a Phase 2 international randomized double-blind placebo-controlled study to assess the effect of istaroxime in patients with early cardiogenic shock due to heart failure. This study included 60 patients (29 assigned to istaroxime and 31 assigned to placebo) receiving study drug infusion over 24 hours. Two istaroxime target doses were utilized in the treatment arm, with approximately half of the patients receiving 1.5 μg/kg/min and approximately half of the patients receiving 1.0 μg/kg/min. The primary endpoint was the change in SBP over six hours after initiating the infusion. Secondary endpoints included characterization of blood pressure changes over 24 hours, the number of patients requiring rescue therapy (vasopressors, inotropes, or mechanical devices), assessment of renal function and measures associated with safety and tolerability. The study also evaluated the safety and side effect profile of istaroxime in this patient population. In March 2022, we completed enrollment. In April 2022, we announced positive topline results with istaroxime in raising SBP. In May 2022, we presented the study results at the European Society of Cardiology Heart Failure Meeting in Madrid, Spain.

- The study met its primary endpoint in SBP profile over six hours, with the istaroxime treated group performing significantly better compared to the control group (p =0.017). The improvement persisted through the 24-hour SBP profile measurement, which was also statistically significant (p=0.025).

- SBP increases were rapid within the first hour and sustained throughout the 96-hour post-infusion measure.

- Istaroxime treatment demonstrated improvement in cardiac index compared to the control (p = 0.016). Patients treated with istaroxime also experienced a substantial increase in stroke volume (the amount of blood pumped from the heart with each contraction).

- Several other secondary cardiac assessments were significantly improved including left atrial area and left ventricular end systolic volume. Left ventricular end diastolic volume was also decreased with treatment.

- Renal function (GFR) was maintained.

- Istaroxime was generally well tolerated with the 1.0 µg/kg/min dose group performing numerically better on efficacy and safety than the 1.5 µg/kg/min dose group. There were more reports of nausea, vomiting and infusion site pain in the istaroxime treated patients. There were no differences in arrhythmias through the 48 hour after study drug administration as determined by Holter monitoring. All-cause mortality was greatest in the 1.5 µg/kg/min istaroxime dose group (3) while the endpoint of all-cause mortality or heart failure readmission through 30 days favored the istaroxime 1.0 µg/kg/min dose group.

The results of this study in early cardiogenic shock due to heart failure confirmed and extended the profile of istaroxime in decompensated heart failure and provided valuable information to advance the program in shock and AHF.

AHF

Istaroxime has been evaluated in six clinical trials assessing various doses in 280 patients, including two AHF Phase 2 clinical trials. In a Phase 2a randomized, double-blind, placebo-controlled, dose-escalation clinical trial, three doses of istaroxime were evaluated in a study of 120 hospitalized patients (approximately 30 patients per cohort) with AHF and reduced left ventricular ejection fraction. The three doses of istaroxime were administered intravenously over six hours. In this clinical trial, the primary endpoint of lowering of PCWP was significantly improved in all three doses relative to placebo, and certain secondary hemodynamic endpoints (increased SBP 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 provided the basis for moving the program forward into a Phase clinical 2b trial and for selecting the doses to study.

The primary endpoint of the istaroxime Phase 2b clinical trial for AHF was a change from baseline to 24 hours after start of infusion (Day 1) in E/e' with istaroxime 0.5 or 1.0 µg/kg/min compared to placebo. The E/e' ratio is a marker of the function of the left ventricle, or LV, of the heart and was measured using doppler echocardiography read by a central laboratory. Secondary endpoints included change in other parameters of cardiac function, such as diastolic function, or E/A, stroke volume, or SVI, left ventricle ejection fraction, or LVEF, LV volumes, left atrial, or LA, area, interior vena cava, or IVC, diameter. A 24-hour infusion of istaroxime was associated with significant improvements in cardiac function, in both dosing groups, with a mean E/e' of -4.55 for the 0.5 µg/kg/min group and -3.16 for the 1.0 µg/kg/min group, compared with mean placebo E/e' ratios of -1.55 and -1.08, respectively. Twenty-four-hour infusions of istaroxime were also associated with substantial increases in stroke volume in both dosing groups, with a mean SVI value of 5.33 ml/beat/m^2 for the 0.5 µg/kg/min group and 5.49 ml/beat/m^2 for the 1.0 µg/kg/min group, compared with the mean placebo SVI of 1.65 ml/beat/m^2 and 3.18 ml/beat/m^2, respectively. Importantly, subjects also maintained or increased SBP, with a mean change in SBP of 2.82 mmHg for the 0.5 µg/kg/min group and 6.1 mmHg for the 1.0 µg/kg/min group, compared with the mean placebo SBP values of -2.47 mmHg and 2.7 mmHg, respectively. 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 decreased, during the infusion with istaroxime. The findings were consistent with the physiologic improvements seen in the Phase 2a study of istaroxime in AHF.

Istaroxime was generally well tolerated. Istaroxime did not appear to be associated with an increased risk for arrhythmias or increases in cardiac troponin T. The rate of cardiovascular-related adverse events was 23% for placebo, 10% for istaroxime low dose, and 18% for istaroxime high dose, with cardiac failure occurring in 3%, 5% and 8% of placebo, low dose and high dose patients, respectively. The cases of cardiac failure were reported by the investigator as "worsening of heart failure" symptoms that occurred approximately 10-14 days after study drug administration and were not considered to be drug related. The most common adverse drug reactions reported included pain at infusion site, generally associated with use of short catheters, and dose-related gastrointestinal adverse events in 5%, 10% and 38% of placebo, low dose and high dose patients, respectively. Serious adverse events included one cardiac death and one case of cardiogenic shock (in the same patient who died) in the istaroxime 1.0 µg/kg/min group, two cases of cardiac failure in the 0.5 µg/kg/min group, three cases of cardiac failure in the 1.0 µg/kg/min group, and one case of renal embolism in the 1.0 µg/kg/min group.

Manufacturing

Istaroxime is manufactured for us by an affiliate of Lee's (HK).

The active pharmaceutical ingredient, or API, used in production of the drug product candidate is manufactured by ScinoPharm Taiwan, Ltd.

We contracted with Clinigen for the receipt, labeling, packaging and distribution of drug and materials to support the istaroxime Phase 2 clinical trial in early cardiogenic shock.

Rostafuroxin

Rostafuroxin is a novel investigational drug product candidate being developed for the treatment of hypertension in patients with a specific genetic profile, which is found in approximately 20% to 25% of the adult hypertensive population.

Hypertension Overview

According to the CDC, patients with high blood pressure have a greater risk for heart disease and stroke, which are leading causes of death in the U.S. Nearly half of adults in the U.S. (116 million, or 47%) have hypertension defined as a SBP ≥ 130 mm Hg or a diastolic blood pressure ≥ 80 mm Hg or are taking medication for hypertension. In 2020, more than half a million deaths in the U.S. included hypertension as a primary or contributing cause. Only about 1 in 4 adults (24%) with hypertension have their condition under control. 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. 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 are currently engaged in a process to test the industry's interest in investing in new drugs in this market, and plan to pursue potential licensing transactions and/or other strategic opportunities with a company that has interest in and/or operates in the anti-hypertension market.

Method of Action

Rostafuroxin 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 targeting vascular alterations associated with this type of hypertension.

Clinical Development

Rostafuroxin has been studied in three Phase 2 clinical trials assessing reduction in blood pressure 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.

Rostafuroxin has demonstrated efficacy in Caucasian patients in treatment naïve hypertension in a Phase 2b trial. As part of our annual quantitative impairment assessment of indefinite-lived in-process research and development, or IPR&D, intangible assets as of December 1, 2022, we reassessed certain assumptions related to our rostafuroxin drug candidate due to the continued difficulties in current macroeconomic conditions which have continued to make it more challenging to secure the funding needed to conduct the additional Phase 2 clinical trial and have therefore further delayed our intended development of rostafuroxin. As a result, we recorded an impairment of the related intangible asset during the year ended December 31, 2022 (See the section titled, "Note 4 – Accounting Policies – Intangible Assets and Goodwill"). We are continuing to pursue licensing arrangements and/or other strategic partnerships for rostafuroxin. We do not intend to conduct the additional Phase 2 clinical trial without securing such an arrangement or partnership.

Manufacturing

The drug product candidate for rostafuroxin is manufactured by an affiliate of Lee's (HK).

The active pharmaceutical ingredient, or API, used in the production of the drug product candidate is manufactured by SciAnda (Changshu) Pharmaceutical, Ltd.

Preclinical Heart Failure Product Candidates

We are pursuing early exploratory research to assess our preclinical follow-on oral and intravenous SERCA2a activator heart failure compounds. To advance these product candidates, we are actively exploring potential licensing transactions, research partnership arrangements, or other strategic opportunities.

Preclinical Heart Failure Product Candidates

We are pursuing early exploratory research to assess our preclinical follow-on oral and intravenous SERCA2a activator heart failure compounds. To advance these product candidates, we are actively exploring potential licensing transactions, research partnership arrangements, or other strategic opportunities.

Preclinical Oncology Product Candidates

Our lead oncology product candidate is an aPKCi inhibitor with potential topical and oral formulations.

Method of Action

Protein kinase inhibitors are a class of anti-cancer therapeutics that has made a significant impact on the treatment of cancers. Among the kinase targets for further development are the PKC family, which are key components of many signaling pathways that drive the formation of cancer. Recently, numerous publications in the scientific literature have identified one member of the PKC family, aPKCi, as important in a number of oncogenic signaling pathways. We believe that our aPKCi compound has the potential to target key signaling pathways that are validated in scientific literature, including the Hedgehog (Hh) pathway, the RAS-RAF-MEK pathway, the TGFbeta pathway and the P13K-AKT-mTOR pathway. These signaling pathways are essential to the formation and growth of many tumor types, including BCC, lung, pancreatic, ovarian and colorectal cancers.

Preclinical Development

Our initial focus is on the topical formulation being developed for cutaneous malignancies. Because of the signaling pathways mentioned previously, basal cell skin cancer is an example of the type of cutaneous malignancy where an aPKCi inhibitor could potentially be efficacious. BCC originates in the basal part of the epidermis in sun-exposed skin surfaces. BCC is the most common form cancer in humans, and the most common form of skin cancer, estimated to occur in more than 3 million Americans annually. While rarely fatal, multiple BCCs (synchronous and metachronous) can occur in a single individual and can be destructive and disfiguring, especially when treatment is inadequate or delayed. BCC occurs on the head and neck (including face) in the majority of cases.

We intend to further refine the full development strategy and by the second half of 2024, we intend to analyze our optimal development path and tumor type program focus by assessing preclinical data, key product candidate attributes, scientific rationale and market opportunities.

Manufacturing

We do not own or operate manufacturing facilities for the production of topical or oral formulations of our aPKCi inhibitor or the APIs. We plan to rely upon third-party contract manufacturing organizations, or CMOs, to produce these product candidates. We believe that any materials required for the manufacture of these drug candidates could be obtained from more than one source.

Material Licenses and Collaborations

License, Development and Commercialization Agreement with Lee's Pharmaceutical (HK) Ltd.

On January 12, 2024, we entered into a License, Development and Commercialization Agreement with Lee's (HK) effective as of January 7, 2024, or the Lee's (HK) License Agreement. Under the Lee's (HK) License Agreement, we granted an exclusive license, with a right to sublicense, to develop, register, make, use, sell, offer for sale, import, distribute and otherwise commercialize products that incorporate istaroxime for intravenous administration, rostafuroxin for oral administration, and our proprietary dual-mechanism SERCA2a activators for intravenous or oral administration, in each case for the prevention, mitigation and/or treatment of any disease, disorder or condition in humans including acute decompensated heart failure, cardiogenic shock, and chronic use following discharge of an individual hospitalized for acute decompensated heart failure in the Greater China region (See the section titled, "Note 18 – Subsequent Events").

Amended and Restated License, Development and Commercialization Agreement with Lee's Pharmaceutical (HK) Ltd. and Zhaoke Pharmaceutical (Hefei) Co. Ltd.

On August 17, 2022, we entered into an Amended and Restated License, Development and Commercialization Agreement, or the A&R License Agreement, with Lee's (HK) and Zhaoke Pharmaceutical (Hefei) Co. Ltd., or Zhaoke, a company organized under the laws of the People's Republic of China, effective as of August 9, 2022. We refer to Zhaoke and Lee's (HK) together as the "Licensee" and each of which is an affiliate of Lee's Pharmaceutical Holdings Limited, or Lee's Holdings. The A&R License Agreement amends, restates and supersedes the Original License Agreement. The Original License Agreement previously granted Lee's (HK) an exclusive license to develop, market and sell non-aerosolized KL4 surfactant for the treatment of human diseases and aerosolized KL4 surfactant (including AEROSURF, our investigative combination drug/device product) for the treatment of human respiratory diseases, in each case in Greater China, Japan, South Korea and certain other Southeast Asia countries. Under the A&R License Agreement, we granted to Licensee an exclusive license, with a right to sublicense, to develop, register, make, use, sell, offer for sale, import, distribute, and otherwise commercialize our KL4 surfactant products, including SURFAXIN®, the lyophilized dosage form of SURFAXIN, and aerosolized KL4 surfactant, in each case for the prevention, mitigation, and/or treatment of any respiratory disease, disorder, or condition in humans worldwide, except for Andorra, Greece, and Italy (including the Republic of San Marino and Vatican City), Portugal, and Spain, or the Licensed Territory, which countries are currently exclusively licensed to Laboratorios Del Dr. Esteve, S.A., or Esteve . If and when the exclusive license granted to Esteve terminates as to any country, such country automatically becomes part of the Licensed Territory of Licensee.

Under the Original License Agreement, Lee's (HK) previously made an upfront payment to us of $1.0 million. Pursuant to the terms of the A&R License Agreement, we may also receive up to $78.9 million in potential clinical, regulatory and commercial milestone payments. We are also entitled to receive a low double-digit percentage of Licensee's non-royalty sublicense income. We are also eligible to receive tiered royalties based on a percentage of Net Sales (as defined in the A&R License Agreement) that ranges from low single digit to low teen percentages, depending on the product. Royalties are payable on a product-by-product and country-by-country basis until the latest of (i) the expiration of the last valid patent claim covering the product in the country of sale, (ii) the expiration or revocation of any applicable regulatory exclusivity in the country of sale, and (iii) ten years after the first commercial sale of the product in the country of sale. Thereafter, in consideration of licensed rights other than patent rights, royalties shall continue for the commercial life of each product but at substantially reduced rates. In addition, the royalty rates are subject to reduction by as much as 50% in a given country based on generic competition in such country.

Under the A&R License Agreement, Licensee will be solely and exclusively responsible for all costs and activities related to the development, manufacturing, regulatory approval and commercialization of licensed products in the Licensed Territory including all royalties payable in respect of third-party intellectual property rights sublicensed by us to Licensee and all intellectual property prosecution, maintenance and defense activities and costs. Licensee may sublicense certain activities under the A&R License Agreement to an affiliate of Licensee but may not grant sublicenses to unaffiliated third parties without our prior consent and, if the proposed sublicense will cover the United States, without first complying with rights of first offer and rights to match granted to us under the A&R License Agreement. A sublicensee and a subcontractor may not be a competitor identified by us. Sublicenses under the A&R License Agreement do not include the right to further sublicense.

The term of the A&R License Agreement will continue on a country-by-country basis for the commercial life of the products. Either party may terminate the A&R License Agreement in the event of bankruptcy or a material breach of the A&R License Agreement by the other party that remains uncured for a period of sixty (60) days (or within 30 days after delivery of a Default Notice (as defined in the A&R License Agreement) if such material breach is solely based on the breaching party's failure to pay amount due under the A&R License Agreement). At any time after the second anniversary of the A&R License Agreement, Licensee may terminate the A&R License Agreement in its entirety or on a product-by-product basis. In addition, either party may terminate the A&R License Agreement with respect to any individual product in a country if a regulatory authority in such country terminates, suspends or discontinues development of such product and such termination, suspension or discontinuance persists for a period in excess of eighteen (18) months. Upon termination of the A&R License Agreement in its entirety or with respect to a particular product or country, generally all related rights and licenses granted to Licensee will terminate, all rights under our technology will revert to us, and Licensee will cease all use of our technology, in each case in relation to the terminated product(s) and country(ies), as applicable.

Universita degli Studi di Milano-Bicocca Collaboration Agreement

In April 2015, our subsidiary, CVie Therapeutics Limited, or CVie Therapeutics, entered into an Agreement for Scientific Collaboration, or the 2015 Agreement, with the Universita degli Studi di Milano-Bicocca, or Bicocca, in Milan, Italy, focused on defining the role of SERCA2a and phospholamban in modulating cardiac contraction, and discovering new small molecules to modulate SERCA2a activity or new drugs for treating chronic and acute human heart failure. The initial term of the 2015 Agreement, which was three years, was extended for approximately an additional year, with an option for further renewal. In June 2019, we entered into a new Agreement for Scientific Collaboration with Bicocca, or the 2019 Agreement, focused on continuing the studies under the 2015 Agreement. The 2019 Agreement supersedes and replaces all prior agreements with Bicocca.

Under the 2019 Agreement, we provided funds aggregating € 0.16 million to extend our use of Bicocca laboratories and to fund research conducted pursuant to the collaboration. (Under the 2015 Agreement, Bicocca had given us exclusive use of a research laboratory for the collaboration work, and nonexclusive access to a physiology laboratory within the university.) Under the 2019 Agreement, any results obtained from the collaboration are jointly owned by the parties. However, Bicocca has agreed to assign to us its interest in patent applications and patents covering any new SERCA2a activator compounds and diagnostic products suitable for further clinical development. We agreed to pay Bicocca (corresponding to stage of development): (i) € 0.1 million for new SERCA2a activator compounds developed up to Phase 1 studies in humans upon the completion and availability of the proof of concept of biological efficacy of new compounds on modulating the SERCA2a activity in cell-free systems, or its functional counterpart in cardiac myocytes and (ii) € 1.5 million upon obtaining marketing authorization in the U.S., EU or China of new compounds with the corresponding companion diagnostic assay. We have also agreed to pay royalties on products generated from the collaboration in the range of a fraction of a single digit to a low single digit percent of net sales for any products sold in any country for a period of ten years from the date of the first commercial sale or until the expiry of patent(s) covering the products.

On March 19, 2021, we entered into an Agreement for Scientific Collaboration, or the New SERCA2a Agreement, with Bicocca, which extends our collaboration. The New SERCA2a Agreement amends and restates the recently expired terms of the 2019 Agreement. Under the New SERCA2a Agreement, we provided Bicocca with approximately € 0.2 million for research activities and to cover laboratory space and operation costs. Results obtained from the collaboration were jointly owned by the parties. However, Bicocca assigned to us its interest in patent applications and patents covering any new SERCA2a compounds and diagnostic products suitable for further clinical development. We agreed to pay Bicocca (corresponding to stage of development): (i) € 25,000 for execution of an assignment to us of Bicocca's interest in the patent at issue, (ii) € 75,000 for new SERCA2a compounds developed up to Phase 1 studies in humans upon the completion and availability of the proof of concept of biological efficacy of new compounds on modulating the SERCA2a activity in cell-free systems, or its functional counterpart in isolated cells and (iii) € 1.5 million upon obtaining marketing authorization in the U.S., EU, or China of new compounds with the corresponding companion diagnostic assay. We have also agreed to pay royalties on products generated from the collaboration in the range of a fraction of a single digit to a low single digit percent of net sales for any products sold in any country for a period of ten years from the date of the first commercial sale or until the expiry of patent(s) covering the products.

Our agreement with Universita Degli Studi di Milano-Bicocca, the institution that has performed many preclinical studies with istaroxime and our preclinical families of compounds, expired on July 31, 2022. If additional preclinical work is required for any reason, we will need to re-engage with Bicocca or find another vendor to provide those services.

Philip Morris License Agreements

In 2008, we entered into an Amended and Restated License Agreement with Philip Morris USA, Inc., or PMUSA, with respect to the U.S., or the U.S. License Agreement, and, as PMUSA had assigned its ex-U.S. rights to Philip Morris Products S.A., or PMPSA, effective on the same date and on substantially the same terms and conditions, we entered into a license agreement with PMPSA with respect to rights outside of the U.S., which we refer to, together with the U.S. License Agreement, as the PM License Agreements. Under the PM License Agreements, we have worldwide exclusive rights to the PMUSA and PMPSA proprietary capillary aerosol technology, which is a key component of our ADS, for use in a drug/device combination product with pulmonary surfactants (alone or in combination with other pharmaceutical compounds) for all respiratory diseases and conditions. In addition, under the U.S. License Agreement, our license to use the capillary aerosol technology includes certain non-surfactant drugs to treat certain designated pediatric and adult respiratory indications in hospitals and other health care institutions. See the section titled, "– Patents and Proprietary Rights – Aerosol Delivery System (ADS) Patent Rights."

The PM License Agreements provide for the payment of royalties at a rate equal to a low single-digit percentage of sales of products sold in the Exclusive Field (as defined in the PM License Agreements) in the territories. In connection with exclusive undertakings of PMUSA and PMPSA not to exploit the aerosol technology for all licensed uses, royalties on all product sales, including sales of certain aerosol devices that are not based on the licensed aerosol technology are contemplated; provided, however, that no royalties are payable to the extent that we exercise our right to terminate the license with respect to a specific indication. While there is no legal obligation under the PM License Agreements to make minimum royalty payments, in the event we do not make quarterly minimum royalty payments, PMUSA and PMPSA can terminate the PM License Agreements. In making such payments, we are entitled to reduce future quarterly royalties above the quarterly minimums in the amount of the true-up payments we make to satisfy minimum royalties for prior quarters. Our license rights extend to innovations to the aerosol technology that are made under the PM License Agreements.

In addition to customary termination provisions for breach of the agreements, we may terminate the PM License Agreements, in whole or in part, upon advance written notice to the licensor. In addition, either party to each PM License Agreement may terminate upon a material breach by the other party (subject to a specified cure period). PMUSA and PMPSA may also terminate the PM License Agreements in the event that we fail to make certain minimum royalty payments. Our license under each PM License Agreement, unless terminated earlier, will expire as to each licensed product, on a country-by-country basis, upon the latest to occur of: the date on which the sale of such licensed product ceases to be covered by a valid patent claim in such country; the date a generic form of the product is introduced in such country; or the tenth anniversary of the first commercial sale of such licensed product.

Pursuant to the A&R License Agreement described above, Licensee has agreed to assume certain of our obligations under the PM License Agreements.

On January 16, 2024, we entered into Amendment No. 1 to the U.S. License Agreement with PMUSA and also entered into Amendment No. 1 to the License Agreement with PMPSA in which the parties extinguished and released their respective rights,

obligations and claims in respect of quarterly payments in effect immediately prior to January 17, 2024 (See the section titled, "Note 9 – Other Current Liabilities").

Battelle Collaboration Agreement

In October 2014, we entered into a Collaboration Agreement with Battelle, or, as amended, the Battelle Collaboration Agreement, for the development of our new ADS for use in our Phase 3 program. We had previously worked with Battelle, which has expertise in developing and integrating aerosol devices using innovative and advanced technologies, in connection with development of our Phase 2 ADS used in the AEROSURF Phase 2b clinical trial. Under the Battelle Collaboration Agreement, we and Battelle shared the costs of development for a three-stage development plan that included planning, executing the project plan and testing and completing verification and documentation of a new Phase 3 ADS, putting us in a position to manufacture a new Phase 3 ADS for use in the remaining AEROSURF development activities, including a potential Phase 3 clinical program, and, if approved, initial commercial activities. We retained final decision-making authority over all matters related to the design, registration, manufacture, packaging, marketing, distribution and sale of the Phase 3 ADS. We and Battelle shared the costs of the project plan equally. Battelle agreed to bear the cost of any cost overruns associated with the project plan and we agreed to bear the cost of any increase in cost resulting from changes in the scope of the product requirements. We also agreed that, if Battelle successfully completed the project plan in a timely manner, we would pay Battelle royalties equal to a low single-digit percentage of the worldwide net sales and license royalties on sales of AEROSURF for the treatment of RDS in premature infants, up to an initial aggregate limit of $25.0 million, which under a payment restructuring agreement (discussed below), was increased to $35.0 million. The Battelle Collaboration Agreement will end at the time we fulfill our payment obligations to Battelle, unless sooner terminated by a party as provided therein.

Pursuant to the A&R License Agreement described above, Licensee has agreed to assume certain of our obligations under the Battelle Collaboration Agreement.

Laboratorios del Dr. Esteve, S.A. Strategic Alliance

We have a strategic alliance with Esteve for the development, marketing and sales of a broad portfolio of potential KL4 surfactant products in Andorra, Greece, and Italy (including the Republic of San Marino and Vatican City), Portugal, and Spain, or, collectively, the Territory. Under the alliance, Esteve will pay us a transfer price on sales of our KL4 surfactant products. We are responsible for the manufacture and supply of all of the covered products and Esteve will be responsible for all sales and marketing in the Territory. Esteve is obligated to make stipulated cash payments to us upon our achievement of certain milestones, primarily upon receipt of marketing regulatory approvals for the covered products. In addition, Esteve has agreed to contribute to Phase 3 clinical trials for the covered products by conducting and funding development performed in the Territory. As part of a 2004 restructuring, Esteve returned certain rights to us in certain territories, or the Former Esteve Territories, and we agreed to pay Esteve 10% of any cash up front and milestone fees (up to a maximum aggregate of $20.0 million) that we receive in connection with any strategic collaborations for the development and/or commercialization of certain of our KL4 surfactant products in the Former Esteve Territories. In addition, with respect to our aerosolized KL4 surfactant, Esteve will pay us $0.5 million upon the initial filing for regulatory approval with the European Medicines Agency, or EMA, and $0.5 million upon receipt of regulatory approval. Esteve will also contribute up to $3 million to support a Phase 3 clinical trial in the Territory. The alliance will terminate as to each covered product, on a country-by-country basis, upon the latest to occur of: the expiration of the last patent claim related to a covered product in such country; the first commercial sale in such country of the first-to-appear generic formulation of the covered product, and the tenth anniversary of the first sale of the covered product in such country. In addition to customary termination provisions for breach of the agreement by a party, the alliance agreement may be terminated by Esteve on 60 days' prior written notice, up to the date of receipt of the first marketing regulatory approval, or, on up to six months' written notice, if the first marketing regulatory approval has issued. We may terminate the alliance agreement in the event that Esteve acquires a competitive product (as defined in the agreement).

Johnson & Johnson License Agreement

Our precision-engineered KL4 surfactant technology was invented at The Scripps Research Institute, or Scripps, and was exclusively licensed to and further developed by Johnson & Johnson, or J&J. Pursuant to a license agreement, dated October 28, 1996, with J&J and its wholly owned subsidiary, Ortho Pharmaceutical Corporation, or the J&J license, we obtained an exclusive, worldwide license and sublicense to a series of over 30 patents and patent filings (worldwide), or the J&J Patents. All J&J Patents have expired. Under the license agreement, we are obligated to pay the licensors fees of up to $3.0 million in the aggregate upon our achievement of certain milestones, primarily upon receipt of marketing regulatory approvals for certain designated products. We have made milestone payments totaling $1.0 million to date. In addition, the agreement provides that we are required to pay royalties at different rates based on the type of revenue and country, in amounts in the range of a high single-digit percent of net sales (as defined in the license agreement) of licensed products sold by us or sublicensees, or, if greater, a percentage of royalty income from sublicensees in the low double digits. The license agreement provides that the license will expire, on a country-by-country basis, upon the payment of royalties for all licensed products for ten years beginning on the date of the first commercial sale of the first licensed product in such country. Thereafter, the license agreement provides that royalties shall be paid in respect of a licensed product until the expiration of the last licensed patent containing a valid claim covering the licensed product in such country. For countries in the EU in which royalties are paid only by virtue of licensed know-how, royalties shall be payable commencing from the date of first commercial sale of the first licensed product in such country and ending on the earlier of (i) the date on which the licensed know-how becomes public or (ii) the tenth anniversary of the first commercial sale of the first licensed product in any country of the EU. In addition to customary termination provisions for breach of the agreement by a party, we may terminate the agreement, as to countries other than the U.S. and Western Europe territories (as defined in the agreement), on a country-by-country basis, on six months' prior written notice; and as to the entire agreement, on 60 days' prior written notice.

Pursuant to the A&R License Agreement described above, Licensee has agreed to assume certain of our obligations under the J&J license agreement.

Intellectual Property

We continue to invest in maintaining and enforcing our potential competitive position through a number of means: (i) by protecting our exclusive rights in our cardiovascular agents including istaroxime, rostafuroxin and SERCA2a activators, (ii) by protecting our exclusive rights in our lyophilized KL4 surfactant, ADS and aerosol-conducting airway connector technologies through patents that we own or exclusively license, (iii) by protecting our exclusive rights in our early-stage oncology platform through patents that we exclusively license, (iv) by seeking regulatory exclusivities, including potential Orphan Drug and new drug product exclusivities, and (v) through protecting our trade secrets and proprietary methodologies that support our manufacturing and analytical processes.

Patents and Proprietary Rights

In addition to the inventions covered by the patents and patent applications described in this Annual Report on Form 10-K, we have been active in identifying and seeking to identify new inventions eligible for patent protection. We have filed and plan to file patent and provisional patent applications to protect our innovations relating to our current and potential future product candidates, including for composition of matter, new dosage forms, formulations, methods of manufacture, methods of use and related processes. We intend to file for patent protection for select inventions, in such markets that we deem material to our patent strategy, as well as for other new inventions that we may identify.

Our Patents and Patent Applications Related to Istaroxime and SERCA2a Activators

We hold a patent portfolio of three patent families that include patents and patent applications directed to compounds, pharmaceutical formulations, methods of manufacturing, methods of delivery, and/or treatment methods using istaroxime and its metabolites and/or derivatives, as well as SERCA2a activators, for the treatment of cardiovascular diseases and related conditions. We plan to continue these patent activities and focus on new follow-on compounds, dosage forms, formulations, and treatment methods related to AHF and persistent hypertension. To benefit from potential non-patent exclusivity within the U.S., we believe that we may qualify istaroxime as a new chemical entity entitled to market exclusivity for a period of years. See the section titled "– Government Regulation – Drug Products – The Hatch-Waxman Act – Market Exclusivity."

Istaroxime-Related Patents and Patent Applications

In November 2019, we filed an international patent application PCT/US2019/060961, directed to methods of treating AHF through an extended istaroxime dosing regimen, as well as to metabolites of istaroxime having SERCA2a stimulating activity. The international application entered the national phase in China on December 31, 2019 (Application No. 201980003356.1), and in the following PCT contracting states/regions in September and October of 2021: Australia, Brazil, Canada, European Patent Office, Israel, Hong Kong (extended from China), Hong Kong (extended from the European Patent Office), Japan, Mexico, Republic of Korea, Singapore, and the United States. This patent family will expire on or about November 12, 2039.

Two United States patents based on PCT/US2019/060961 have issued. On February 21, 2023, the United States Patent and Trademark Office, or the USPTO, issued U.S. Patent No. 11,583,540, providing expanded patent coverage for istaroxime administration. The new U.S. patent, titled: "Istaroxime-Containing Intravenous Formulation for the Treatment of Acute Heart Failure (AHF)," issued from a continuing patent application following the expedited U.S. Track One filing by us, which resulted in U.S. Patent No. 11,197,869 that was issued December 14, 2021. The claims of the newly issued patent cover longer durations of istaroxime infusion for improved outcomes in treatment of acute heart failure. In particular, the claims are directed to an improvement in diastolic heart function following administration of istaroxime by intravenous infusion for 6 hours or more, which we attribute to the SERCA2a mechanism of action of istaroxime and its metabolites.

SERCA2A Activators-Related Patents

Two patent application families have resulted from research under the 2019 Agreement with Bicocca. Pursuant to that agreement, those patent families have been assigned to CVie (or to us). In July 2018, the parties to the 2019 Agreement filed European Application No. EP18185753.3, directed to 17ß-heterocyclyl-digitalis like compounds and their use for the treatment of heart failure and related conditions. International application PCT/EP2019/069283, based on the European application, was filed in July 2019. National stage applications based on PCT/EP2019/069283 were filed in January and February 2021 in Australia, Brazil, Canada, China, Hong Kong (extended from China), Hong Kong (extended from the European Patent Office), Israel, Japan, Mexico, Republic of Korea, Singapore, and the United States. Patents granted on this family of applications will expire on or about July 17, 2039.

In April 2023, we announced that the European Patent Office has granted Patent No. 3599243, providing patent coverage for the dual mechanism SERCA2a Activator class of drug candidates. This patent provides protection until July 2038 for the family of compounds with a dual mechanism of action. In August 2023, we announced that the USPTO issued US Patent No. 11,730,746 providing patent coverage for the dual mechanism SERCA2a Activators. The new composition of matter patent, titled: "17BETA-HETEROCYCLYL-DIGITALIS LIKE COMPOUNDS FOR THE TREATMENT OF HEART FAILURE," provides patent protection through late 2039. Since then, patents have issued in China, Hong Kong, and Japan.

In October 2019, the parties to the 2019 Agreement filed European Application No. 19202257.2, directed to androstane derivatives with activity as pure or predominantly pure stimulators of SERCA2a for the treatment of heart failure and related conditions. International application PCT/EP2020/078253 and Taiwan Application No. 109134997, both based on the European application, were filed in October 2020. National stage applications based on PCT/EP/2020/078253 were filed in Australia, Brazil, Canada, China, Hong Kong (extended from the European Patent Office), Israel, Japan, Mexico, Republic of Korea, Singapore, and the United States. Patents granted on this family of applications will expire on or about October 8, 2040.

In November 2023, we announced that the European Patent Office has granted Patent No. 3805243, providing patent coverage for the pure or predominantly pure SERCA2a stimulators class of drug candidates. The patent provides protection until October 2039.

Our KL4 -Related Patents and Patent Rights

We have been active in seeking patent protection for our innovations relating to new dosage forms, formulations and methods of manufacturing and delivering synthetic peptide containing pulmonary surfactants. Our patent activities have focused particularly on improved dosage forms and delivery of aerosolized pulmonary surfactant.

In January 2006, we filed U.S. and international patent applications (U.S. 11/326,885 which is now U.S. Patent No. 7,541,331 issued on June 2, 2009 and PCT/US06/000308), directed to a surfactant treatment regimen for Bronchopulmonary Dysplasia, or BPD. U.S. Patent No. 7,541,331 will expire on or about January 6, 2026.

In September 2007, we filed U.S. and international patent applications (U.S. 11/901,866 which is now U.S. Patent No. 8,221,772 and PCT US/2007/020260), directed to surfactant compositions and methods of promoting mucus clearance and treating pulmonary disorders such as cystic fibrosis. U.S. Patent No. 8,221,772 will expire on or about September 19, 2027.

In March 2013, we filed international patent applications (PCT/US13/34364 and PCT/US13/34464, which entered national phase and commenced expedited examination in the U.S. and EPO) directed to lyophilized pulmonary surfactant and methods of manufacture. In this patent family, two U.S. Patents Nos. 8,748,396 and 8,748,397, were issued on June 10, 2014, European patent 2723323B1 granted on September 23, 2015, U.S. Patent No. 9,554,999, issued on January 31, 2017 and multiple foreign counterparts are granted. U.S. Patents Nos. 8,748,396; 8,748,397 and 9,554,999 and European Patent No. 2723323B1 will expire on or about March 28, 2033.

Aerosol Delivery System (ADS) Patent Rights

Pursuant to the PM Licenses Agreements, we have worldwide exclusive rights to the proprietary capillary aerosol technology incorporated into the ADS for use in a drug/device combination product. The ADS is the medical device component of our AEROSURF product candidate. We completed design verification of the new ADS for use in the remaining AEROSURF development activities, including a Phase 2b bridging study to be conducted in China, potentially a Phase 3 clinical program and, if approved, initial commercial activities.

Our ADS technology and our new ADS are protected by a portfolio of issued patents and pending patent applications covering various components of the system. While certain of the earlier patents on the technology have expired, there remain 90 in-force patents worldwide that protect, among other things, core elements of the ADS technology and the new ADS. These patents and applications will expire on dates ranging from the third quarter of 2023 to 2039. As an illustrative example, important components of our new ADS technology are covered by a patent family represented by US Patent No. 9,713,687, expiring on or about February 10, 2035, and European Patent No. 2887984B1, expiring on or about August 21, 2033. In addition, several key components of our new ADS are covered by recently issued U.S. Patent No. 10,874,818, which expires on or about January 22, 2039.

Aerosol-Conducting Airway Connector Technology Patents and Patent Rights

In March 2009, we filed an international patent application (PCT US/2009/037409) directed to aerosol-conducting airway connectors and improvements of an ADS using AFECTAIR®. The claims of this application are directed to a novel ventilation circuit adaptor (an aerosol-conducting airway connector) and related aerosol circuitry that are intended to (i) increase the efficiency of aerosol delivery to the patient by allowing more efficient delivery of aerosols to the patient and (ii) reduce drug compound dilution and wastage and result in more precise aerosol dosing. This patent family will expire on or about March 17, 2029. Representative examples of patents in this family include U.S. Patent Nos. 8,701,658, 9,352,114 and 9,592,361, as well as European Patent No. 2265309 and counterparts in several other countries.

Our Early-Stage Oncology Platform-Related Patents

Pursuant to the Varian asset purchase, which included an exclusive license from CRT, we have worldwide exclusive rights to a class of PKC inhibitors that have been shown to play a key role in signaling pathways involved in cancer development. The asset platform includes two formulations (topical and oral), which are covered by two patent families directed to azaquinazoline inhibitors of aPKC. There are 43 granted patents, based on international patent applications PCT/US2013/062085 and PCT/US2015/022368, included in these patent families worldwide, expiring on or about September 27, 2033 and March 25, 2035, respectively. Representative examples include U.S. Patent Nos. 9,896,446, 9,914,730, and 10,414,763, as well as European Patent Nos. 2900666 and 3129372.

In addition, methods of using these azaquinazoline inhibitors to treat Hedgehog signaling pathway-related cancers are covered by another patent family represented by international patent application PCT/US2020/025437, which is now in the national phase in the United States, the European Patent Office, and several other nations.

Another patent family in the early-stage oncology platform is directed to thieonpyrimidine inhibitors of aPKC. There are 23 granted patents, based on international patent application PCT/US2012/065831, included in this patent family worldwide, expiring on or about November 19, 2032. Representatives of this patent family include U.S. Patent Nos. 9,604,994,10, 183,950, and 10,954,251, as well as European Patent Nos. 2782917 and 3048106.

Trademarks

AEROSURF®, AFECTAIR®, SURFAXIN®, SURFAXIN LS™, WINDTREE THERAPEUTICS® (logo), WINDTREE™ and WINDTREE THERAPEUTICS™ are our material registered and common law trademarks.

Trade Secrets

In addition to our patent exclusivities, we rely on trade secrets to protect and maintain our competitive position. We take measures to protect and maintain our trade secrets and know-how licensed to us or developed by us by entering in confidentiality agreements with third parties. Our trade secrets and know-how include information related to manufacturing processes for our drug product candidates and devices, analytical methods and procedures, research and development activities, provisional patent applications, as well as certain information provided to the FDA that was not made public which relates to our regulatory activities and clinical trials.

Other Regulatory Designations

Orphan Drug and Orphan Medicinal Product Designations

The FDA has granted Orphan Drug designation for (i) our KL4 surfactant (lucinactant) for the treatment of RDS in premature infants, (ii) our KL4 surfactant for the prevention and treatment of BPD in premature infants, (iii) our KL4 surfactant for the treatment of ARDS in adults, and (iv) our KL4 surfactant for the treatment of CF. See the section titled "– Government Regulation – Drug Products – Orphan Drugs."

The European Commission, or EC, grants orphan medicinal product designation for medicinal products which are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition and either (i) such condition affects no more than 5 in 10,000 people in EU, or (ii) it is unlikely that the marketing of the medicine would generate sufficient returns to justify the necessary investment in its development. In each case, there must also be no satisfactory method of diagnosis, prevention or treatment of the condition concerned authorized in the EU, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition. In the EU, orphan medicinal product designation provides for exclusive marketing rights for the orphan indication in the EU for 10 years (which may be reduced to six years if, at the end of the fifth year, it is established that the orphan designation criteria are no longer met) following marketing approval by the EMA. In addition, the designation would enable us to receive regulatory assistance in the further development process, and to access reduced regulatory fees throughout its marketing life. The EC has granted orphan medicinal product designation for (i) our KL4 surfactant for the prevention of RDS in premature neonates of less than 32 weeks gestational age, (ii) our KL4 surfactant for the treatment of RDS in premature neonates of less than 37 weeks gestational age, (iii) our KL4 surfactant for the treatment of ALI (which in this circumstance encompasses ARDS), and (iv) our KL4 surfactant for the treatment of CF. In submitting the requests to the EMA for orphan medicinal product designations, instead of listing the drug product under the USAN name (lucinactant) as we have in the U.S., we were required to submit our requests under the names of the four APIs in our KL4 surfactant (lucinactant) as follows: sinapultide (KL4), dipalmitoylphosphatidylcholine, palmitoyl-oleoyl phosphatidylglycerol and palmitic acid.

Fast Track Designations

The FDA has granted Fast Track designation for (i) istaroxime for the treatment of AHF, (ii) AEROSURF for the treatment of RDS in premature neonates, and (iii) SURFAXIN® for the prevention and treatment of BPD in premature neonates and the treatment of ARDS in adults. We believe that other of our product candidates may qualify for Fast Track or Breakthrough Therapy designation or other expedited programs. These designations and programs are intended to facilitate and expedite development and review of a New Drug Application, or NDA, to address unmet medical needs in the treatment of serious or life-threatening conditions. See the section titled "– Government Regulation – Drug Products – Fast Track Designation."

Competition

The biotechnology industry is a highly competitive industry. As we work to gain marketing authorization for our product candidates, in some therapeutic areas, competition from numerous existing pharmaceutical companies and other companies entering our fields is expected to be intense and expected to increase. In fact, our future competitors are competing with us currently to secure access to development resources, including clinical sites and their patients to advance development programs. We expect that those companies that are successful at being the first to introduce new products and technologies to the market may gain significant advantages over their competitors in the establishment of a customer base and track record for the performance of their products and technologies. Moreover, there are also existing therapies that may compete with the products we are developing. Therefore, as a development stage biotechnology company, our competitors are comprised of other biotechnology firms and pharmaceutical companies that have existing products or are developing products for our primary markets -- respiratory and cardiovascular indications.

Government Regulation

In the U.S., drug products, medical devices, and drug/medical device combination products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act, or the FDC Act, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, clearance, labeling, promotion, advertising and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of drug products, medical devices, and drug/medical device combination products. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve or clear pending new submissions to market drugs or devices, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution,

injunctions, fines, civil penalties, and criminal prosecution. Drug products, medical devices, and drug/medical device combination products must receive all relevant regulatory approvals or clearances before they may be marketed in the U.S. Drug products, medical devices, and drug/medical device combination products are subject to extensive regulation, including premarket review and marketing authorization, by similar agencies in other countries.

Drug Products

Pharmaceutical product development for a new product or certain changes to an approved product in the U.S. typically involves preclinical laboratory and animal tests, the submission to the FDA of an IND application, which must be accepted before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity, and novelty of the product or disease.

Preclinical tests include laboratory evaluation of product chemistry, formulation, and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements, including good laboratory practices. The results of preclinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long-term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. The FDA may also impose clinical holds on a product candidate at any time before or during clinical trials due to safety concerns, non-compliance, or other issues affecting the integrity of the trial. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial and, once begun, issues may arise that could cause the trial to be suspended or terminated.

Clinical trials involve the administration of the investigational product to volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with good clinical practices, or GCPs, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators, and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with the FDA requirements or presents an unacceptable risk to the clinical trial patients. The study protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board, or IRB, for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the drug into human subjects or patients, the drug is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence on effectiveness. Phase 2 usually involves trials in a limited patient population to determine the effectiveness of the drug for a particular indication, dosage tolerance, and optimum dosage, and to identify common adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to obtain the additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit the FDA to evaluate the overall benefit- risk relationship of the drug and to provide adequate information for the labeling of the drug. In most cases the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the drug. A single Phase 3 trial with other confirmatory evidence may be sufficient in rare instances where the study is a large multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible. Data from clinical trials conducted outside the U.S. may be accepted by the FDA subject to certain conditions. For example, the clinical trial must be conducted in accordance with GCPs and the FDA must be able to validate the data from the clinical trial through an onsite inspection if it deems such inspection necessary. Where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the U.S., the FDA will not approve the application on the basis of foreign data alone unless those data are considered applicable to the U.S. patient population and U.S. medical practice, the clinical trials were performed by clinical investigators of recognized competence, and the data is considered valid without the need for an onsite inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an onsite inspection or other appropriate means.

The manufacturer of an investigational drug in a Phase 2 or 3 clinical trial for a serious or life-threatening disease is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for expanded access to such investigational drug.

After completion of the required clinical testing, an NDA is prepared and submitted to the FDA. The FDA approval of the NDA is required before marketing of the product may begin in the U.S. The NDA must include the results of all preclinical, clinical, and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture, and controls. The cost of preparing and submitting an NDA is substantial. The submission of most NDAs is additionally subject to a substantial application user

fee, currently $3,242,026 for fiscal year 2023, and the applicant under an approved new drug application is also subject to an annual program fee, currently $393,000 per product for fiscal year 2023. These fees are typically increased annually.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be filed based on the agency's threshold determination that it is sufficiently complete to permit substantive review. If the NDA submission is filed, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use. The FDA has agreed to certain performance goals in the review of NDAs. Most such applications for standard review drug products are reviewed within ten to twelve months; most applications for priority review drugs are reviewed in six to eight months. Priority review can be applied to drugs that the FDA determines offer major advances in treatment or provide a treatment where no adequate therapy exists. The review process for both standard and priority review may be extended by the FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission.

The FDA may also refer applications for novel drug products, or drug products that present difficult questions of safety or efficacy, to an advisory committee - typically a panel that includes clinicians and other experts - for review, evaluation, and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCPs. Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. The FDA will not approve the product unless compliance with current good manufacturing practices, or cGMPs, is satisfactory and the NDA contains data that provide substantial evidence that the drug is safe and effective in the indication studied.

After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, or information, in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require a Risk Evaluation and Mitigation Strategy, or REMS, to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the drug. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and the FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

Companion Diagnostics

Companion diagnostics are subject to regulation by the FDA and comparable foreign regulatory authorities as medical devices and require separate marketing authorization prior to their commercialization. To date, the FDA has required premarket approval for nearly all companion diagnostics for cancer therapies. In January 2024, the FDA announced its intention to initiate the reclassification process for most in vitro diagnostics, including companion diagnostics. Further, FDA indicated that in addition to the reclassification process, FDA will continue taking a risk-based approach in the initial classification of individual in vitro diagnostics to determine whether a new test may be classified into class II through the de novo classification process. In so doing, FDA indicated that it may regulate most future companion diagnostics as class II devices.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant Orphan Drug designation to drugs intended to treat a rare disease or condition - generally a disease or condition that affects fewer than 200,000 individuals in the U.S., or 200,000 or more individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan drug designation must be requested before submitting an NDA. After the FDA grants Orphan Drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first NDA applicant to receive FDA approval for a particular active moiety to treat a particular disease with FDA Orphan Drug designation is entitled to a seven- year exclusive marketing period in the U.S. for that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with Orphan Drug exclusivity by means of greater effectiveness, greater safety, or providing a major contribution to patient care. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Among the other benefits of Orphan Drug designation are tax credits for certain research and a waiver of the NDA application user fee.

Fast Track Designation

The FDA is required to facilitate the development, and expedite the review, of drugs that are intended for the treatment of a serious or life-threatening disease and which demonstrate the potential to address unmet medical needs for the condition. Under the Fast Track program, the sponsor of a new drug candidate may request that the FDA designate the drug candidate for a specific indication as a Fast Track drug concurrent with, or after, the filing of the IND for the drug candidate. The FDA must determine if the drug candidate qualifies for Fast Track designation within 60 days of receipt of the sponsor's request.

Under the Fast Track program, sponsors have the opportunity to engage in more frequent interactions with the FDA. In addition, the FDA may initiate review of sections of a Fast Track drug's NDA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing an application does not begin until the last section of the NDA is submitted. Additionally, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Breakthrough Therapy Designation

FDA is also required to expedite the development and review of the application for approval of drugs that are intended to treat a serious or life-threatening disease or condition where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. Under the Breakthrough Therapy program, the sponsor of a new drug candidate may request that FDA designate the drug candidate for a specific indication as a Breakthrough Therapy concurrent with, or after, the filing of the IND for the drug candidate. FDA must determine if the drug candidate qualifies for Breakthrough Therapy designation within 60 days of receipt of the sponsor's request.

The Hatch-Waxman Act

Orange Book Listing

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims covering the applicant's product or method of using the product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an abbreviated new drug application, or ANDA. An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown to be bioequivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, preclinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way are commonly referred to as generic equivalents to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a Section VIII statement certifying that its proposed ANDA labeling does not contain (or carves out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been received by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA applicant.

An applicant submitting an NDA under Section 505(b)(2) of the FDC Act, which permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant and for which the applicant has not obtained a right of reference, is required to certify to the FDA regarding any patents listed in the Orange Book for the approved product it references to the same extent that an ANDA applicant would.

Market Exclusivity

Market exclusivity provisions under the FDC Act also can delay the submission or the approval of certain applications. The FDC Act provides a five-year period of non-patent exclusivity within the U.S. to the first applicant to gain approval of an NDA for a new chemical entity, or NCE. A drug is entitled to NCE exclusivity if it contains a drug substance no active moiety of which has been previously approved by the FDA. During the exclusivity period, the FDA may not receive for review an ANDA or file a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a Paragraph IV certification. The FDC Act also provides three years of market exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions for use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs for the original conditions of use, such as the originally approved indication. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all the non-clinical studies and adequate and well- controlled clinical trials necessary to demonstrate safety and effectiveness.

Patent Term Extension

After NDA approval, the owner of a relevant drug patent may apply for up to five years of patent term extension. Only one patent may be extended for each regulatory review period, which is composed of two parts: a testing phase, and an approval phase. The allowable patent term extension is calculated as half of the drug's testing phase - the time between the day the IND becomes effective and NDA submission - and all of the review phase - the time between NDA submission and approval - up to a maximum of five years. The time can be shortened if the FDA determines that the applicant did not pursue approval with due diligence. The total remaining patent term after the extension may not exceed 14 years.

For patents that might expire during the application phase, the patent owner may request an interim patent extension. An interim patent term extension increases the patent term by one year and may be renewed up to four times. For each interim patent term extension granted, the post-approval patent term extension is reduced by one year. The director of the USPTO must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely. Interim patent term extensions are not available for a drug for which an NDA has not been submitted.

Post-Approval Requirements

Once an NDA is approved, a product will be subject to certain post-approval requirements. For instance, the FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to- consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling.

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA. The FDA also may require post-marketing testing, known as Phase 4 testing, a REMS program, and surveillance to monitor the effects of an approved product, or the FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality-control, drug manufacture, packaging, and labeling procedures must continue to conform to cGMPs, after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies. Registration with the FDA subjects entities to periodic unannounced inspections by the FDA, during which the agency inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money, and effort in the areas of production and quality-control to maintain compliance with cGMPs and other regulatory requirements. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered. In addition, prescription drug manufacturers in the U.S. must comply with applicable provisions of the Drug Supply Chain Security Act and provide and receive product tracing information, maintain appropriate licenses, ensure they only work with other properly licensed entities, and have procedures in place to identify and properly handle suspect and illegitimate products.

Pediatric Information

Under the Pediatric Research Equity Act, or PREA, NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDC Act requires that a sponsor who is planning to submit a marketing application for a product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within sixty days of an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA. The FDA and the sponsor must reach agreement on the PSP. The FDA may grant full or partial waivers, or deferrals, for submission of data. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted.

The Best Pharmaceuticals for Children Act, or BPCA, provides NDA holders a six-month extension of any exclusivity—patent or non-patent—for a drug if certain conditions are met. Conditions for exclusivity include the FDA's determination that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, the FDA making a written request for pediatric studies, and the applicant agreeing to perform, performing, and reporting on, the requested studies within the statutory timeframe. Applications under the BPCA are treated as priority applications, with all of the benefits that designation confers.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA-regulated products are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, trial sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed in certain circumstances for up to two years after the date of completion of the trial. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Medical Device Products

A medical device is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component part, or accessory which is: (i) recognized in the official National Formulary, or the US Pharmacopoeia, or any supplement to them; (ii) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or (iii) intended to affect the structure or any function of the body of man or

other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

The FDC Act classifies medical devices into one of three categories based on the risks associated with the device and the level of control necessary to provide reasonable assurance of safety and effectiveness. Class I devices are deemed to be low risk and are subject to the fewest regulatory controls. Class III devices are generally the highest risk devices and are subject to the highest level of regulatory control to provide reasonable assurance of the device's safety and effectiveness. Class III devices must typically be approved by the FDA before they are marketed.

Generally, establishments that manufacture and/or distribute devices, including manufacturers, contract manufacturers, sterilizers, repackagers and relabelers, specification developers, reprocessors of single-use devices, remanufacturers, initial importers, manufacturers of accessories and components sold directly to the end user, and U.S. manufacturers of export-only devices, are required to register their establishments with the FDA and provide the FDA a list of the devices that they handle at their facilities.

Pre-market Authorization and Notification

While most Class I and some Class II devices can be marketed without prior FDA authorization, most medical devices can be legally sold within the U.S. only if the FDA has: (i) approved a premarket approval application, or PMA, prior to marketing, generally applicable to Class III devices; or (ii) cleared the device in response to a premarket notification, or 510(k) submission, generally applicable to Class I and II devices. Some devices that have been classified as Class III are regulated pursuant to the 510(k) requirements because the FDA has not yet called for PMAs for these devices. Other less common regulatory pathways to market for certain devices include the de novo classification process, the humanitarian device exception, or a product development protocol.

The 510(k) Clearance Process

Under the 510(k) process, the manufacturer must submit to the FDA a premarket notification, demonstrating that the device is "substantially equivalent," as defined in the statute, to a legally marketed predicate device.

A predicate device is a legally marketed device that is not subject to premarket approval, i.e., a device that was legally marketed prior to May 28, 1976, often referred to as a preamendments device, and for which a PMA is not required, a device that has been reclassified from Class III to Class II or I, or a device that was previously found substantially equivalent through the 510(k) process. To be "substantially equivalent," the proposed device must have the same intended use as the predicate device, and either have the same technological characteristics as the predicate device or have different technological characteristics and not raise different questions of safety or effectiveness than the predicate device. Clinical data is sometimes required to support substantial equivalence.

After a 510(k) premarket notification is submitted, the FDA determines whether to accept it for substantive review. If it lacks necessary information for substantive review, the FDA will refuse to accept the 510(k) notification. If it is accepted for filing, the FDA begins a substantive review. By statute, the FDA has a performance goal to complete its review of 95% of 510(k) submissions within 90 days of receipt. As a practical matter, clearance often takes longer, because the FDA can request additional date and information, which pauses the review clock for up to 180 days, and clearance is never assured. Although many 510(k) premarket notifications are cleared without clinical data, the FDA may require further information, including clinical data, to make a determination regarding substantial equivalence. If the FDA agrees that the device is substantially equivalent, it will grant clearance to commercially market the device.

If the FDA determines that the device is not "substantially equivalent" to a predicate device, or if the device is automatically classified into Class III, the device sponsor must then fulfill the much more rigorous premarketing requirements of the PMA approval process, or seek reclassification of the device through the de novo process. A manufacturer can also submit a petition for direct de novo review if the manufacturer is unable to identify an appropriate predicate device and the new device or new use of the device presents a moderate or low risk.

After a device receives 510(k) clearance, any modification that could significantly affect its safety or effectiveness, or that would constitute a new or major change in its intended use, will require a new 510(k) clearance or, depending on the modification, could require a PMA application or de novo classification. The FDA requires each manufacturer to determine whether the proposed change requires submission of a 510(k) or a PMA in the first instance, but the FDA can review any such decision and disagree with a manufacturer's determination. Many minor modifications are accomplished by a letter-to-file in which the manufacturer documents the change in an internal letter-to-file. The letter-to-file is in lieu of submitting a new 510(k) to obtain clearance for such change. The FDA can always review these letters to file in an inspection. If the FDA disagrees with a manufacturer's determination regarding whether a new premarket submission is required for the modification of an existing device, the FDA can require the manufacturer to cease marketing and/or recall the modified device until 510(k) clearance or approval of a PMA application is obtained. In addition, in these circumstances, the FDA can impose significant regulatory fines or penalties for failure to submit the requisite PMA application(s).

The PMA Approval Process

Following receipt of a PMA application, the FDA conducts an administrative review to determine whether the application is sufficiently complete to permit a substantive review. If it is not, the agency will refuse to file the PMA. If it is, the FDA will accept the application for filing and begin the review. The FDA, by statute and by regulation, has a performance goal to review 90% of PMA applications within 180 days, if advisory committee input is not required, and within 320 days, if advisory committee input is required, although the review of an application more often occurs over a significantly longer period of time. During this review period, the FDA may request additional information or clarification of information already provided, and the FDA may issue a major deficiency letter to the applicant, requesting the applicant's response to deficiencies communicated by the FDA. The FDA considers a PMA or PMA

supplement to have been voluntarily withdrawn if an applicant fails to respond to an FDA request for information (i.e., major deficiency letter) within a total of 360 days. Before approving or denying a PMA, an FDA advisory committee may review the PMA at a public meeting and provide the FDA with the committee's recommendation on whether the FDA should approve the submission, approve it with specific conditions, or not approve it. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Prior to approval of a PMA, the FDA may conduct inspections of the clinical trial data and clinical trial sites, as well as inspections of the manufacturing facility and processes. Overall, the FDA review of a PMA application generally takes between one and three years, but may take significantly longer. The FDA can delay, limit or deny approval of a PMA application for many reasons, including:

- the device may not be shown safe or effective to the FDA's satisfaction;
- the data from preclinical studies and/or clinical trials may be found unreliable or insufficient to support approval;
- the manufacturing process or facilities may not meet applicable requirements; and
- changes in FDA approval policies or adoption of new regulations may require additional data.

If the FDA evaluation of a PMA is favorable, the FDA will issue either an approval letter, or an approvable letter, the latter of which usually contains a number of conditions that must be met in order to secure final approval of the PMA. When and if those conditions have been fulfilled to the satisfaction of the FDA, the agency will issue a PMA approval letter authorizing commercial marketing of the device, subject to the conditions of approval and the limitations established in the approval letter. If the FDA's evaluation of a PMA application or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. The FDA also may determine that additional tests or clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and data is submitted in an amendment to the PMA, or the PMA is withdrawn and resubmitted when the data are available. The PMA process can be expensive, uncertain and lengthy and a number of devices for which the FDA approval has been sought by other companies have never been approved by the FDA for marketing.

New PMA applications or PMA supplements are required for modification to the manufacturing process, equipment or facility, quality control procedures, sterilization, packaging, expiration date, labeling, device specifications, ingredients, materials or design of a device that has been approved through the PMA process. PMA supplements often require submission of the same type of information as an initial PMA application, except that the supplement is limited to information needed to support any changes from the device covered by the approved PMA application and may or may not require as extensive technical or clinical data or the convening of an advisory panel, depending on the nature of the proposed change. In approving a PMA application, as a condition of approval, the FDA may also require some form of post-approval study or post-market surveillance, whereby the applicant conducts a follow-up study or follows certain patient groups for a number of years and makes periodic reports to the FDA on the clinical status of those patients when necessary to protect the public health or to provide additional or longer term safety and effectiveness data for the device. The FDA may also require post-market surveillance for certain devices cleared under a 510(k) notification, such as implants or life-supporting or life- sustaining devices used outside a device user facility. The FDA may also approve a PMA application with other post-approval conditions intended to ensure the safety and effectiveness of the device, such as, among other things, restrictions on labeling, promotion, sale, distribution and use.

Exempt Devices

If a manufacturer's device falls into a generic category of Class I or Class II devices that the FDA has exempted by regulation, a premarket notification is not required before marketing the device in the U.S. Manufacturers of such devices are required to register their establishments and list the proprietary device name and the generic category or classification regulation into which the device fits. Some 510(k)-exempt devices are also exempt from Quality System Regulation requirements.

Post-market Requirements

After a device is placed on the market, numerous regulatory requirements apply. These include: Quality System Regulation, labeling regulations, the FDA's general prohibition against promoting products for unapproved or off-label uses, the Medical Device Reporting regulation (which requires that manufacturers report to the FDA if their device may have caused or contributed to a death or serious injury or malfunctioned in a way that would likely cause or contribute to a death or serious injury if it were to recur), and the Reports of Corrections and Removals regulation (which requires manufacturers to report recalls and field actions to the FDA if initiated to reduce a risk to health posed by the device or to remedy a violation of the FDC Act).

The FDA enforces these requirements by inspection and market surveillance. If the FDA finds a violation, it can institute a wide variety of enforcement actions, ranging from a public warning letter to more severe sanctions such as: fines, injunctions, and civil penalties; recall or seizure of products; operating restrictions, partial suspension or total shutdown of production; refusing requests for 510(k) clearance or PMA approval of new products; withdrawing 510(k) clearance or PMA approvals already granted; and criminal prosecution.

Combination Products

A combination product is a product comprised of (i) two or more regulated components, i.e., drug/medical device, biologic/medical device, drug/biologic, or drug/medical device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity; (ii) two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products; (iii) a drug, device, or biological product

packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect and where, upon approval of the proposed product, the labeling of the approved product would need to be changed, i.e., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or (iv) any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

The FDA is divided into various branches, or Centers, by product type. Different Centers typically review drug, biologic, or device applications. In order to review an application for a combination product, the FDA must decide which Center should be responsible for the review. FDA regulations require that the FDA determine the combination product's primary mode of action, or PMOA, which is the single mode of a combination product that provides the most important therapeutic action of the combination product. The Center that regulates that portion of the product that generates the PMOA becomes the lead evaluator. If there are two independent modes of action, neither of which is subordinate to the other, the FDA makes a determination as to which Center to assign the product based on consistency with other combination products raising similar types of safety and effectiveness questions or to the Center with the most expertise in evaluating the most significant safety and effectiveness questions raised by the combination product. When evaluating an application, a lead Center may consult other Centers but still retain complete reviewing authority, or it may collaborate with another Center, by which the Center assigns review of a specific section of the application to another Center, delegating its review authority for that section. Typically, the FDA requires a single marketing application submitted to the Center selected to be the lead evaluator, although the agency has the discretion to require separate applications to more than one Center. One reason to submit multiple evaluations is if the applicant wishes to receive some benefit that accrues only from approval under a particular type of application, like new drug product exclusivity. If multiple applications are submitted, each may be evaluated by a different lead Center.

Regulation Outside the U.S.

In addition to regulations in the U.S., we are subject to a variety of regulations in other jurisdictions governing clinical studies, commercial sales, and distribution of our products. Most countries outside the U.S. require that clinical trial applications be submitted to and approved by the local regulatory authority for each clinical study. In addition, whether or not we obtain FDA approval for a product, we must obtain approvals by the comparable regulatory authorities of countries outside the U.S. before we can commence clinical studies or marketing of the product in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval.

Similar to the United States, the various phases of preclinical and clinical research in the EU are subject to significant regulatory controls. In April 2014, the EU adopted the new Clinical Trials Regulation (EU) No 536/2014, which replaced the Clinical Trials Directive 2001/20/EC on January 31, 2022. The new Regulation is directly applicable in all Member States (and so does not require national implementing legislation in each Member State) and aims at simplifying and streamlining the approval of clinical studies in the EU. The main characteristics of the new Regulation include: a streamlined application procedure via a single-entry point through the Clinical Trials Information System, or CTIS; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts (Part I contains scientific and medicinal product documentation and Part II contains the national and patient-level documentation). Part I is assessed by a coordinated review by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned) of a draft report prepared by a reference Member State. Part II is assessed separately by each Member State concerned. Strict deadlines have also been established for the assessment of clinical trial applications.

To obtain regulatory approval of an orphan product in the EU, we are mandated to submit a marketing authorization application, or MAA, under the centralized procedure. The centralized procedure allows applicants to obtain a marketing authorization that is valid throughout the EU and the additional Member States of the European Economic Area (Iceland, Liechtenstein and Norway), or EEA. It is compulsory for medicinal products manufactured using biotechnological processes, orphan medicinal products, advanced-therapy medicinal products (gene therapy, somatic cell therapy or tissue-engineered medicines) and for human products containing a new active substance indicated for the treatment of HIV/AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for any other products containing new active substances not authorized in the EEA or for products which constitute a significant therapeutic, scientific or technical innovation or for which an EEA-wide authorization is in the interests of public health. When a company wishes to place on the market a medicinal product that is eligible for the centralized procedure, it sends an application directly to the EMA, to be assessed by the Committee for Medicinal Products for Human Use, or CHMP. The procedure results in an EC decision, which is valid and enables products to be marketed throughout the EEA.

In the centralized procedure, full copies of the MAA are sent to a rapporteur and a co-rapporteur designated by the competent EMA scientific committee. They coordinate the EMA's assessment of the medicinal product and prepare draft reports. Once the draft reports are prepared (other experts might be called upon for this purpose), they are sent to the CHMP, whose comments or objections are communicated to the applicant. The rapporteur is therefore the privileged interlocutor of the applicant and continues to play this role, even after the MAA has been granted. The rapporteur and co-rapporteur then assess the applicant's replies, submit them for discussion to the CHMP and, taking into account the conclusions of this debate, prepare a final assessment report. Once the evaluation is completed, the CHMP gives a favorable or unfavorable opinion as to whether to grant the authorization. When the opinion is favorable, it shall include the draft summary of products characteristics, or SmPC, the package leaflet and the texts proposed for the various packaging materials. The maximum timeframe for the evaluation of an MAA by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Clock stops may extend the timeframe of evaluation of an MAA considerably beyond 210 days. Where the CHMP gives a positive opinion, the EMA provides the opinion together with supporting documentation to the European Commission, who make the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated assessment might be granted by the

CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of an MAA under the accelerated assessment procedure is of 150 days, excluding stop-clocks, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment.

For products not within the mandatory scope of the centralized procedure, other procedures are available for the grant of a marketing authorization in multiple EU Member States. The decentralized procedure provides for approval by one or more other, or concerned, Member States of an assessment of an application performed by one Member State, known as the reference Member State. Under this procedure, an applicant submits an application, or dossier, and related materials including a draft SmPC, and draft labeling and package leaflet, to the reference Member State and concerned Member States. The reference Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference Member State's assessment report, each concerned Member State must decide whether to approve the assessment report and related materials. If a Member State cannot approve the assessment report and related materials on the grounds of potential serious risk to the public health, the disputed points may eventually be referred to the EC, whose decision is binding on all Member States. Where a product has already been authorized for marketing in a Member State of the EU, this national authorization can be recognized in other Member States through the mutual recognition procedure.

Applications from persons or companies seeking "orphan medicinal product designation" for products they intend to develop for the diagnosis, prevention, or treatment of life-threatening or chronically debilitating conditions that affect no more than 5 in 10,000 persons in the EU are reviewed by the EMA's Committee for Orphan Medicinal Products, or COMP. In addition, orphan designation can be granted in the EU if the product is intended for a life threatening, seriously debilitating, or serious and chronic condition and where, without incentives, it is unlikely that sales of the product in the EU would be sufficient to justify the necessary investment in developing the drug. Orphan designation is only available if there is no other satisfactory method approved in the EU of diagnosing, preventing, or treating the condition, or if such a method exists, the proposed orphan product will be of significant benefit to patients affected by the applicable condition. Orphan designation provides opportunities for fee reductions, protocol assistance and access to the centralized procedure for marketing approval. In addition, if a product which has an orphan designation in the EU subsequently receives EMA marketing approval for the indication for which it has such designation, the product is entitled to market exclusivity, which means the EMA and the competent authorities of the EU Member States may not approve any other application to market a "similar medicinal product" to the authorized orphan product for the same indication for a period of 10 years. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The exclusivity period may be reduced to six years if, at the end of the fifth year, it is established that the designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. During the period of market exclusivity, a marketing authorization may only be granted to a "similar medicinal product" for the same therapeutic indication if: (i) a second applicant can establish that its product, although similar to the authorized product, is safer, more effective or otherwise clinically superior; (ii) the marketing authorization holder for the authorized product consents to a second orphan medicinal product application; or (iii) the marketing authorization holder for the authorized product cannot supply enough orphan medicinal product.

A pediatric investigation plan, or PIP, is a development plan aimed at ensuring that the necessary data are obtained to support the authorization of a medicine for children, through studies in children. All applications for marketing authorization for new medicines have to include the results of studies as described in an agreed PIP, unless the medicine is exempt because of a deferral or waiver. This requirement also applies when a marketing-authorization holder wants to add a new indication, pharmaceutical form, or route of administration for a medicine that is already authorized and covered by intellectual property rights. The EMA's pediatric committee, or PDCO, can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults, in which case the pediatric clinical trials must be completed at a later date. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when this data is not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Several rewards and incentives for the development of pediatric medicines for children are available in the EU. Medicines authorized across the EU with the results of studies from a PIP included in the product information are eligible for an extension of their supplementary protection certificate by six months. This is the case even when the studies' results are negative. For orphan medicines, the incentive is an additional two years of market exclusivity. Scientific advice and protocol assistance at the EMA are free of charge for questions relating to the development of pediatric medicines. Medicines developed specifically for children that are already authorized but are not protected by a patent or supplementary protection certificate are eligible for a pediatric-use marketing authorization, or PUMA. If a PUMA is granted, the product will benefit from 10 years of market protection as an incentive.

In the EU, medical devices were previously regulated under Directive 93/42/EEC, also known as the Medical Device Directive, or MDD, and the implementing legislation in each Member State of the EU. On May 26, 2021, EU Regulation 2017/745, also known as the Medical Devices Regulation, or MDR, became fully applicable and repealed and replaced the MDD. The changes which are brought in by the MDR were prompted by divergent interpretations of the MDD and to address issues concerning product quality and performance. The MDR is intended to establish a uniform, transparent, predictable and sustainable regulatory framework across the EU for medical devices, and it:

- strengthens the rules on placing devices on the market and reinforces surveillance once they are available;
- establishes explicit provisions on manufacturers' responsibilities for the follow-up of the quality, performance, and safety of devices placed on the market;
- improves the traceability of medical devices throughout the supply chain to the end-user or patient through a unique identification number;

- sets up a central database (Eudamed) to provide patients, healthcare professionals, and the public with comprehensive information on products available in the EU; and
- strengthens rules for the assessment of certain high-risk devices, such as implants, which may have to undergo an additional check by experts before they are placed on the market.

Under the MDR, the system of regulating medical devices operates by way of a certification for each medical device, which confirms that the device meets the relevant general safety and performance requirements laid down in Annex I of the MDR. Each certificated device is marked with a Conformitè Europëenne mark, or CE mark, which shows that the device has a Certificat de Conformité, also referred to as a certificate of conformity. The means for achieving the requirements for a CE mark varies according to the nature of the device. Devices are classified in accordance with their perceived risks, similarly to the U.S. system. The class of a product determines the requirements to be fulfilled in accordance with the MDR before a CE mark can be placed on a product. The procedure by which a device is assess to confirm if it complies with the general safety and performance requirements is known as a conformity assessment. Conformity assessment procedures require an assessment of available clinical evidence, literature data for the product and post-market experience in respect of similar products already marketed. Specifically, a manufacturer must demonstrate that the device achieves its intended performance during normal conditions of use, that the known and foreseeable risks, and any adverse events, are minimized and acceptable when weighed against the benefits of its intended performance, and that any claims made about the performance and safety of the device are supported by suitable evidence. Except for low-risk medical devices (Class I non-sterile, non-measuring devices), where the manufacturer can self-certify compliance with the MDR based on a self-assessment of the conformity of its products with the general safety and performance requirements of the MDR, a conformity assessment procedure requires the intervention of an independent organization accredited by a Member State of the EEA to conduct conformity assessments, known as a notified body. If satisfied that the relevant product conforms to the relevant general safety and performance requirements, the notified body issues a certificate of conformity, which the manufacturer uses as a basis for its own declaration of conformity. The manufacturer may then apply the CE mark to the device, which allows the device to be placed on the market throughout the EEA.

Under transitional provisions provided in the MDR, medical devices that had valid certificates of conformity issued under the MDD prior to May 26, 2021 may, provided certain obligations under the MDR are respected, continue to be placed on the EEA market for the remaining validity of the certificate, and until May 27, 2024 at the latest. After the expiry of any applicable transitional period, only devices that have been CE marked on the basis of the MDR may be placed on the market in the EEA. However, in response to concerns raised about notified body capacity and the ability for devices to be re-certified within such time period, the European Commission has adopted a proposal to extend the transition period by some years, depending on the risk class of the device. Such proposal is currently being considered for adoption by the European Parliament and Council.

Post-Brexit, the MDR does not apply in the United Kingdom, or UK, (except for Northern Ireland, which under the Northern Ireland Protocol is bound by certain EU laws). The medical device legislative framework in the UK is set out in the Medical Devices Regulations 2002. These regulations are based on the previous medical device directives of the EU, but have been amended so that they function properly now that the UK is no longer part of the EU. The Medical Devices Regulations 2002 have introduced several changes including (but not limited to) replacing the CE mark with a UK Conformity Assessed marking, requiring manufacturers outside of the UK to appoint a UK Responsible Person if they place devices on the market in the UK and more wide-ranging device registration requirements. Manufactures can continue placing CE marked medical devices on the Great Britain market for the time being, however from July 2024, transitional arrangements will apply for CE marked medical devices placed on the Great Britain market. These transitional arrangements have not yet been brought into force through the UK medical devices regulations, but the UK Government intends to introduce legislation by Spring 2023 that will bring these into force.

International Approvals

Drug products, medical devices, and drug/medical device combination products are subject to extensive regulation, including premarket review and marketing authorization, by similar agencies in other countries. Regulatory requirements and approval processes are similar in approach to that of the U.S. but are not harmonized. International regulators are independent and not bound by the findings of the FDA and there is a risk that foreign regulators will not accept clinical trial design/results or may require additional data or other information not requested by the FDA. In addition, international regulators may require different manufacturing practices than the FDA's cGMPs.

Reimbursement

In the United States and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels.

Potential sales of any of our product candidates, if approved, will depend, at least in part, on the extent to which such products will be covered by third-party payors, such as government health care programs, commercial insurance and managed healthcare organizations. In the U.S., no uniform policy of coverage and reimbursement for drug or biological products exists. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will be made on a payor-by-payor basis. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly limiting coverage and/or reducing reimbursements for medical products and services. A third-party payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our future revenues and results of operations. Decreases in third-party reimbursement or a decision by a third-party payor to not cover a product candidate, if approved, or any future approved products could reduce physician usage of our products, and have a material adverse effect on our sales, results of operations and financial condition.

In the U.S., the Medicare Part D program provides a voluntary outpatient drug benefit to Medicare beneficiaries for certain products. We do not know whether our product candidates, if approved, will be eligible for coverage under Medicare Part D, but individual Medicare Part D plans offer coverage subject to various factors such as those described above. Furthermore, private payors often follow Medicare coverage policies and payment limitations in setting their own coverage policies.

Anti-Kickback, False Claims Laws and Other Regulations

In addition to the FDA restrictions on marketing of pharmaceutical products, medical devices, and combination products, several other types of state and federal laws have been applied to restrict certain marketing practices in the medical product industry in recent years. These laws include federal and state anti-kickback statutes, false claims statutes, and other statutes pertaining to health care fraud and abuse. The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid, or other federally financed healthcare programs. The Patient Protection and Affordable Care Act, or PPACA, amended the intent element of the federal statute so that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other. Violations of the anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties, and exclusion from participation in federal healthcare programs. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. This includes claims made to programs where the federal government reimburses, such as Medicaid, as well as programs where the federal government is a direct purchaser, such as when it purchases off the Federal Supply Schedule. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. Additionally, PPACA amended the healthcare program anti-kickback statute such that a violation can serve as a basis for liability under the federal false claims law. The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

The U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors or making any false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their implementing regulations, impose obligations on certain types of individuals and entities regarding the electronic exchange of information in common healthcare transactions, as well as standards relating to the privacy and security of individually identifiable health information.

Other federal statutes pertaining to healthcare fraud and abuse include the civil monetary penalties statute, which prohibits the offer or payment of remuneration to a Medicaid or Medicare beneficiary that the offeror/payor knows or should know is likely to influence the beneficiary to order a receive a reimbursable item or service from a particular supplier, and the healthcare fraud statute, which prohibits knowingly and willfully executing or attempting to execute a scheme to defraud any healthcare benefit program or obtain by means of false or fraudulent pretenses, representations, or promises any money or property owned by or under the control of any healthcare benefit program in connection with the delivery of or payment for healthcare benefits, items, or services.

Additionally, to the extent that our product is sold in a foreign country, we may be subject to similar foreign laws.

Privacy and Security laws

HIPAA, as amended by HITECH, and their respective implementing regulations, impose privacy, security transmission and breach reporting obligations with respect to individually identifiable health information, including protected health information, or PHI, upon entities subject to the law, such as health plans, healthcare clearinghouses and certain healthcare providers, and their respective business associates that perform services on their behalf that involve individually identifiable health information, including PHI. HIPAA imposes criminal liability and amends provisions on the reporting, investigation, enforcement, and penalizing of civil liability for, among other things, knowingly and recklessly executing a scheme or artifice to defraud any healthcare benefit program, including private payors, as well as knowingly and willfully falsifying, concealing, or covering up a material fact by any trick, scheme, or device or making any materially false, fictitious, or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items, or services. A violation of this statute is a felony and may result in fines, imprisonment, or exclusion from government-sponsored programs. Similar to the federal Anti-Kickback Statute, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, state attorney generals have authority to file civil actions for damages or injunctions in federal courts to enforce the HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. Although we are not directly subject to HIPAA, other than potentially with respect to providing certain employee benefits, we could be subject to criminal penalties if we knowingly obtain or disclose individually identifiable health information maintained by a HIPAA covered entity in a manner that is not authorized or permitted by HIPAA.

Many states have laws that protect the privacy and security of personal information, including health or other categories of sensitive personal information.

Federal and state laws that govern the privacy and security of health information or personally identifiable information in certain circumstances, including state health information privacy and data breach notification laws which govern the collection, use, disclosure, and protection of health-related and other personal information, many of which differ from each other in significant ways, may require us to undertake compliance efforts that could be costly and time consuming or subject us to liability for a failure to comply.

Other Federal and State Regulatory Requirements

Manufacturers of prescription drugs are required to collect and report information on certain payments or transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other licensed health care practitioners (i.e. physician assistants, nurse practitioners or clinical nurse specialists, certified registered nurse anesthetists, and certified nurse-midwives), and teaching hospitals, as well as any investment interests held by the physicians and their immediate family members. The reports must be submitted on an annual basis and the reported data are posted in searchable form on a public website on an annual basis. Failure to submit required information may result in civil monetary penalties.

In addition, several states now require prescription drug companies to report certain expenses relating to the marketing and promotion of drug products and to report gifts and payments to individual healthcare practitioners in these states. Other states prohibit various marketing-related activities, such as the provision of certain kinds of gifts or meals. Still other states require the posting of information relating to clinical studies and their outcomes. Some states require the reporting of certain pricing information, including information pertaining to and justifying price increases, or prohibit prescription drug price gouging. In addition, states such as California, Connecticut, Nevada, Massachusetts, and Vermont require pharmaceutical companies to implement compliance programs and/or marketing codes. Additional jurisdictions, such as the City of Chicago and the District of Columbia, require pharmaceutical sales representatives to be licensed and meet continuing education requirements. Several additional states are considering similar proposals. Compliance with these laws is difficult and time-consuming, and companies that do not comply with these state laws face civil penalties.

Healthcare Reform

The U.S. and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system. The U.S. government, state legislatures and foreign governments also have shown significant interest in implementing cost-containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Payors, whether domestic or foreign, or governmental or private, are developing increasingly sophisticated methods of controlling healthcare costs and those methods are not always specifically adapted for new technologies such as gene therapy and therapies addressing rare diseases such as those we are developing. In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell our products profitably. In particular, in 2010, the PPACA was enacted, which, among other things, subjected biologic products to potential competition by lower-cost biosimilars; addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations; subjected manufacturers to new annual fees and taxes for certain branded prescription drugs; created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and provided incentives to programs that increase the federal government's comparative effectiveness research.

In recent years, Congress has considered reductions in Medicare reimbursement levels for drugs. CMS, the agency that administers the Medicare and Medicaid programs, also has authority to revise reimbursement rates and to implement coverage restrictions for some drugs. Cost reduction initiatives and changes in coverage implemented through legislation or regulation could decrease utilization of and reimbursement for any approved products. While Medicare regulations apply only to drug benefits for Medicare beneficiaries, private payers often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from federal legislation or regulation may result in a similar reduction in payments from private payers.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the Affordable Care Act, substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacts the pharmaceutical industry. The Affordable Care Act is intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on pharmaceutical and medical device manufacturers, and impose additional health policy reforms. Among other things, the Affordable Care Act expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum Medicaid rebate for both branded and generic drugs, expanded the 340B program, and revised the definition of AMP, which could increase the amount of Medicaid drug rebates manufacturers are required to pay to states. The legislation also extended Medicaid drug rebates, previously due only on fee-for-service Medicaid utilization, to include the utilization of Medicaid managed care organizations as well and created an alternative rebate formula for certain new formulations of certain existing products that is intended to increase the amount of rebates due on those drugs. On February 1, 2016, CMS issued final regulations to implement the changes to the Medicaid Drug Rebate program under the Affordable Care Act. These regulations became effective on April 1, 2016. Since that time, there have been significant ongoing efforts to modify or eliminate the Affordable Care Act.

Other legislative changes have been proposed and adopted since passage of the Affordable Care Act. The Budget Control Act of 2011 and subsequent legislation, among other things, created measures for spending reductions by Congress that include aggregate reductions to Medicare payments to healthcare providers of up to 2.0% per fiscal year, which remain in effect until 2031 unless additional Congressional action is taken. Due to the Statutory Pay-As-You-Go Act of 2010, estimated budget deficit increases resulting from the American Rescue Plan Act of 2021, and subsequent legislation, Medicare payments to providers will be further reduced starting in 2025 absent further legislation. Further, the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

The Affordable Care Act has been subject to challenges in the courts. On December 14, 2018, a Texas U.S. District Court Judge ruled that the Affordable Care Act is unconstitutional in its entirety because the “individual mandate” was repealed by Congress. On December 18, 2019, the Fifth Circuit U.S. Court of Appeals held that the individual mandate is unconstitutional and remanded the case to the Texas District Court to reconsider its earlier invalidation of the entire Affordable Care Act. An appeal was taken to the U.S. Supreme Court which heard oral arguments in the case on November 10, 2020. On June 17, 2021, the Supreme Court ruled that the plaintiffs lacked standing to challenge the law as they had not alleged personal injury traceable to the allegedly unlawful conduct. As a result, the Supreme Court did not rule on the constitutionality of the Affordable Care Act or any of its provisions.

The Affordable Care Act requires pharmaceutical manufacturers of branded prescription drugs to pay a branded prescription drug fee to the federal government. Each individual pharmaceutical manufacturer pays a prorated share of the branded prescription drug fee, based on the dollar value of its branded prescription drug sales to certain federal programs identified in the law. Furthermore, the law requires manufacturers to provide a 50% discount off the negotiated price of prescriptions filled by beneficiaries in the Medicare Part D coverage gap, referred to as the “donut hole.” The Bipartisan Budget Act of 2018, among other things, amended the Affordable Care Act, effective January 1, 2019, to close the coverage gap in most Medicare drug plans by increasing from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D.

Payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives as well. For example, CMS may develop new payment and delivery models, such as bundled payment models. Recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Such scrutiny has resulted in several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for pharmaceutical products.

Further changes to and under the Affordable Care Act remain possible, but it is unknown what form any such changes or any law proposed to replace or revise the Affordable Care Act would take, and how or whether it may affect our business in the future.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that additional federal, state and foreign healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in limited coverage and reimbursement and reduced demand for our products, once approved, or additional pricing pressures.

Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act, or FCPA, prohibits U.S. businesses and their representatives from offering to pay, paying, promising to pay or authorizing the payment of money or anything of value to a foreign official in order to influence any act or decision of the foreign official in his or her official capacity or to secure any other improper advantage in order to obtain or retain business. The FCPA also obligates companies whose securities are listed in the U.S. to comply with accounting provisions requiring us to maintain books and records, which in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the corporation, including international subsidiaries, if any, and to devise and maintain a system of internal accounting controls sufficient to provide reasonable assurances regarding the reliability of financial reporting and the preparation of financial statements. Our industry is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers are subject to regulation under the FCPA. Recently, the Securities and Exchange Commission, or the SEC, and Department of Justice have increased their FCPA enforcement activities with respect to pharmaceutical companies. Violations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of our facilities, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Recent enacted legislation has expanded the SEC's power to seek disgorgement in all FCPA cases filed in federal court and extended the statute of limitations in SEC enforcement actions in intent-based claims such as those under the FCPA from five years to ten years.

International laws

In Europe, and throughout the world, other countries have enacted anti-bribery laws and/or regulations similar to the FCPA. Violations of any of these antibribery laws, or allegations of such violations, could have a negative impact on our business, results of operations and reputation. There are also international privacy laws that impose restrictions on the access, use, including the EU's General Data Protection Regulation, and disclosure of health information. All of these laws may impact our business. Our failure to comply with these privacy laws or significant changes in the laws restricting our ability to obtain required patient information could significantly impact our business and our future business plans.

Employees and Human Capital Resources

As of April 16, 2024, we had 15 full-time employees, 12 of whom are based in the U.S. Our employees are skilled in drug development, including clinical trial design, clinical operations in support of our clinical trials and related activities, corporate administration, finance and business development. None of our employees are represented by a labor union or covered by collective bargaining agreements, and we believe our relationship with our employees is good. We also work with independent professional advisors and consultants to support our program development activities, particularly in the areas of drug product development, regulatory, compliance, and international clinical operations.

We believe our human capital resources are fundamental to our success; as such, our corporate objectives include recruiting, retaining, incentivizing and integrating existing and new employees, advisors and consultants for the common purpose of increasing stockholder value and promoting the success of our company. Our compensation and equity incentive programs are designed to attract, retain and reward personnel through cash-based compensation and granting of stock-based awards intended to motivate such individuals to perform to the best of their abilities and advance our corporate objectives. We endeavor to provide competitive benefits that will reward and retain our employees. Our compensation program includes competitive salary and annual bonus programs, comprehensive healthcare benefits for employees and dependent family members, paid time off, paid holidays, family medical leave and flexible work schedules. We sponsor a 401(k) plan and automatically enroll all employees when eligible and generally provide a discretionary matching corporate contribution.

Corporate Information

We were incorporated in Delaware on November 6, 1992. Our principal executive offices are located at 2600 Kelly Road, Suite 100, Warrington, Pennsylvania, 18976, and our telephone number is 215-488-9300. Our website address is www.windtreetx.com. The information contained in, or accessible through, our website does not constitute part of this Annual Report on Form 10-K. We have included our website address as an inactive textual reference only.

Available Information

We file annual, quarterly and current reports, proxy or stockholder information statements and other information with the SEC. The SEC maintains an Internet site that contains reports, proxy and information statements, certain and other information that we may file electronically with the SEC (http://www.sec.gov). We maintain our corporate website at http://www.windtreetx.com. Our website and the information contained therein or connected thereto are not incorporated into this Annual Report on Form 10-K.

ITEM 1A. RISK FACTORS.

You should carefully consider the following risks and uncertainties when reading this Annual Report on Form 10-K. If any of the following risks actually occurs, our business, financial condition and results of operations could be materially and adversely affected. In that event, the trading price of our common stock could decline. Although we believe that we have identified and discussed below the key risk factors affecting our business, there may be additional risks and uncertainties that are not presently known or that are not currently believed to be significant that may adversely affect our performance or financial condition.

Information concerning the shares of our common stock and related share prices in these risk factors has been adjusted to reflect the 1-for-50 reverse split of our common stock that was made effective on February 24, 2023.

Risks Related to Our Financial Condition

Our current cash position, losses, negative cash flows from operations, and accumulated deficit raise substantial doubt about our ability to continue as a going concern absent obtaining adequate new debt or equity financings.

The auditor's opinion on our audited financial statements for the year ended December 31, 2023 includes an explanatory paragraph stating that we have incurred recurring losses from operations that raise substantial doubt about our ability to continue as a going concern. Management has also concluded that substantial doubt exists about our ability to continue as a going concern. As of December 31, 2023, we had cash and cash equivalents of $4.3 million and current liabilities of $4.0 million. In April 2024, we entered into a Securities Purchase Agreement, or the Purchase Agreement, with the buyers named therein, pursuant to which we agreed to sell senior convertible notes, or the Notes, for $1.5 million of gross proceeds. As a result, we believe that we have sufficient resources available to fund our business operations through April 2024. We do not have sufficient cash and cash equivalents as of the date of this Annual Report on Form 10-K to support our operations for at least the 12 months following the date that the financial statements are issued. These conditions raise substantial doubt about our ability to continue as a going concern.

To alleviate the conditions that raise substantial doubt about our ability to continue as a going concern, management plans to secure additional capital, potentially through a combination of public or private securities offerings; convertible debt financings; and/or strategic transactions, including potential licensing arrangements, alliances and drug product collaborations focused on specified geographic markets; however, none of these alternatives are committed at this time. There can be no assurance that we will be successful in obtaining sufficient funding on terms acceptable to us to fund continuing operations, if at all, or identify and enter into any strategic transactions that will provide the capital that we will require. If none of these alternatives is available, or if available, we are unable to raise sufficient capital through such transactions, we will not have sufficient cash resources and liquidity to fund our business operations for at least the next 12 months following the date that the financial statements are issued. In addition, we may be unable to pay our vendors and other service partners on time, or at all. If any of our key vendors and service providers were to cease working with us or subject the delivery of products or services to timing or payment preconditions, our development activities may be adversely affected, which could have a material adverse effect on our business and operations. Additionally, if we are unable to regain compliance with the listing standards of Nasdaq, our common stock may become delisted, which could have a material adverse effect on the liquidity of our common stock and our ability to raise funding. If additional financing is not available on satisfactory terms, or is not available in sufficient amounts, we may be require required to delay, limit, or eliminate the development of business opportunities and our ability to achieve our business objectives and our competitiveness, and our business, financial condition, and results of operations will be materially adversely affected. In addition, market instability, including as a result of geopolitical instability, may reduce our ability to access capital, which could negatively affect our liquidity and ability to continue as a going concern. Further, the perception that we may not be able to continue as a going concern may cause others to choose not to deal with us due to concerns about our ability to meet our contractual obligations.

Our forecast of the period of time through which our financial resources will be adequate to support our operating requirements is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors, including the factors discussed elsewhere in this "*Risk Factors*" section. We have based this estimate on a number of assumptions that may prove to be wrong and changing circumstances beyond our control may cause us to consume capital more rapidly than we currently anticipate. Our inability to obtain additional funding when we need it could seriously harm our business.

We have incurred significant operating losses since inception, we expect to incur operating losses in the future, and we may not be able to achieve or sustain profitability.

We have incurred operating losses since our incorporation on November 6, 1992. For the years ended December 31, 2023 and 2022, we had operating losses of $20.6 million and $41.3 million, respectively. As of December 31, 2023, we had an accumulated deficit of $844.8 million. To date, we have financed our operations primarily through private placements and public offerings of our common and preferred stock and borrowings from investors and financial institutions. As of December 31, 2023, we had cash and cash equivalents of $4.3 million and current liabilities of $4.0 million. In April 2024, we entered into the Purchase Agreement pursuant to which we agreed to sell the Notes for $1.5 million of gross proceeds. As a result, we believe that we have sufficient resources available to fund our business operations through April 2024.

We expect to continue to incur significant research and clinical development, regulatory and other expenses as we (i) develop product candidates; (ii) seek regulatory clearances or approvals for our planned or future product candidates; (iii) conduct clinical trials on our planned or future product candidates; and (iv) manufacture, market, and sell any product candidates for which we may obtain regulatory approval. As a result, we expect to continue to incur operating losses for the foreseeable future and may never achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on an ongoing basis. If we do not achieve or sustain profitability, it will be more difficult for us to finance our business and accomplish our strategic objectives, either of

which would have a material adverse effect on our business, financial condition and results of operations and may cause the market price of our common stock to decline.

We have incurred indebtedness, which could adversely affect our operating flexibility and financial condition.

We have, and may from time to time in the future have, third-party debt service obligations pursuant to our outstanding indebtedness, which currently includes $1.5 million in aggregate principal amount, or the Notes. The degree to which we are leveraged could have important consequences. For example, it could:

- make it more difficult for us to satisfy our obligations with respect to our existing indebtedness;
- increase our vulnerability to general adverse economic and industry conditions;
- require us to dedicate a substantial portion of our cash flows from operations to payments on our indebtedness, thereby reducing the availability of our cash flows to fund working capital and capital expenditures, and for other general corporate purposes;
- limit our flexibility in planning for, or reacting to, changes in our business and industry, which may place us at a competitive disadvantage compared to our competitors that have less debt;
- restrict us from making strategic acquisitions or other investments or cause us to make non-strategic divestitures; and
- limit, along with the financial and other restrictive covenants in the documents governing our indebtedness, among other things, our ability to obtain additional financing for working capital and capital expenditures, and for other general corporate purposes.

If we cannot maintain an adequate cash balance to service our debt, we may be unable to pay amounts due under our outstanding indebtedness or to fund other liquidity needs and it may be required to refinance all or part of our then existing indebtedness, sell assets, reduce or delay capital expenditures or seek to raise additional capital, any of which could have a material adverse effect on our business, results of operations and financial condition. We cannot assure you that our business will generate sufficient cash flows from operations in an amount sufficient to enable us to pay our indebtedness or to fund our other liquidity needs. Further, we cannot assure you that we will be able to refinance any of our indebtedness on commercially reasonable terms, or at all.

In addition, in some cases, the Notes allow for the interest to be paid in a combination of cash and shares of our common stock, and allows for the interest to be convertible into shares of our common stock, which may dilute our existing stockholders. Such conversion is also subject to adjustment, which may cause further dilution to our existing stockholders.

The Notes are subject to restrictive and other covenants that may limit our discretion and the discretion of our subsidiaries with respect to certain business matters. A breach of any of these covenants could result in a default under our outstanding indebtedness, which would have a material adverse effect on our business, results of operations and financial condition.

We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development programs, or other operations.

The development of biopharmaceutical product candidates is capital-intensive. We expect our expenses to increase in connection with our ongoing activities, particularly as we conduct our planned clinical trials under our key clinical development programs, continue research and development and potentially initiate clinical trials under our other development programs and seek regulatory approval for any product candidates we may develop. In addition, as our product candidates progress through development and toward commercialization, we may need to make milestone payments to licensors and other third parties from whom we have in-licensed or acquired our product candidates. Furthermore, if and to the extent we seek to acquire or in-license additional product candidates in the future, we may be required to make significant upfront payments, milestone payments, and/or licensing payments. If we obtain regulatory approval for any of our product candidates, we also expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Because the outcome of any clinical trial or preclinical study is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. Moreover, a small group of investors that hold a significant portion of our issued and outstanding common stock may be in a position to influence the terms of a funding transaction, potentially making it more difficult to reach agreement on terms that are acceptable to investors participating in the financing, in a timely manner, if at all. If we are unable to raise sufficient capital to fund our activities when needed and on acceptable terms, we could be forced to delay, reduce or eliminate our research and development programs or, if our product candidates are approved, any future commercialization efforts.

We have based estimates included in our operating plan on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our operating plans and other demands on our cash resources may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings or other capital sources, including potentially collaborations, licenses and other similar arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Attempting to secure additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to develop our product candidates.

Our future capital requirements will depend on many factors, including:

- the type, number, scope, progress, expansions, results, costs and timing of our clinical trials and preclinical studies of our product candidates, which we are pursuing or may choose to pursue in the future;
- the costs and timing of manufacturing for our product candidates, including commercial manufacturing if any product candidate is approved;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of obtaining, maintaining and enforcing our patents and other intellectual property rights;
- the timing and amount of the milestone or other payments we must make to the licensors and other third parties from whom we have in-licensed or acquired our product candidates;
- the costs and timing of establishing or securing sales and marketing capabilities if any product candidate is approved;
- the costs, terms and timing of establishing and maintaining collaborations, licenses and other similar arrangements;
- costs associated with any product candidates or technologies that we may in-license or acquire; and
- our ability to achieve sufficient market acceptance, coverage and adequate reimbursement from payors and adequate market share and revenue for any approved products.

Conducting clinical trials and preclinical studies is a time consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success.

Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us at any time on acceptable terms, or at all.

Our strategy to expand our pipeline on our own, through acquisitions of early-stage product candidates, or through research partnerships, may not be successful.

Our business is focused on advancing early and late-stage innovative therapies for critical conditions and diseases. In this regard, we continue to pursue internal discovery efforts or partnerships with pharmaceutical and biotech companies, with the goal of identifying new product candidates to advance into clinical trials. Our efforts to identify new product candidates will require substantial technical, financial and human resources. These discovery efforts may initially show promise in identifying potential product candidates, yet ultimately fail to yield product candidates for clinical development for a number of reasons. For example, potential product candidates may, on later stage clinical trial, be shown to have inadequate efficacy, harmful side effects, suboptimal pharmaceutical profiles or other characteristics suggesting that they are unlikely to be commercially viable products.

Apart from our internal efforts, we may continue to seek to broaden and diversify our product portfolio through acquisitions. This strategy is dependent on our ability to successfully identify and acquire relevant product candidates. For example, in April 2024, we entered into an Asset Purchase Agreement, or the Asset Purchase Agreement, with Varian Biopharmaceuticals, Inc., or Varian, to acquire certain of Varian's assets, including a proprietary aPKCi inhibitor.

The acquisition of a product is a highly competitive area, and many other companies are pursuing the same or similar product candidates to those that we may consider attractive. In particular, larger companies with more well-established and diverse revenue streams may have a competitive advantage over us due to their size, financial resources and more extensive clinical development and commercialization capabilities. Furthermore, companies that perceive us to be a competitor may be unwilling to assign rights to us. The success of this strategy depends partly upon our ability to identify, select and acquire promising product candidates. The process of proposing, negotiating and implementing an acquisition of a product candidate is lengthy and complex, and we may be unable to acquire the rights to any such products or product candidates from third parties for several reasons. We may also be unable to acquire additional relevant product candidates on acceptable terms. Further, even if we identify acquisition targets, we may not be able to complete the transactions or we may determine after due diligence investigation not to pursue identified targets. Even if we succeed in our efforts to obtain rights to suitable product candidates, the success of our investments in these areas, our investment strategy will remain subject to the inherent risks associated with the development and commercialization of the product, and with the competitive business environment in which we operate

In addition, acquisitions may entail numerous operational, financial and legal risks, including:

- potential failure of the due diligence process to identify significant problems, liabilities or other shortcomings or challenges of an acquired product candidate or technology, including problems, liabilities or other shortcomings or challenges with respect to intellectual property, product quality, partner disputes or issues and other legal and financial contingencies and known and unknown liabilities;
- assumption of unknown or contingent liabilities or incurrence of unanticipated expenses;
- exposure to known and unknown liabilities, including possible intellectual property infringement claims, violations of laws, tax liabilities and commercial disputes;
- incurrence of substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions;
- incurrence of large one-time expenses and acquiring intangible assets that could result in significant future amortization expense and significant write-offs;
- higher than expected acquisition and integration costs; and
- inability to maintain uniform standards, controls, procedures and policies.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until we can generate substantial product revenues to support our operations, we expect to finance our cash needs through equity offerings, debt financings or other capital sources, including potentially collaborations, licenses and other strategic transactions. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect their rights as common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through future collaborations, licenses and other similar arrangements, we may have to relinquish valuable rights to our future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us and/or that may reduce the value of our common stock.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition, and stock price.

Global financial markets have recently, and may continue to, experience extreme volatility and disruptions, declines in consumer confidence, declines in economic growth, increases in unemployment rates, and uncertainty about economic stability as a result of geopolitical unrest, liquidity constraints, failures and instability in U.S. and international financial banking systems, inflation, and other factors beyond control. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy and ability to raise capital may be adversely affected by any such economic downturn, volatile business environment, or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance, and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers, and other partners may not survive these difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget.

In addition, the stock markets have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many companies, including in connection with the COVID-19 pandemic, which resulted in decreased stock prices for many companies notwithstanding the lack of a fundamental change in their underlying business models or prospects. These fluctuations have often been unrelated or disproportionate to the operating performance of those companies. For additional information regarding the impact of the COVID-19 pandemic, please see "*Risk Factors—The COVID-19 pandemic has negatively impacted, and may continue to negatively impact, our ability to develop our product candidates.*"

Further, the impacts of political unrest, including as a result geopolitical tension, such as a deterioration in the relationship between the U.S. and China or continued conflict between Russia and Ukraine, including any additional sanctions, export controls or other restrictive actions that may be imposed by the U.S. and/or other countries against governmental or other entities in, for example, China or Russia, also could lead to disruption, instability, and volatility in the global markets, which may have an adverse impact on our business or ability to access the capital markets. Broad market and industry factors, including potentially worsening economic conditions, inflationary pressures, and other adverse effects, political, regulatory, and other market conditions, may negatively affect the market price of shares of our common stock, regardless of our actual operating performance.

Adverse developments affecting the financial services industry, including events or concerns involving liquidity, defaults or non-performance by financial institutions or transactional counterparties, could adversely affect our business, financial condition or results of operations.

Events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. Most recently, on March 10, 2023, Silicon Valley Bank was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation as receiver. Similarly, on March 12, 2023, Signature Bank and Silvergate Capital Corp. were each swept into receivership. Although we assess our banking and customer relationships as we believe necessary or appropriate, our access to funding sources and other credit arrangements in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect us, the financial services industry or economy in general. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry.

In addition, investor concerns regarding the U.S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, result in breaches of our contractual obligations or result in violations of federal or state wage and hour laws. Any of these impacts, or any other impacts resulting from the factors described above or other related or similar factors not described above, could have material adverse impacts on our liquidity and our business, financial condition or results of operations.

Due to the significant resources required to develop our product candidates, we must prioritize development of certain product candidates and/or certain disease indications. We may be delayed in advancing a product candidate or potential indication if our plan does not include sufficient funding to execute a clinical program. If we expend our limited resources on candidates or indications that do not yield a successful product and fail to capitalize on other product candidates or indications that may be more profitable or for which there is a greater likelihood of success, such failure could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We are currently focused on developing product candidates to address unmet medical needs in acute cardiovascular diseases. We seek to allocate our limited capital among our programs in an efficient manner and to advance our cardiovascular product candidate. However, due to the significant resources required to advance the development of our product candidates, we also must focus on specific indications and disease pathways and decide which product candidates and indications to pursue and the amount of resources to allocate to each such product candidate.

Our ability to advance a product candidate depends on our ability to secure the additional capital required to execute each phase of product development. In developing our plan, we were aware of the size and projected costs of our planned late stage development of istaroxime to improve cardiac function and clinical outcomes in patients with AHF. We have allocated our limited resources initially toward cardiogenic shock as we believe this may be a less resource intensive and faster development program. Such decisions concerning the allocation of research and development funds towards, or away from, particular product candidates or therapeutic areas may not lead to the development of any viable commercial product and may divert resources away from better opportunities. Similarly, any decision to delay, terminate or engage with third parties in respect of certain programs may subsequently also prove to be suboptimal and could cause us to miss valuable opportunities. In that event, our business, financial condition and results of operations could be materially adversely affected. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases and disease pathways that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to such product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain development and commercialization rights.

We have a significant amount of intangible assets recorded on our consolidated balance sheets which may lead to potentially significant impairment charges.

As a result of the acquisition of CVie Therapeutics in December 2018, we have recorded significant intangible assets on our consolidated balance sheets, which could become impaired and lead to material charges in the future. The identifiable intangible assets resulting from the CVie Therapeutics acquisition relate to IPR&D of istaroxime and rostafuroxin, which, as of December 31, 2023, were $22.3 million and $2.9 million, respectively, recorded in aggregate on our consolidated balance sheet as intangible assets of $25.3 million. As of December 31, 2023, goodwill was zero on our consolidated balance sheet.

Throughout the year, we consider whether any events or changes in the business environment have occurred which indicate that intangible assets or goodwill may be impaired. If an impairment exists, we would be required to take an impairment charge with respect to the impaired asset. Events giving rise to impairment are difficult to predict, including the uncertainties associated with the development of product candidates and the success of business development activities, and are an inherent risk in the pharmaceutical industry. Based on our annual quantitative impairment assessment of our indefinite-lived IPR&D intangible assets as of December 1, 2023, we concluded that the assets were not impaired.

Since early 2022, we have experienced a declining trend in the closing share price of our common stock, on a split-adjusted basis. During each of the first and second quarters of 2023, the continued declining trend in the closing share price of our common stock, on a split-adjusted basis, suggested that the fair value of our reporting unit was more likely than not less than its carrying value. As a result, in each quarter, we performed the interim goodwill impairment test consistent with the methodology that we use when performing our annual goodwill impairment assessment and determined that the fair value of our reporting unit was more likely than not less than its carrying value. We recorded a loss on impairment of goodwill of $0.5 million in the first quarter of 2023 and an additional loss of $2.6 million, representing the remaining balance of goodwill, in the second quarter of 2023. For the year ended December 31, 2023, the aggregate loss on impairment of goodwill is $3.1 million, recognized within operating expenses in our consolidated statement of operations. As of December 31, 2023, goodwill was zero on our consolidated balance sheet.

If we fail to maintain proper and effective internal control over financial reporting, our ability to produce accurate and timely financial statements could be impaired, investors may lose confidence in our financial reporting and the trading price of our common stock may decline.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, as amended, we are required to furnish a report by our management on our internal control over financial reporting. We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If our financial statements are not accurate, investors may not have a complete understanding of our operations. If we do not file our financial statements on a timely basis as required by the SEC, we could face severe consequences. If we are unable to conclude that our internal control over financial reporting is effective, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by the Nasdaq Stock Market LLC, or Nasdaq, the SEC or other regulatory authorities. Moreover, responding to such investigations, are likely to consume a significant amount of our management resources and cause us to incur significant legal and accounting expense. Failure to remedy any material weakness in our internal control over financial reporting, or to maintain effective control systems, could also restrict our future access to the capital markets. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Risks Related to our Development Activities and Regulatory Approval of our Product Candidates

We are substantially dependent on the success of our lead product candidate istaroxime. To the extent that our clinical development of istaroxime is not successful, our business, financial condition, and results of operations may be materially adversely affected and the price of our common stock may decline.

We currently have no product candidates approved for sale, and we may never be able to develop marketable products. We are focusing a significant portion of our activities and resources on our lead product candidate, istaroxime, and we believe our prospects are highly dependent on, and a significant portion of the value of our company relates to, our ability to successfully obtain regulatory approval for istaroxime. We currently do not have sufficient capital to fully execute clinical trials with respect to istaroxime. Furthermore, the clinical development and regulatory approval of istaroxime is subject to many risks, including the risks discussed in other risk factors, and istaroxime may not receive marketing approval from any regulatory agency. If we are unable to continue to advance istaroxime through clinical development, or if the results or timing of regulatory filings, the regulatory process, regulatory developments, clinical trials or preclinical studies, or other activities, actions or decisions related to istaroxime do not meet our or others' expectations, the market price of our common stock could decline significantly. Should the results of our clinical development program be insufficient to support regulatory approval, we may be forced to rely on our other product candidates, which will require additional time and resources to potentially obtain regulatory approval. There can be no assurance that we will be able to successfully develop istaroxime.

Clinical development involves a lengthy and expensive process with an uncertain outcome, and results of preclinical studies and early clinical trials are not necessarily predictive of future results. In addition, our assumptions about why certain of our product candidates are worthy of future development and potential approval are based on data primarily collected by other companies. Our product candidates may not have favorable results in later clinical trials, if any, or receive regulatory approval on a timely basis, if at all.

Clinical drug development is expensive and can take many years to complete, and its outcome is inherently uncertain. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all, and failure can occur at any time during the preclinical study or clinical trial process as a result of inadequate study design, inadequate performance of a drug, inadequate adherence by patients or investigators to clinical trial protocols, or other factors. For example, conducting a toxicology study as part of a preclinical program, to be included in a required regulatory submission, could result in unanticipated findings that could potentially negatively impact the clinical program. Despite promising preclinical or clinical results, any product candidate can unexpectedly fail at any stage of preclinical or clinical development. The historical failure rate for product candidates in our industry is high.

Product candidates in later stages of clinical trials may fail to achieve the desired safety and efficacy outcomes despite having progressed through earlier clinical trials. As a result, data we obtain from our phase 2 clinical trials may not accurately predict phase 3 trial results, whether due to differences in sample size, study arms, duration, endpoints, or other factors. If any of our product candidates should fail to perform as designed in their respective phase 3 clinical programs, such failures could adversely affect the results of our clinical development program despite promising results in earlier trials. If clinical trials for any of our product candidates fail to demonstrate safety or efficacy to the satisfaction of the U.S. Food and Drug Administration, or FDA, or the equivalent regulatory authorities in other countries, the FDA or the equivalent regulatory authorities in other countries will not approve that drug and we would not be able to commercialize it, which could have a material adverse effect on our business, financial condition, results of operations, and

prospects. Moreover, if we are required to cease development activities on any of our recently acquired product candidates due to adverse clinical results or otherwise, it could result in impairment of related intangible assets and goodwill on our consolidated balance sheets.

Even if later stage clinical trials are successful, regulatory authorities may question the trial design or sufficiency for approval of the endpoints we select for our clinical trials or add new requirements, such as the completion of additional studies, as conditions for obtaining approval or obtaining an indication. For the foregoing reasons, we cannot be certain that our planned clinical trials and preclinical studies will be successful. Any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications, which could have a material adverse effect on our business, financial condition and results of operations, and result in significant additional costs and expenses, require additional time and have an adverse effect on our business, including our financial condition and results of operations.

Delays in clinical trials are common and have many causes, and any delay could result in increased costs to us and jeopardize or delay our ability to continue development activities, including our ability to obtain trial results, regulatory approval and commence product sales or allow for competition to emerge.

We may experience delays in clinical trials of our product candidates, or the time required to complete clinical trials for our product candidates may be longer than anticipated. Our planned clinical trials may not begin on time, have an effective design, enroll a sufficient number of patients, or be completed on schedule, if at all. Our clinical trials can be delayed for a variety of reasons, including, but not limited to:

- our inability to raise funding necessary to initiate or continue a trial;
- delays in obtaining regulatory approval to commence a trial or reaching a consensus with regulatory authorities on trial design or product standards;
- delays in reaching an agreement with the FDA or the equivalent foreign regulatory authorities in other countries on final trial design or the scope of the development program;
- inability to develop studies that are acceptable in all markets of interest;
- inability to come to an agreement on clinical trial design or execution factors with potential development partners;
- imposition of a clinical hold following an inspection of our clinical trial operations or trial sites by the FDA or the equivalent regulatory authorities in other countries;
- failures or delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- delays associated with severe acute respiratory syndrome coronavirus 2, the causative agent in a novel strain of coronavirus, which have and may continue to impact our healthcare systems and our trial sites ability to conduct trials to varied degrees and times. Coronavirus creates risk of interrupting availability of necessary clinical supplies, local regulatory reviews, hospital ethics committee reviews, professional staff, site monitors and other necessary travel;
- delays in obtaining contracts with clinical sites and required IRB approval at each site;
- IRBs refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing their approval of the trial;
- competition with other studies for study patients;
- changes to clinical trial protocol;
- delays in recruiting suitable patients to participate in a trial;
- subjects choosing an alternative treatment for the indication for which we are developing our product candidates, or participating in competing clinical trials;
- delays in having subjects complete participation in a trial or return for post-treatment follow-up;
- clinical sites deviating from trial protocol or dropping out of a trial to the detriment of enrollment;
- subjects experiencing severe or unexpected adverse events;
- occurrence of serious adverse events in trials of the same class of agents conducted by other companies;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;

- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, GCPs, or other regulatory requirements;
- third-party contractors not performing data collection or analysis in a timely or accurate manner;
- third-party contractors lacking adequate certification to provide services in all regions where we conduct our business activities;
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications;
- manufacturing timing and/or obtaining sufficient quantities of product candidate or obtaining sufficient quantities of combination therapies for use in clinical trials or changes in the manufacturing process or inability to meet analytical standards for product release or use that may be necessary or desired;
- time required to add new clinical sites; or
- delays by our contract manufacturers to produce and deliver a sufficient supply of clinical trial materials or being ordered by the FDA or comparable foreign regulatory authorities to temporarily or permanently shut down due to violations of cGMP regulations or other applicable requirements, or infections or cross-contaminations of product candidates in the manufacturing process.

In addition, we may not reach agreement with the FDA, or a foreign regulator on the extent of our phase 3 programs, the design of any one or more of the clinical trials necessary for approval, or we may be unable to reach agreement on a single design that would permit us to conduct a common pivotal phase 3 clinical development program in all markets of interest. For example, we may not be able to design a study that is acceptable to both the FDA and the EMA regulators, which would cause us to limit the scope of our geographical activities or greatly increase our investment. Even if we complete the clinical trial within our anticipated time, if our results are inconclusive or non-compelling or otherwise insufficient to support a strategic or financing transaction, we potentially could be forced to limit or cease our development activities, which would have a material adverse effect on our business.

We have conducted, and may in the future conduct, clinical trials for our product candidates at clinical sites located in the U.S. and outside of the U.S. If the FDA and other foreign equivalents raise concerns about certain of the clinical sites based on location and regulatory environment, they may not accept data from such trials, in which case our development plans will be delayed, which could materially harm our business.

We have conducted and are expecting in the future to conduct one or more of our clinical trials for our product candidates at clinical sites located in the U.S. and outside of the U.S., including the EU, China, Russia, Israel, and South America. Although the FDA may accept data from clinical trials conducted outside the U.S., acceptance of this data may be subject to certain conditions imposed by the FDA. For example, the FDA requires the clinical trial to have been conducted in accordance with GCPs, and the FDA must be able to validate the data from the clinical trial through an onsite inspection if it deems such inspection necessary. Where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the U.S., the FDA will not approve the application on the basis of foreign data alone unless those data are considered applicable to the U.S. patient population and U.S. medical practice, the clinical trials were performed by clinical investigators of recognized competence, and the data is considered valid without the need for an onsite inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an onsite inspection or other appropriate means. There can be no assurance the FDA will accept data from clinical trials conducted outside of the U.S. If the FDA does not accept data from our clinical trials of our product candidates, it would likely result in the need for additional clinical trials, which would be costly and time consuming and delay or permanently halt our development of our product candidates.

For example, we have previously conducted clinical trials in Russia. The February 2022 invasion of Ukraine by Russia and the resulting imposition of economic and other sanctions by the U.S., EU, and many other nations on Russia, individuals in Russia, Russian businesses, and the Russian central bank, has impacted the way we executed certain trial procedures as we completed the first part of our trial in early cardiogenic shock. This geopolitical disruption could also disrupt or delay our ability to conduct clinical trial activities in Russia in the future. Although the length and impact of any military action are highly unpredictable, making them unavailable for follow-up could result in increased costs and could delay our anticipated timeline for the completion of our future clinical trials.

The COVID-19 pandemic has negatively impacted, and may continue to negatively impact, our ability to develop our product candidates.

The impact of the COVID-19 pandemic resulted in, and may in the future result in, significant disruptions to the global economy, as well as businesses and capital markets around the world. Efforts to contain the spread of COVID-19 have intensified at times to manage surges in the infection rate and deaths, and many countries have at times implemented severe travel restrictions, social distancing, and delays or cancellations of elective surgeries at different times. Notwithstanding the introduction of effective vaccines, COVID-19 may in the future affect our ability and the ability of our employees, contractors, suppliers, and other partners in the U.S. and abroad to conduct normal business activities from time to time, including due to shutdowns that may be requested or mandated by governmental authorities.

The spread of COVID-19 globally has previously adversely impacted trial conduct and operations and may do so again in the future. We have, in the past, initiated several clinical trials for istaroxime in the EU and other worldwide locations impacted by the COVID-19 outbreak. Our clinical trials have suffered delays and interruptions and our previous decision to cease enrollment in the AEROSURF clinical trial was partially due to such delays and escalating expenses. Our efforts to conduct trials could be materially delayed in the future by governmental restrictions and enrollment difficulties as hospitals reduce and divert staffing, divert resources to patients suffering from the infectious disease and limit hospital access for nonpatients.

Similarly, there is a risk that clinical supplies of our product candidates may be significantly delayed or may become unavailable as a result of COVID-19 and the resulting impact on our suppliers' labor forces and operations, including as a result of governmental restrictions on business operations and the movement of people and goods in an effort to curtail the spread of the virus. There can be no assurance that we would be able to timely implement any mitigation plans. Disruptions in our supply chain, whether as a result of restricted travel, quarantine requirements or otherwise, could negatively impact clinical supplies of our product candidates, which could materially adversely impact our clinical trial and development timelines.

The effects of COVID-19 or any other pandemic, including identification of potential new variants, has led and may in the future lead to periodic disruption and volatility in the global capital markets, which could increase our cost of capital and adversely affect our ability to access the capital markets in the future. It is possible that the spread of COVID-19 in the future could cause an economic slowdown or recession or cause other unpredictable events, each of which could adversely affect our business, results of operations or financial condition.

The extent to which COVID-19 or any other pandemic impacts our financial results going forward will depend on future developments, which are highly uncertain and cannot be predicted, including new information which may emerge concerning the severity of the COVID-19 outbreak, the rise of variants, which may be more contagious and potentially more lethal, and the actions recommended to contain the outbreak or treat its impact, among others. Moreover, the COVID-19 outbreak has had and may in the future have indeterminable adverse effects on general commercial activity and the world economy, and our business and results of operations could be adversely affected to the extent that COVID-19 or any other pandemic harms the global economy generally.

Use of our product candidates could be associated with side effects, adverse events or other properties or safety risks, which could delay or preclude approval, cause us to suspend or discontinue clinical trials, abandon a product candidate, limit the commercial profile of an approved label or result in other significant negative consequences that could severely harm our business, prospects, operating results and financial condition.

As is the case with pharmaceuticals generally, there may be adverse events in patients treated with our product candidates. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. Adverse events could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Moreover, if our product candidates are associated with undesirable side effects in clinical trials or have characteristics that are unexpected, we may elect to abandon their development or limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, which may limit the commercial expectations for the product candidate if approved. We may also be required to modify our study plans based on findings in our clinical trials. Many compounds that initially show promise in early-stage testing have later been found to cause side effects that prevented further development of the compound. In addition, regulatory authorities may draw different conclusions or require additional testing to confirm these determinations.

It is possible that as we test our product candidates in larger, longer and more extensive clinical trials, or as the use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by subjects. If such side effects become known later in development or upon approval, if any, such findings may harm our business, financial condition and prospects significantly.

In addition, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw, suspend or limit approvals of such product;
- we may be required to recall a product or change the way such product is administered to patients;
- regulatory authorities may require additional warnings on the label, such as a "black box" warning or a contraindication;
- we may be required to implement a REMS or create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way a product is distributed or administered, conduct additional clinical trials or change the labeling of a product or be required to conduct additional post-marketing studies or surveillance;
- we could be sued and held liable for harm caused to patients;
- sales of the product may decrease significantly, or the product could become less competitive; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations, and prospects.

Our product candidates are subject to extensive regulation and compliance, which is costly and time consuming, and such regulation may cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates.

The clinical development, manufacturing, labeling, storage, record-keeping, advertising, promotion, import, export, marketing and distribution of investigational new drugs and approved new drugs are subject to extensive regulation by the FDA in the U.S. and by comparable foreign regulatory authorities in foreign markets. In the U.S., the process of obtaining regulatory approval is expensive, often takes many years following the commencement of clinical trials and can vary substantially based upon the type, complexity and novelty of the product candidates involved, as well as the target indications and patient population. Approval policies or regulations may change, and the FDA has substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed. We are not permitted to market any of our product candidates in the U.S. until we receive approval of an NDA from the FDA.

Prior to obtaining approval to commercialize a product candidate, if approved, in the U.S. or abroad, we must demonstrate with substantial evidence from adequate and well-controlled clinical trials, and to the satisfaction of the FDA or comparable foreign regulatory authorities, that such product candidates are safe and effective for their intended uses.

Even if we believe the nonclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authorities, as the case may be, may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post-approval, or may object to elements of our clinical development program.

The FDA or comparable foreign regulatory authorities can delay, limit, or deny approval of a product candidate for many reasons, including:

- such authorities may disagree with the design or implementation of our clinical trials;
- negative or ambiguous results from our clinical trials or results may not meet the level of statistical significance required by the FDA or comparable foreign regulatory agencies for approval;
- such authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- such authorities may not agree that the data collected from clinical trials of our product candidates are acceptable or sufficient to support approval;
- serious and unexpected adverse events may be experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- the population studied in the clinical trial may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- such authorities may not accept clinical data from trials which are conducted at clinical facilities or in countries where the standard of care or patient characteristics are potentially different from that of the U.S.;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks or the safety data base may not be large enough;
- such authorities may not accept the submission of an NDA or other submission to obtain regulatory approval in the U.S. or elsewhere, and such authorities may impose requirements for additional preclinical studies or clinical trials;
- such authorities may disagree regarding the formulation, labeling and/or the specifications of our product candidates;
- approval may be granted only for indications that are significantly more limited than what we apply for and/or with other significant restrictions on distribution and use;
- such authorities may find deficiencies in the manufacturing processes or facilities of our third-party manufacturers with which we contract for clinical and, if approved, commercial supplies; or the approval policies;
- regulations of such authorities may significantly change in a manner rendering our or any of our potential future collaborators' clinical data insufficient for approval; or
- such authorities may not accept a submission due to, among other reasons, the content or formatting of the submission.

We may conduct clinical development in the U.S., Canada, the EU, Eastern Europe, Latin America, and Asia Pacific regions and sell our products, if approved, in the U.S. and potentially in other major markets. To accomplish this objective, we must obtain and maintain regulatory approvals and comply with regulatory requirements in each jurisdiction. To avoid the significant expense and lengthy time required to complete multiple regional clinical development programs, we expect to meet with relevant regulatory authorities. While we would prefer to design a single, global clinical development program that would satisfy the regulators in all of our target markets, there can be no assurance that our efforts will be successful. If we are unable to reach agreement with the various regulatory authorities, we may not be able to pursue regulatory approval of our product candidates in all of our selected markets.

With respect to foreign markets, approval procedures vary among countries and, in addition to the foregoing risks, may involve additional product testing, administrative review periods and agreements with pricing authorities. In addition, events raising questions about the safety of certain marketed pharmaceuticals may result in increased cautiousness by the FDA and comparable foreign regulatory authorities in reviewing new drugs based on safety, efficacy or other regulatory considerations and may result in significant delays in obtaining regulatory approvals. Any delay in obtaining, or inability to obtain, applicable regulatory approvals would prevent us or any of our potential future collaborators from commercializing our product candidates. In addition, delays associated with COVID-19 may impact local regulatory reviews occurring in a timely manner and result in delays for trial and site initiations.

Of the large number of drugs in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, financial condition, results of operations and prospects.

Although we have multiple product candidates or potential indications of those candidates in our clinical pipeline, we may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on other product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we may focus on specific product candidates, indications and development programs at any time. As a result, we may forgo or delay pursuit of opportunities with other product candidates that could have had greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through future collaborations, license agreements and other similar arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Additionally, we may pursue additional in-licenses or acquisitions of development-stage assets or programs, which entails additional risk to us. For example, in connection with the Asset Purchase Agreement entered into on April 2, 2024, we acquired certain assets from Varian, which includes topical and oral formulations of our aPKCi inhibitor. Because we were not involved in the preclinical development of these drug candidates prior to such date, we have relied on Varian having conducted such research and development in accordance with the applicable protocol, legal, regulatory and scientific standards, having accurately reported the results of all preclinical studies conducted prior to our agreement with Varian and having correctly collected and interpreted the data from these studies. To the extent any of these has not occurred, expected development time and costs may be increased which could adversely affect any future revenue from the assets acquired from Varian.

Identifying, selecting and acquiring promising product candidates requires substantial technical, financial and human resources expertise. Efforts to do so may not result in the actual acquisition or license of a particular product candidate, potentially resulting in a diversion of our management's time and the expenditure of our resources with no resulting benefit. If we are unable to identify programs that ultimately result in approved products, we may spend material amounts of our capital, management and other resources evaluating, acquiring and developing products that ultimately do not provide a return on our investment.

Even though some of our product candidates have Fast Track designation, the FDA may not approve them at all or any sooner than other product candidates that do not have Fast Track designation.

We have received Fast Track designation from the FDA for istaroxime for the treatment of AHF. Fast Track designation does not ensure that we will receive marketing approval or that approval will be granted within any particular timeframe. We may not experience a faster development, regulatory review or approval process with Fast Track designation compared to conventional FDA procedures. Additionally, the FDA may withdraw Fast Track designation, for reasons such as it comes to believe a drug candidate no longer adequately addresses an unmet medical need. Fast Track designation alone does not guarantee qualification for the FDA's priority review procedures. If we seek Fast Track designation for other product candidates, we may not receive such a designation from the FDA.

Although we may pursue expedited regulatory programs for a product candidate or an indication, it may not qualify for expedited development or, if it does qualify for expedited development, it may not actually lead to a faster development or regulatory review or approval process.

Although we have received Fast Track designation for certain of our product candidates, we believe there may be an opportunity to expedite the development of other product candidates or indications through one or more of the FDA's expedited programs, such as Fast Track, Breakthrough Therapy or priority review, we cannot be assured that any of our product candidates or indications will qualify for such programs.

For example, a product candidate may be eligible for designation as a Breakthrough Therapy if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. Although Breakthrough Therapy designation or access to any other expedited program may expedite the development or approval process, it does not change the standards for approval. If we apply for Breakthrough Therapy designation or any other expedited program for our product candidates, the FDA may determine that our proposed target indication or other aspects of our clinical development plans do not qualify for such expedited program. For example, we believe that istaroxime may fulfill an unmet medical need in early and more severe cardiogenic shock based on the profile observed in prior phase 2 clinical studies in AHF and early cardiogenic shock, in which increases in SBP as well as improvements in cardiac function were observed suggesting that istaroxime could potentially contribute to the

clinical improvement of select patients in cardiogenic shock due to heart failure. However, the FDA may not agree with our assessment, and we may not be able to obtain Breakthrough Therapy designation.

Even if we are successful in obtaining a Breakthrough Therapy designation or access to any other expedited program, we may not experience faster development timelines or achieve faster review or approval compared to conventional FDA procedures. Access to an expedited program may also be withdrawn by the FDA if it believes that the designation is no longer supported by data from our clinical development program. Additionally, qualification for any expedited program does not ensure that we will ultimately obtain regulatory approval for such product candidate.

We may not be able to obtain or maintain Orphan Drug exclusivity for our product candidates.

Regulatory authorities in some jurisdictions, including the U.S. and Europe, may designate drugs for relatively small patient populations as Orphan Drugs. In the U.S., Orphan Drug designation entitles a party to financial incentives such as tax advantages and user-fee waivers. In addition, if a product candidate that has Orphan Drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to Orphan Drug exclusivity, which means that the FDA may not approve any other applications, including an NDA, to market the same drug for the same indication for seven years, except in limited circumstances, including if the FDA concludes that the later drug is clinically superior to the approved drug. A drug is clinically superior if it is safer, more effective, or makes a major contribution to patient care. The FDA has granted Orphan Drug designation for our (i) KL4 surfactant (lucinactant) for the treatment of RDS in premature infants, (ii) our KL4 surfactant for the prevention and treatment of BPD in premature infants, (iii) our KL4 surfactant for the treatment of ARDS in adults, and (iv) our KL4 surfactant for the treatment of cystic fibrosis.

If we obtain Orphan Drug exclusivity, we may lose such exclusivity if the FDA or the European Commission, or EC, determines that the request for designation was materially defective or if we are unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. Moreover, Orphan Drug exclusivity may not effectively protect our product candidates from competition because different drugs can be approved for the same condition. Even after an Orphan Drug is approved, the FDA or comparable foreign regulatory authority can subsequently approve the same drug for the same condition if such regulatory authority concludes that the later drug is clinically superior if it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a product candidate nor gives the product candidate any advantage in the regulatory review or approval process.

Interim, topline and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or topline or data from our clinical studies, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available. From time to time, we may also disclose interim data from our clinical studies. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

Even if we receive regulatory approval for any product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions on marketing or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them are approved.

Following potential approval of any our product candidates, the FDA may impose significant restrictions on a product's indicated uses or other aspects of the directions for use or marketing or impose ongoing requirements for potentially costly and time-consuming post-approval studies, post-market surveillance or clinical trials to monitor the safety and efficacy of the product. The FDA may also require a REMS as a condition of approval of our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our products will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and GCP requirements for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with our products, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- restrictions on product distribution or use, or requirements to conduct post-marketing studies or clinical trials;

- fines, restitutions, disgorgement of profits or revenues, warning letters, untitled letters, Form 483s, or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of our products; and
- injunctions or the imposition of civil or criminal penalties.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates, if approved, and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

In addition, if any of our product candidates is approved, our product labeling, advertising and promotion will be subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

If we fail to obtain and maintain regulatory approval in foreign jurisdictions, our market opportunities will be limited.

In order to market our product candidates in the EU or other foreign jurisdictions, we must obtain and maintain separate regulatory approvals and comply with numerous and varying regulatory requirements. The approval procedure varies from country to country and can involve additional testing. The time required to obtain approval abroad may be longer than the time required to obtain FDA clearance or approval. Foreign regulatory approval processes include many of the risks associated with obtaining FDA clearance or approval and we may not obtain foreign regulatory approvals on a timely basis, if at all. FDA clearance or approval does not ensure approval by regulatory authorities in other countries, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries. However, the failure to obtain clearance or approval in one jurisdiction may have a negative impact on our ability to obtain clearance or approval elsewhere. If we do not obtain or maintain necessary approvals to commercialize our product candidates in markets outside the U.S., it would negatively affect our overall market penetration.

If the FDA or other applicable regulatory authorities approve generic products with claims that compete with our product candidates, it could reduce our sales of our product candidates if approved.

In the U.S., after an NDA is approved, the product covered thereby becomes a "listed drug" which can, in turn, be cited by potential competitors in support of approval of an abbreviated NDA, or ANDA. The Federal Food, Drug, and Cosmetic Act, or the FDC Act, FDA regulations and other applicable regulations and policies provide incentives to manufacturers to create modified, non-infringing versions of a drug to facilitate the approval of an ANDA or other application for generic substitutes. These manufacturers might only be required to conduct a relatively inexpensive study to show that their product has the same active ingredients, dosage form, strength, route of administration, and conditions of use, or product labeling, as our product candidates and that the generic product is absorbed in the body at the same rate and to the same extent as, or is bioequivalent to, our product candidates. These generic equivalents would be significantly less costly than ours to bring to market and companies that produce generic equivalents are generally able to offer their products at lower prices. Thus, after the introduction of a generic competitor, a significant percentage of the sales of any branded product are typically lost to the generic product. Accordingly, competition from generic equivalents to our product candidates would substantially limit our ability to generate revenues and therefore to obtain a return on the investments we have made in our product candidates.

Even if we receive regulatory approval for any of our product candidates, we may not be able to successfully commercialize the product and the revenue that we generate from its sales, if any, may be limited.

If approved for marketing, the commercial success of our product candidates will depend upon the acceptance of each product by the medical community, including physicians, patients and health care payors. The degree of market acceptance for any of our product candidates, if approved, will depend on a number of factors, including:

- demonstration of clinical safety and efficacy;
- efficacy of our product candidates compared to competing products;
- relative convenience, dosing burden and ease of administration;
- the prevalence and severity of any adverse effects;
- the willingness of physicians to prescribe our product candidates, if approved, and the target patient population to try new therapies;

- our ability to obtain and maintain sufficient third-party coverage or reimbursement from government health care programs, including Medicare and Medicaid, global government payors, private health insurers and other third-party payors or to receive the necessary pricing approvals from government bodies regulating the pricing and usage of therapeutics;
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage or reimbursement or government pricing approvals;
- government health care payor imposed mandatory pricing discounting and reductions;
- delays in achieving hospital formulary acceptance or limitations of use that are more restrictive than the approved label;
- the introduction of any new products that may in the future become available targeting indications for which our product candidates may be approved;
- new procedures or therapies that may reduce the incidences of any of the indications in which our product candidates, if approved, may show utility;
- pricing and cost-effectiveness;
- the inclusion or omission of our product candidates, if approved, in applicable therapeutic guidelines;
- the effectiveness of our own or any future collaborators' sales and marketing strategies; and
- limitations or warnings contained in approved labeling from regulatory authorities.

If any of our product candidates are approved, but do not achieve an adequate level of acceptance by physicians, health care payors, and patients, we may not generate sufficient revenue and we may not be able to achieve or sustain profitability. Our efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may never be successful.

In addition, even if we obtain regulatory approvals, the timing or scope of any approvals may prohibit or reduce our ability to commercialize our product candidates successfully. For example, if the approval process takes too long, we may miss market opportunities and give other companies the ability to develop competing products or establish market dominance. Any regulatory approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render our product candidates not commercially viable. For example, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve any of our product candidates with a label that does not include the labeling claims necessary or desirable for the successful commercialization for that indication. Further, the FDA or comparable foreign regulatory authorities may place conditions on approvals or require risk management plans or a REMS to assure the safe use of the drug. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of our product candidates, if approved. Moreover, product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following the initial marketing of the product. Any of the foregoing scenarios could materially harm the commercial success of our product candidates, if approved.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off- label uses. If we are found or alleged to have improperly promoted any of our products, if approved, for off-label uses, we may become subject to significant liability.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products, as our product candidates would be, if approved. In general, a product may not be promoted for uses that are not approved by the FDA or in ways that may not be consistent with the product's approved labeling. If we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA and other regulatory agencies have also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

We currently have no sales and marketing organization. If we are unable to establish satisfactory sales and marketing capabilities or secure a sales and marketing partner, we may not successfully commercialize any of our product candidates.

We may not be able to enter into collaboration agreements on terms acceptable to us or at all. In addition, even if we enter into such relationships, we may have limited or no control over the sales, marketing and distribution activities of these third parties. Our future revenues may depend heavily on the success of the efforts of these third parties. If we elect to establish a sales and marketing infrastructure, we may not realize a positive return on this investment. In addition, we will have to compete with established and well-funded pharmaceutical and biotechnology companies to recruit, hire, train and retain sales and marketing personnel. Factors that may inhibit our efforts to commercialize our product candidates, if approved, without strategic partners or licensees include:

- the inability of sales personnel to obtain access to or educate and appropriately persuade adequate numbers of physicians to prescribe any of our product candidates, if approved;
- inability to obtain a competitive share of voice and frequency of meeting with physicians against multiple, larger competitors;
- unforeseen costs and expenses associated with creating an independent sales and marketing organization; and

- inability to control or influence partner sales and marketing personnel or their prioritization of promotion of our product candidates, if approved.

The successful commercialization of our product candidates, if approved, will depend in part on the extent to which hospitals and hospital systems, governmental authorities and health insurers establish coverage, adequate reimbursement levels and favorable pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those product candidates and decrease our ability to generate revenue.

The availability of coverage and the adequacy of reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford prescription medications such as our product candidates, if approved. Our ability to achieve coverage and acceptable levels of reimbursement for our product candidates by third-party payors will have an effect on our ability to successfully commercialize our product candidates, if approved. Even if we obtain coverage for a given product candidate, if approved, by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the U.S., the EU or elsewhere will be available for any product candidate that we may develop and for which we receive approval, and any reimbursement that may become available may be decreased or eliminated in the future. See the section titled, "Item 1. Business – Reimbursement."

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs when an equivalent generic drug or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates, if approved, as substitutable and only offer to reimburse patients for the less expensive product. Even if we are successful in demonstrating improved efficacy or improved convenience of administration with our product candidates, if approved, pricing of existing drugs may limit the amount we will be able to charge for our product candidates, if approved. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in product development. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates, if approved and may not be able to obtain a satisfactory financial return on products that we may develop.

Obtaining and maintaining reimbursement status is time consuming, costly and uncertain. The Medicare and Medicaid programs increasingly are used as models for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs. However, no uniform policy for coverage and reimbursement for products exists among third-party payors in the U.S. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates, if approved, to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases at short notice, and we believe that changes in these rules and regulations are likely.

Outside the U.S., international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other countries has and will continue to put pressure on the pricing and usage of our product candidates, if approved. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Additional foreign price controls, discounts or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates, if approved. Accordingly, in markets outside the U.S., the reimbursement for product candidates for which we receive approval may be reduced and experience continual mandatory price reductions compared with the U.S. and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the U.S. and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates, if approved. We expect to experience pricing pressures in connection with the sale of any of our product, candidates, if approved, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

Risks Related to Our Reliance on Third Parties

We rely on third parties, primarily outside of the U.S., to conduct many of our preclinical studies and clinical trials. Any failure by a third party to conduct the clinical trials according to GCPs and other requirements and in a timely and quality manner may delay or prevent our ability to seek or obtain regulatory approval for or commercialize our product candidates.

We are dependent on third parties to conduct our clinical trials and preclinical studies for our development programs. Specifically, we have used and relied on, and intend to continue to use and rely on, medical institutions, clinical investigators, CROs and consultants to conduct our clinical trials in accordance with our clinical protocols and regulatory requirements. These CROs, investigators and other third parties play a significant role in the conduct and timing of these trials and subsequent collection and analysis of data. While we have agreements governing the activities of our third-party contractors, we have limited influence over their actual performance. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and any third-party that we rely upon are required to comply with GCP requirements, which are

regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any third-party that we rely on or trial sites fail to comply with applicable GCPs or to provide adequate data with respect to such trials, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our clinical trials must be conducted with product produced under cGMP and/or Quality System Regulation requirements. Our failure or our vendors' failure to comply with these regulations may require us to delay or to repeat clinical trials, which would delay the regulatory approval process.

There is no guarantee that any such CROs, investigators or other third parties will devote adequate time and resources to such trials or perform as contractually required. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, or otherwise performs in a substandard manner, our clinical trials may be extended, delayed or terminated. In addition, many of the third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the study, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection by the FDA of any NDA we submit. Any such delay or rejection could prevent us from commercializing our product candidates, if approved.

If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative third parties or do so on commercially reasonable terms. Switching or adding additional CROs, investigators and other third parties involves additional costs and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, investigators and other third parties, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects. Our agreement with Universita Degli Studi di Milano-Bicocca, the institution that has performed many preclinical studies with istaroxime and our preclinical families of compounds, expired on July 31, 2022. If additional preclinical work is required for any reason, we will need to re-engage with Bicocca or find another vendor to provide those services.

We currently do not have a back-up facility for our CMO for our drug product candidates, or our suppliers of API. If the parties we depend on for supplying our APIs and manufacturing our drug product candidates do not supply these products in a timely and quality manner, it may delay or impair our ability to execute our development plans for our current and potential pipeline products. Such delays could adversely impact our operations and financial condition.

In most cases, we are dependent upon a single supplier to provide all of our requirements for each of our active pharmaceutical ingredients, or APIs. We rely on a single CMO, located in China, to manufacture each of our cardiovascular drug product candidates that meets appropriate content, quality and stability standards for use in preclinical programs and clinical trials. Legislative proposals are pending that, if enacted, could negatively impact U.S. funding for certain biotechnology providers having relationships with foreign adversaries or which pose a threat to national security. The potential downstream adverse impacts on entities having only commercial relationships with any impacted biotechnology providers is unknown but may include supply chain disruptions or delays. In most cases, we submit purchase orders to our CMO and API suppliers as needed and do not have contractual commitments to manufacture for us in the future. Additionally, we intend to rely on CMOs to produce topical or oral formulations of our aPKCi inhibitor. If we do not establish or maintain these manufacturing and service relationships that are important to us and are not able to identify replacement suppliers, vendors and laboratories, our ability to obtain regulatory approval for our product candidates could be impaired or delayed and our costs could substantially increase.

We may be unable to identify additional manufacturers with whom we might establish appropriate arrangements on acceptable terms, if at all, because the number of potential CMOs is limited. Even if we are able to find replacement manufacturers, suppliers, vendors and service providers when needed, we may not be able to enter into agreements with them on terms and conditions favorable to us or there could be a substantial delay before such manufacturer, vendor or supplier, or a related new facility is properly qualified and registered with the FDA or other foreign regulatory authorities. A new manufacturer currently not qualified with the FDA would have to be educated in, or develop substantially equivalent processes for, production of our approved products after receipt of FDA approval. To qualify and receive regulatory approval for a new manufacturer could take as long as two years. The process of changing a supplier could have an adverse impact on our current clinical development programs if supplies of drug substances or materials on hand are insufficient to satisfy demand. Such delays could have a material adverse effect on our development activities and our business.

Our product candidates are temperature sensitive and may have other attributes that lead to limited shelf life. These attributes may pose risks to supply, inventory and waste management and increased cost of goods.

Our product candidates may prove to have a stability profile that leads to a lower than desired shelf life. This poses risk in supply requirements, wasted stock, and higher cost of goods.

Our product candidates are temperature sensitive, and we may learn that any or all of our product candidates are less stable than desired. It is also possible that we may find that transportation conditions negatively impact product quality. This may require changes to the formulation or manufacturing process for one or more of our product candidates and result in delays or interruptions to clinical or commercial supply. In addition, the cost associated with such transportation services and the limited pool of vendors may also add additional risks of supply disruptions.

We have established a number of analytical testing strategies, and may have to establish several more, to assess the quality of our product candidates. We may identify gaps in our analyses that might prevent release of product or could require product withdrawal or recall. For example, new or existing impurities that have an impact on product safety, efficacy, or stability may be discovered. This may lead to an inability to release or use our product candidates until the manufacturing or testing process is rectified or specifications are changed. This could potentially result in delays to our key program.

We plan to rely on third parties, some of which are located outside the U.S., to manufacture our drug product candidates, which exposes us to risks that may affect our ability to maintain supplies of our clinical materials, and subject us to uncertainty associated with the international political climate, and could potentially delay or cease our research and development activities, as well as eventual regulatory approval and commercialization of our drug product candidates.

Our manufacturing strategy involves manufacturing our drug product candidates using a CMO. We do not own or operate manufacturing facilities and have no plans to build our own clinical or commercial scale manufacturing capabilities. We rely, and expect to continue to rely, on third parties for the manufacture of our drug product candidates and related raw materials for clinical and preclinical development, as well as for commercial manufacture if any of our product candidates receive marketing approval. The facilities used by third-party manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit an NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, third-party manufacturers for compliance with cGMP requirements for manufacture of drug products and other government regulations and corresponding international standards. If these third-party manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, including requirements related to the manufacturing of high potency compounds, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities.

Istaroxime and rostafuroxin are currently manufactured by an affiliate of Lee's Pharmaceutical (HK) Ltd., or Lee's (HK), in Hefei, China. We expect that Lee's (HK) will manufacture KL4 surfactant drug product candidate at an affiliate of Lee's (HK) in Hefei, China. The APIs for istaroxime and rostafuroxin are manufactured in China. If the FDA is unable to inspect the manufacturing site in China or if it is able to inspect the site but finds it deficient in any way, to secure marketing approval for our product candidates in the U.S., and potentially other markets, we may be required to designate a different manufacturer for each of our drug product candidates. A technology transfer of a manufacturing process from one CMO to another can be time consuming and expensive and there can be no assurance that such a transfer will be successful or that a new manufacturer will be able to manufacture our drug product candidates successfully. Moreover, a technology transfer from one country to another may be subject to changing international legal and regulatory requirements in a potential difficult political climate. In addition, we have limited control over the ability of third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel and the third-party manufacturers may fail to manufacture our product candidate according to our schedule or at all. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates. In addition, any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval, and any related remedial measures may be costly or time consuming to implement. We do not currently have arrangements in place for redundant supply or a second source for all required raw materials used in the manufacture of our product candidates. If our current third-party manufacturer cannot perform as agreed, we may be required to replace such manufacturers and we may be unable to replace them on a timely basis or at all.

A third party's failure to execute on our manufacturing requirements, technology transfers of our manufacturing and our planned future reliance on CMOs exposes us, among other things, to the following risks:

- an inability to initiate or continue clinical trials of istaroxime or any future product candidates under development;
- subjecting third-party manufacturing facilities to additional inspections by regulatory authorities;
- we may implement a plan to execute a technology transfer of our manufacturing process to a CMO and, after investing significant time and resources, learn that the CMO we chose is unable to successfully complete the technology transfer and thereafter manufacture our product candidates in accordance with our plan;
- CMOs might be unable to manufacture our product candidates in the volume and to our specifications to meet our clinical and commercial needs, or we may have difficulty scheduling the production of drug product in a timely manner to meet our timing requirements;
- if we desire to make our drug product candidates available outside the U.S. for clinical or commercial purposes, our CMOs would become subject to, and may not be able to comply with, corresponding manufacturing and quality system regulations or standards of the various foreign regulators having jurisdiction over our activities abroad. Such failures (such as in-country quality testing) could result in not only a loss of approved supply to that country, but a total loss of a lot (or lots) of materials globally and could restrict our ability to execute our business strategies;
- we may have difficulty implementing changes or necessary modifications to our manufacturing processes that may be required by the FDA or foreign regulator or our CMO, if, for example, such changes would burden our CMO or otherwise disrupt operations, or our CMO could impose significant financial terms to implement any such change that could adversely affect our business. We may fail to adequately develop new manufacturing processes. Failure to achieve such required changes or modifications could delay or prevent our gaining regulatory approval for our product candidates or prevent us from continuing to market our approved products, which would have a material adverse effect on our business, financial condition and operations;

- we may fail to adequately scale manufacturing to achieve our objectives for cost of goods and profit margins;
- we may be subject to disputes arising with respect to the ownership of rights to any technology developed with third parties; and
- we may be subject to the misappropriation of our proprietary information, including our trade secrets and know-how.

Each of the foregoing risks and others could delay our development programs and, if approved, commercial manufacturing plans, limit our ability to maintain continuity of supply for our approved products, delay or impair the approval, if any, of our product candidates by the FDA, or result in higher costs or deprive us of potential product revenues.

In addition, our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or products, if approved, may adversely affect our future profit margin and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

Our ability to manufacture our product candidates depends upon receiving adequate supplies and related services, which may be difficult or uneconomical to procure.

Supply chain or manufacturing interruptions could negatively impact our operations and financial performance. We do not have fully redundant systems and equipment to respond promptly in the event of a significant loss at a CMO's manufacturing operations. Under certain conditions, we may be unable to produce our drug product candidates at the required volumes or to appropriate standards, if at all. The supply of any of our manufacturing materials may be interrupted because of supply shortages, poor vendor performance or other events outside our control, which may require us, among other things, to identify alternate vendors, which could involve a lengthy process, and result in increased expenses.

We are dependent on Lee's (HK) and Zhaoke for the successful development and commercialization of our KL4 surfactant products. If Lee's (HK) and Zhaoke do not devote sufficient resources to the development of those product candidates, are unsuccessful in their efforts, or chooses to terminate their agreement with us, the potential licensing revenue will not materialize.

On August 17, 2022, we entered into an Amended and Restated License, Development and Commercialization Agreement, or the A&R License Agreement, with Lee's (HK) and Zhaoke effective as of August 9, 2022. The A&R License Agreement amends, restates and supersedes the Original License Agreement.

Under the A&R License Agreement, Lee's is solely and exclusively responsible for all costs and activities related to the development, manufacturing, regulatory approval and commercialization of KL4 surfactant products, including SURFAXIN®, the lyophilized dosage form of SURFAXIN, and aerosolized KL4 surfactant. Lee's (HK) and Zhaoke may determine however, that it is commercially reasonable to de-prioritize or discontinue the development of the KL4 surfactant products. These decisions may occur for many reasons, including internal business reasons, results from clinical trials or because of unfavorable regulatory feedback.

Further, on review of the safety and efficacy data, the FDA may impose requirements on the programs that render them commercially nonviable. In addition, under the A&R License Agreement, Lee's (HK) and Zhaoke have certain decision-making rights in determining the development and commercialization plans and activities for the programs. We may disagree with Lee's (HK) and Zhaoke about the development strategy they employ, but we will have limited rights to impose our development strategy on Lee's (HK) and Zhaoke. Similarly, they may decide to seek marketing approval for, and limit commercialization of, the KL4 surfactant products to narrower indications than we would pursue. More broadly, if Lee's (HK) and Zhaoke elect to discontinue the development of the KL4 surfactant products, we may be unable to advance the product candidate ourselves.

On January 12, 2024, we entered into a License, Development and Commercialization Agreement with Lee's (HK) effective as of January 7, 2024 under which we granted an exclusive license, with a right to sublicense, to develop, register, make, use, sell, offer for sale, import, distribute and otherwise commercialize products that incorporate istaroxime for intravenous administration, rostafuroxin for oral administration, and our proprietary dual-mechanism SERCA2a activators for intravenous or oral administration, in each case for the prevention, mitigation and/or treatment of any disease, disorder or condition in humans including acute decompensated heart failure, cardiogenic shock, and chronic use following discharge of an individual hospitalized for acute decompensated heart failure in the Greater China region.

Risks Related to our Business and Operations

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or any guidance we may provide.

Our quarterly and annual operating results may fluctuate significantly, which makes it difficult for us to predict our future operating results.

These fluctuations may occur due to a variety of factors, many of which are outside of our control, including, but not limited to:

- the timing and cost of, and level of investment in, research, development, including manufacturing development regulatory approval and commercialization activities relating to our product candidates, which may change from period to period;
- the timing and success or failure of preclinical studies or clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;
- the level of investment funding we are able to achieve and apply to our development operations;
- the cost of manufacturing our product candidates, which may vary depending on the quantity of production and the terms of our agreements with third-party manufacturers;
- the potential for our identifiable intangible assets to become impaired, and the timing of such impairments, if any;
- the timing and amount of the milestone or other payments we must make to the licensors and other third parties from whom we have in-licensed our acquired our product candidates;
- expenditures that we may incur to acquire, develop or commercialize additional product candidates and technologies;
- our allocation of resources and ability to raise additional capital;
- future changes in requirements to achieve regulatory approval;
- future accounting pronouncements or changes in our accounting policies.
- the capital markets stability and openness to investing;
- delays associated with COVID-19 or future pandemics which will impact the ability of our healthcare systems and trial sites to conduct trials to varied degrees and times;
- coverage and reimbursement policies with respect to our product candidates, if approved, and potential future drugs that compete with our products; and
- the level of demand for any approved products, which may vary significantly.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance.

This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue or earnings guidance we may provide.

Our acquisition of Varian's assets may divert resources away from existing operations or expose us to liabilities, which could adversely affect our business, results of operations and financial condition.

On April 2, 2024, we entered into the Asset Purchase Agreement with Varian. Pursuant to the Asset Purchase Agreement, we purchased all of the assets of Varian's business associated with a Licence Agreement, dated as of July 5, 2019, by and between Varian and Cancer Research Technology Limited, or the Licence Agreement, including the Licence Agreement, all rights in molecules and compounds subject to the Licence Agreement, know-how and inventory of drug substance, or the Transferred Assets. We also assumed all liabilities arising on or after April 2, 2024, relating to the research, development, manufacturing, registration, commercialization, use, handling, supply, storage, import, export or other disposition or exploitation of any and all products associated with the Transferred Assets.

We may invest a substantial amount of time, resources and efforts in connection with our acquisition of the Transferred Assets. All of these actions divert resources away from our other initiatives and operations. These efforts may not result in product candidates, efficiencies or revenues for our company, which could adversely affect our business, operating results and financial condition as a result.

We are continually evaluating our business strategy and may modify this strategy to respond to developments in our business and other factors, and any such modification, if not successful, could have a material adverse effect on our business, financial condition, and results of operations.

We plan to continually evaluate our business strategy and will modify our plans as necessary to achieve our objectives. As part of our shift in priorities, we entered into a global licensing agreement in 2022 to support the development of our KL4 surfactant platform and were able to eliminate the remaining costs associated with the KL4 surfactant platform. If for any reason, our licensee does not proceed with development of the KL4 surfactant platform, such action could have a material adverse effect on our potential to realize licensing revenue.

Similarly, our strategy currently contemplates that we will seek to out-license rostafuroxin and invest the proceeds in our other core programs. If we are not successful in our efforts, we may be forced to accept a significant write down of our rostafuroxin asset on our balance sheet and reassess our strategy. This action also could have a material adverse effect on our business, financial condition and results of operations.

The execution of a clinical program is complex and involves the cooperation of many individuals and entities, including third parties that we may not be able to control, and require the coordination of a number of components, any one of which could experience delays or unforeseen events or circumstances that may require the development of alternative strategies. If we encounter such events or circumstances, if we believe that certain changes would be in our best interest, we will consider adjusting our strategy and planning. If we conclude that an alternative approach may improve our ability to achieve our objectives, we will consider adopting such other approach. Similarly, if a third party were to share observations or make recommendations concerning the focus, sequence or approach of any or all of our research and development programs, we may consider taking such recommendations into account in our planning process and future activities.

There can be no assurance, whether or not we alter our strategy or plans, that we will be successful, or that we will secure regulatory approval for our product candidates and execute any product launches effectively and on time, if at all, in all markets that we may identify. Our ability to discover and/or develop new product candidates depends in part on our internal research capabilities and whether we have the resources required to conduct a development program or to acquire new product candidates. Our limited resources may not be sufficient to discover and develop or to acquire new product candidates. To support our efforts to develop our product candidates and, if approved, commercialize our products in the world markets, including the U.S., we continue to evaluate potential licensing transactions, collaboration arrangements and other strategic transactions. However, there can be no assurance that our efforts will be successful or that, even if we identify and enter into any strategic transactions, that such transactions will be successfully implemented, if at all, within our expected time frames.

We plan to continue evaluating our business strategy and may modify our strategy again in the future. To respond to changing circumstances, we may expand or alter our research and development activities from time to time and allocate resources to work on development of different product candidates or may pace, delay or halt the development of potential product development programs. As a result of changes in our strategy, we may also change or refocus our existing drug development and manufacturing activities or our plans for commercialization of our product candidates, if approved. These decisions could require changes in our facilities and personnel and restructuring various financial arrangements. There can be no assurances that any product development or other changes that we implement will be successful or that, after implementation of any such changes, that we will not refocus our efforts on new or different objectives.

Our industry is highly competitive, and we have less capital and resources than many of our competitors, which may give them an advantage in developing and marketing products similar to ours or make our product candidates obsolete.

Our industry is highly competitive and subject to rapid technological innovation and evolving industry standards. We compete with numerous existing companies in many ways. We need to successfully introduce new products to achieve our strategic business objectives. If we cannot successfully introduce new products, adapt to changing technologies or anticipate changes in our current and potential customers' requirements, our product candidates may become obsolete, and our business could suffer.

Many of our competitors' companies have substantially greater research and development, manufacturing, marketing, financial, and technology personnel and managerial resources than we have. In addition, many of these competitors, either alone or with their collaborative partners, have significantly greater experience than we do in developing products, preclinical testing and human clinical trials management, obtaining FDA approval and other regulatory approvals, and manufacturing and marketing products. Accordingly, our competitors may succeed in receiving FDA or foreign regulatory approval or commercializing products and obtaining patent protection before us. Our competitors may successfully secure regulatory exclusivities in various markets, which could have the effect of barring us or limiting our ability to market our product candidates, if approved, in such markets. In addition, developments by our competitors may render our drug product candidates obsolete or noncompetitive.

We also face, and will continue to face, competition from colleges, universities, governmental agencies and other public and private research organizations. These competitive forces frequently and aggressively seek patent protection and licensing arrangements to collect royalties for technologies that they develop. Some of these technologies may compete directly with the technologies that we are developing. These institutions will also compete with us in recruiting highly qualified scientific personnel.

The political and healthcare policy and reimbursement environment is becoming more challenging for pharmaceutical companies and manufacturers and may adversely affect our business.

Political, economic and regulatory influences globally are subjecting the healthcare industry to potential fundamental challenges that could substantially affect our business and results of operations. Government and private sector initiatives to limit the growth of healthcare costs, including price regulation, competitive pricing, coverage and payment policies, comparative effectiveness of therapies, technology assessments and managed-care arrangements, are continuing to arise in many countries where we potentially may seek to do business, including the U.S. There is increasing pressure on pricing, reimbursement and demands for value-based data to gain access to patients and healthcare funds globally. This may increase the costs of development, risks of commercialization and overall value of the opportunity. The Inflation Reduction Act of 2022 contains substantial drug pricing reforms, including the establishment of a drug price negotiation program within the U.S. Department of Health and Human Services that would require manufacturers to charge a negotiated "maximum fair price" for certain selected drugs or pay an excise tax for noncompliance, the establishment of rebate payment requirements on manufacturers of certain drugs payable under Medicare Parts B and D to penalize price increases that outpace inflation, and requires manufacturers to provide discounts on Part D drugs. Substantial penalties can be assessed for noncompliance with the drug pricing provisions in the Inflation Reduction Act of 2022. The Inflation Reduction Act of 2022 could have the effect of reducing the prices we can charge and reimbursement we receive for our product candidates, if approved, thereby reducing our profitability, and could have a material adverse effect on our financial condition, results of operations and growth prospects. The effect of Inflation Reduction Act of 2022 on our business and the pharmaceutical industry in general is not yet known. We also cannot predict the likelihood, nature or extent of additional government regulation that may arise from future legislation, administrative, judicial, or executive action, either in the U.S. or abroad. In addition, we rely on our CMO located in China to manufacture drug product and APIs for us, such that the supply lines for our drug product, and APIs may be affected by trade and political considerations.

Given the increasing uncertainty in the healthcare and pharmaceutical industries as well as increased regulatory scrutiny on foreign investment, capital investment in our industry and our ability to attract capital investment is becoming more challenging. This trend, if continued, may restrict or impair our ability to gain necessary funding for continued development and, if approved, commercialization of our product candidates.

We depend upon key employees and consultants in a competitive market for skilled personnel. If we or our strategic partners or collaborators are unable to attract and retain key personnel, it could adversely affect our ability to develop and market our product candidates.

We have assembled a team of qualified personnel to advance the development programs for our product candidates. We have competed and will continue to compete for qualified individuals with numerous biopharmaceutical companies, universities and other research institutions. Competition for such individuals is significant and attracting and retaining qualified personnel will be critical to our success, and any failure to do so successfully may have a material adverse effect on us.

We are highly dependent upon the members of our executive management team and certain employees and consultants who are subject matter experts. Many of these individuals have been involved with us for many years, have played integral roles in our progress and we believe that they continue to provide value to us. We have over the last few years lost long-term members of our executive team and certain professional, scientific and management personnel, due to retirement, shifts in our focus and other causes. The loss of such personnel potentially exposes us to a lack of ready recall and knowledge of past corporate events, risks previously identified and related learnings. As such, loss of any of our remaining key personnel may further increase the associated risk and may have a material adverse effect on aspects of our business and clinical development and regulatory programs. The loss of services from any of our executives could significantly adversely affect our ability to develop and market our product candidates and obtain necessary regulatory approvals. Further, we do not maintain key man life insurance.

Our future success also will depend on the continued service of our key professional, scientific and management personnel and our ability to recruit and retain additional personnel. While we attempt to provide competitive compensation packages to attract and retain key personnel at all levels in our organization, many of our competitors have greater resources and more experience than we do, making it difficult for us to compete successfully for key personnel. We may experience intense competition for qualified personnel and the existence of non-competition agreements between prospective employees and their former employers may prevent us from hiring those individuals or subject us to lawsuits brought by their former employers.

If our business development activities are unsuccessful, our business could suffer, and our financial performance could be adversely affected.

As part of our long-term growth strategy, we engage in business development activities intended to identify strategic opportunities, including potential strategic alliances, joint development opportunities, acquisitions, technology licensing arrangements and other similar opportunities. Such opportunities may result in substantial investments in our business. Our success in developing product candidates or expanding into new markets from such activities will depend on a number of factors, including our ability to find suitable opportunities for investment, alliance or acquisition; whether we are able to complete an investment, alliance or acquisition on terms that are satisfactory to us; the strength of our underlying technology, product candidates and our ability to execute our business strategies; any intellectual property and litigation related to these product candidates or technology; and our ability to successfully integrate the investment, alliance or acquisition into our existing operations, including to fund our share of any IPR&D projects. If we are unsuccessful in our business development activities, we may be unable to secure needed capital and expertise to support our development programs and our financial condition could be adversely affected.

We may seek to enter into licensing transactions, collaboration arrangements, and other similar transactions and strategic opportunities, and may not be successful in doing so, and even if we are, we may not realize the benefits of such relationships.

We may seek to enter into licensing transactions, collaboration arrangements, and other similar transactions and strategic opportunities for the development or commercialization of our product candidates, or to secure the capital required to develop or commercialize a product candidate or address manufacturing constraints. We may not be successful in our efforts to establish such collaborations for our product candidates because our research and development pipeline may be insufficient, our product candidates may be deemed to be at too early of a stage of development for collaborative effort or third parties may not view our product candidates as having the requisite potential to demonstrate safety and efficacy or significant commercial opportunity. In addition, we face significant competition in seeking appropriate strategic partners, and the negotiation process can be time consuming and complex. Further, any future collaboration agreements may restrict us from entering into additional agreements with potential collaborators. We cannot be certain that, following a strategic transaction or licensing agreement, we will achieve an economic benefit that justifies such transaction.

Even if we are successful in our efforts to establish such collaborations, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such collaborations if, for example, development or approval of a product candidate is delayed, the safety of a product candidate is questioned or sales of an approved product candidate are unsatisfactory.

In addition, any potential future collaborations may be terminable by our strategic partners, and we may not be able to adequately protect our rights under these agreements. Furthermore, strategic partners may negotiate for certain rights to control decisions regarding the development and commercialization of our product candidates, if approved, and may not conduct those activities in the same manner as we do. Any termination of collaborations we enter into in the future, or any delay in entering into collaborations related to our product candidates, could delay the development and commercialization of our product candidates and reduce their competitiveness if they reach the market, which could have a material adverse effect on our business, financial condition and results of operations.

We could be adversely affected by any interruption, including from breaches in cybersecurity, in our ability to conduct business at our current location.

We are increasingly dependent on sophisticated information technology for our infrastructure. Our information systems require an ongoing commitment of significant resources to maintain, protect and enhance existing systems. Despite our implementation of security measures, our information systems, like those of other companies, are vulnerable to damages from computer viruses, natural disasters, unauthorized access, cyber-attack, including ransomware, and other similar disruptions. Any system failure, accident or security breach could result in disruptions to our operations. For example, third parties may attempt to hack into systems and may obtain our proprietary information or other sensitive information, which could cause significant damage to our reputation, lead to claims against us and ultimately harm our business.

We do not have redundant facilities. We perform substantially all of our research and development and back office activity in a small number of locations, including our headquarters in Warrington, Pennsylvania, and a research laboratory at Chang Gung University in Taiwan under a separate collaboration agreement. We also depend upon third-party manufacturers and laboratories to manufacture our drug product candidates, APIs and perform important API and drug product release testing and stability work.

Our facilities, equipment and inventory would be costly to replace and could require substantial lead time to repair or replace. Our facilities and those of our third-party manufacturers and laboratories may be harmed or rendered inoperable by natural or man-made disasters, including, but not limited to, tornadoes, flooding, fire and power outages, which may render it difficult or impossible for us to perform our research, development and commercialization activities for some period of time. The inability to perform those activities, combined with the time it may take to rebuild our inventory of finished product, may result in the loss of customers or harm to our reputation. Although we have insurance for damage to our property and the disruption of our business, this insurance may not be sufficient to cover all of our potential losses and this insurance may not continue to be available to us on acceptable terms, or at all.

The failure to prevail in litigation or the costs of litigation, including securities class actions, product liability claims and patent infringement claims, could harm our financial performance and business operations.

We are potentially susceptible to litigation. For example, as a public company, we may be subject to claims asserting violations of securities laws. Even if such actions are found to be without merit, the potential impact of such actions, which generally seek unquantifiable damages and attorneys' fees and expenses, is uncertain. There can be no assurance that an adverse result in any future proceeding would not have a potentially material adverse effect on our business, results of operations and financial condition.

Our business activities, including development, manufacture and, if our product candidates are approved, marketing of our drug products also exposes us to liability risks. Using our drug product candidates, including in clinical trials, may expose us to product liability claims. Even if approved, our products may be subject to claims resulting from unintended effects that result in injury or death. Product liability claims alleging inadequate disclosure and warnings in our package inserts also may arise.

We presently carry comprehensive general liability, property damage, product liability, workers' compensation, health benefits and other insurance coverage in amounts that we believe to be adequate for the protection of our assets and operations and customary for companies in our industry of comparable size and level of activity. However, our insurance policies contain various deductibles, limitations and exclusions from coverage, and in any event might not fully cover any potential claims. There can be no assurance that the insurance coverage we maintain is sufficient or will be available in adequate amounts or at a reasonable cost. A successful claim brought against us in excess of available insurance or not covered by indemnification agreements, or any claim that results in significant adverse publicity against us, could have an adverse effect on our business and our reputation.

Product liability claims may be brought by individuals or by groups seeking to represent a class. The outcome of litigation, particularly class action lawsuits, is difficult to assess or quantify. Plaintiffs in these types of lawsuits often seek recovery of very large or indeterminate amounts, and the magnitude of the potential loss relating to such lawsuits may remain unknown for substantial periods of time.

We face a potential risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any of our product candidates, if approved, or any other future product. For example, we may be sued if any product we develop, including any of our product candidates, or any materials that we use in our product candidates allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. In the U.S., claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates, if approved. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for any of our product candidates, if approved, or any future products that we may develop;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management's time, attention and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- the inability to commercialize some or all of our product candidates, if approved; and
- a decline in the value of our stock.

There can be no assurance that the insurance coverage we maintain is sufficient or will be available in adequate amounts or at a reasonable cost. A successful claim brought against us in excess of available insurance or not covered by indemnification agreements, or any claim that results in significant adverse publicity against us, could have an adverse effect on our business and our reputation.

We may be required to obtain additional product liability insurance coverage. However, such insurance is expensive and may not be available when we need it. In the future, we may not be able to obtain adequate insurance, with acceptable limits and retentions, at an acceptable cost. Any product, general liability or product liability claim, even if such claim is within the limits of our insurance coverage or meritless and/or unsuccessful, could adversely affect the availability or cost of insurance generally and our cash available for other purposes, such as research and development. In addition, such claims could result in:

- uninsured expenses related to defense or payment of substantial monetary awards to claimants;
- a decrease in demand for our drug product candidates, if approved;
- damage to our reputation; and
- an inability to complete clinical trial programs or to commercialize our drug product candidates, if approved.

Risks Related to Government Regulation

Our activities are subject to various and complex laws and regulations, and we are susceptible to a changing regulatory environment. Violations or allegations of violations of these laws may result in large civil and criminal penalties, debarment from participating in government programs, diversion of management time, attention and resources and may otherwise have a material adverse effect on our business, financial condition and results of operations.

Our product candidates and our operations are regulated by numerous government agencies, both inside and outside the U.S. Our drug product candidates must undergo lengthy and rigorous testing and other extensive, costly and time-consuming procedures mandated by the FDA and foreign regulatory authorities. Our facilities and those of our third-party providers must pass inspection and/or be approved or licensed prior to production and remain subject to inspection at any time thereafter. Failure to comply with the requirements of the FDA or other regulatory authorities could result in warning or untitled letters, Form 483s, product recalls or seizures, monetary sanctions, injunctions to halt the manufacture and distribution of our product candidates, if approved, civil or criminal sanctions, refusal of a government to grant approvals or licenses, restrictions on operations or withdrawal of existing approvals and licenses. Any of these actions could damage our reputation and have a material adverse effect on our sales.

If our product candidates are approved for commercial sale, we will be required to comply with not only the requirements of applicable regulators, but also will become subject to various laws regulating the sales, marketing, and distribution of healthcare-related products. The sales and marketing of products and relationships that pharmaceutical companies have with healthcare providers are under increasing scrutiny by federal, state and foreign government agencies. The FDA and other federal regulators have increased their enforcement activities with respect to the Anti-Kickback Statute, False Claims Act, off-label promotion of products, and other healthcare related laws, antitrust and other competition laws. Foreign governments have also increased their scrutiny of pharmaceutical companies' sales and marketing activities and relationships with healthcare providers.

Of particular importance, federal and state anti-kickback laws make it illegal for a prescription drug manufacturer to solicit, offer, receive, or pay any remuneration in exchange for, or to induce, the referral of business, including the purchase or prescription of a particular drug. These laws can be complicated, are subject to frequent change and may be violated unknowingly. In addition, a number of states require that companies implement compliance programs or comply with industry ethics codes, adopt spending limits, and report to state governments any gifts, compensation, and other remuneration provided to physicians. Sanctions under these laws may include civil monetary penalties, exclusion of a manufacturer's products from reimbursement under government programs (including Medicare and Medicaid), criminal fines, and imprisonment. Companies that have chosen to settle these alleged violations have typically paid multi-million-dollar fines to the government and agreed to abide by corporate integrity agreements, which often include significant and costly burdens.

There has been a recent trend of increased federal and state regulation of payments and transfers of value provided to healthcare professionals and entities. For example, the Physician Payment Sunshine Act imposes annual reporting requirements on certain manufacturers of drugs, biologics and medical supplies with respect to payments and other transfers of value provided by them, directly or indirectly, to physicians and teaching hospitals, as well as with respect to certain ownership and investment interests held by physicians and their family members. A manufacturer's failure to submit timely, accurately and completely the required information regarding all payments, transfers of value or ownership or investment interests may result in civil monetary penalties. Certain states also mandate implementation of commercial compliance programs, impose restrictions on manufacturers' marketing practices, and require the tracking and reporting of gifts, compensation and other remuneration to healthcare professionals and entities under certain circumstances.

We are continually evaluating our compliance programs, including policies, training and various forms of monitoring, designed to address the requirements outlined above. However, no compliance program can mitigate risk in its entirety. Violations or allegations of violations of these laws may result in large civil and criminal penalties, debarment from participating in government programs, diversion of management time, attention and resources and may otherwise have a material adverse effect on our business, financial condition and results of operations.

Failure in our information technology systems could disrupt our operations and cause the loss of confidential information and business opportunities.

In the ordinary course of our business, we and our third-party contractors maintain sensitive data on our and their respective networks, including our intellectual property and proprietary or confidential business information relating to our business and that of our clinical trial participants and business partners and electronically stored work product, including clinical data, analyses, research, communications and other materials necessary to gain regulatory approval of our product candidates. The secure maintenance of this sensitive information is critical to our business and reputation. Despite the implementation of security measures, our internal computer systems and those of our third-party contractors are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, unintended loss, human error, natural disasters, terrorism, war and telecommunication and electrical failures. For information stored with our third-party contractors, we rely upon, and the integrity and confidentiality of such information is dependent upon, the risk mitigation and data preservation efforts such third-party contractors have in place. Our and our third-party contractors' respective network and storage applications and policies may not be sufficient to protect our sensitive business information and may be subject to loss, unauthorized access by hackers or breached due to operator error, malfeasance or other system disruptions. It is often difficult to anticipate or immediately detect such incidents and the damage caused by such incidents. Such incidents could compromise our intellectual property, expose sensitive business information, result in loss of data necessary to secure regulatory approval of our product candidates, cause interruptions in our operations, result in a material disruption of our operations, or require substantial expenditures of resources to remedy.

We face risks related to our collection and use of data, including personal information, which could result in investigations, inquiries, litigation, fines, legislative and regulatory action and negative press about our privacy and data protection practices.

Our business processes personal data, including some data related to health. When conducting clinical trials, we face risks associated with collecting trial participants' data, especially health data, in a manner consistent with applicable laws and regulations. We also face risks inherent in handling large volumes of data and in protecting the security of such data. We could be subject to attacks on our systems by outside parties or fraudulent or inappropriate behavior by our service providers or employees. Third parties may also gain access to users' accounts using stolen or inferred credentials, computer malware, viruses, spamming, phishing attacks or other means, and may use such access to obtain users' personal data or prevent use of their accounts. Data breaches could subject us to individual or consumer class action litigation and governmental investigations and proceedings by federal, state and local regulatory entities in the U.S. and by international regulatory entities, resulting in exposure to material civil and/or criminal liability. Further, our general liability insurance and corporate risk program may not cover all potential claims to which we are exposed and may not be adequate to indemnify us for all liability that may be imposed.

Our business requires that we and our third-party service providers collect and store sensitive data, including legally protected health information, personally identifiable information about patients, credit card information, and our proprietary business and financial information. As a covered entity, we must comply with the HIPAA privacy and security regulations, which may increase our operational costs. Furthermore, the privacy and security regulations provide for significant fines and other penalties for wrongful use or disclosure of protected health information, or PHI, including potential civil and criminal fines and penalties. We face a number of risks relative to our protection of, and our service providers' protection of, this critical information, including loss of access, fraudulent modifications, inappropriate disclosure and inappropriate access, as well as risks associated with our ability to identify and audit such events. The secure processing, storage, maintenance and transmission of this critical information is vital to our operations and business strategy, and we devote significant resources to protecting such information. Although we take measures to protect sensitive information from unauthorized access or disclosure, our information technology and infrastructure may be vulnerable to attacks by hackers or viruses or otherwise breached due to employee error, malfeasance or other activities. If such event would occur and cause interruptions in our operations, our networks would be compromised and the information we store on those networks could be accessed by unauthorized parties, publicly disclosed, modified without our knowledge, lost or stolen.

Additionally, we share PHI with third-party contractors who are contractually obligated to safeguard and maintain the confidentiality of PHI. Unauthorized persons may be able to gain access to PHI stored in such third-party contractors' computer networks. Any wrongful use or disclosure of PHI by us or our third-party contractors, including disclosure due to data theft or unauthorized access to our or our third-party contractors' computer networks, could subject us to fines or penalties that could adversely affect our business and results of operations. Although the HIPAA statute and regulations do not expressly provide for a private right of damages, we also could incur damages under state laws to private parties for the wrongful use or disclosure of confidential health information or other private personal information by us or our third-party contractors. Unauthorized access, loss, modification or dissemination could disrupt our operations, including our ability to process tests, provide test results, bill payers or patients, process claims, provide customer assistance services, conduct research and development activities, collect, process and prepare company financial information, provide information about our solution and other patient and physician education and outreach efforts through our website, manage the administrative aspects of our business and damage our reputation, any of which could adversely affect our business. In addition, the interpretation and application of consumer, health-related and data protection laws in the U.S. are often uncertain, contradictory and in flux. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices. Complying with these various laws could cause us to incur substantial costs or require us to change our business practices, systems and compliance procedures in a manner adverse to our business.

As our operations and business grow, we may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities, including various domestic and international privacy and security regulations. The legislative and regulatory landscape for privacy and data protection continues to evolve. In the U.S., certain states may adopt privacy and security laws and regulations that may be more stringent than applicable federal law.

A number of US states have proposed new privacy laws. Such proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies. The existence of comprehensive privacy laws in different states in the country would make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance.

Our international operations are subject to international laws and regulations, regulatory guidance, and industry standards relating to data protection, privacy, and information security. This includes the EU General Data Protection Regulation, or GDPR, as well as other national data protection legislation in force in relevant EU member states (including the GDPR in such form as incorporated into the law of England and Wales, Scotland and Northern Ireland by virtue of the European Union (Withdrawal) Act 2018 and any regulations thereunder and the UK Data Protection Act 2018, or UK GDPR.

The GDPR and UK GDPR are wide-ranging in scope and impose numerous additional requirements on companies that process personal data, including imposing special requirements in respect of the processing of health and other sensitive data, requiring that consent of individuals to whom the personal data relates is obtained in certain circumstances, requiring additional disclosures to individuals regarding data processing activities, requiring that safeguards are implemented to protect the security and confidentiality of personal data, creating mandatory data breach notification requirements in certain circumstances, requiring data protection impact assessments for high risk processing and requiring that certain measures (including contractual requirements) are put in place when engaging third-party processors. The GDPR and the UK GDPR also provide individuals with various rights in respect of their personal data, including rights of access, erasure, portability, rectification, restriction and objection.

The GDPR and UK GDPR impose strict rules on the transfer of personal data to countries outside the European Economic Area, including the U.S. The UK and Switzerland have adopted similar restrictions. Although the UK is regarded as a third country under the EU's GDPR, the EC has now issued a decision recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EU to the UK remain unrestricted. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the UK to countries not regarded by the UK as providing adequate protection. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing.

To enable the transfer of personal data outside of the EEA or the UK, adequate safeguards must be implemented in compliance with European and UK data protection laws. On June 4, 2021, the EC issued new forms of standard contractual clauses for data transfers from controllers or processors in the EU/EEA (or otherwise subject to the GDPR) to controllers or processors established outside the EU/EEA (and not subject to the GDPR). The new standard contractual clauses replace the standard contractual clauses that were adopted previously under the EU Data Protection Directive. The UK is not subject to the EC's new standard contractual clauses but has published a draft version of a UK-specific transfer mechanism, which, once finalized, will enable transfers from the UK. We will be required to implement these new safeguards when conducting restricted data transfers under the EU and UK GDPR and doing so will require significant effort and cost.

The GDPR and UK GDPR may increase our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR and UK GDPR. Implementing legislation in applicable EU member states and the UK, including by seeking to establish appropriate lawful bases for the various processing activities we carry out as a controller or joint controller, reviewing security procedures and those of our vendors and collaborators, and entering into data processing agreements with relevant vendors and collaborators, we cannot be certain that our efforts to achieve and remain in compliance have been, and/or will continue to be, fully successful. Given the breadth and depth of changes in data protection obligations, preparing for and complying with the GDPR and UK GDPR and similar laws' requirements are rigorous and time intensive and require significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data.

Other countries around the world in which we conduct business have also enacted strict privacy and data protection laws. Further, in addition to general privacy and data protection requirements, many jurisdictions around the world have adopted legislation that regulates how businesses operate online and enforces information security, including measures relating to privacy, data security and data breaches. Many of these laws require businesses to notify data breaches to the regulators and/or to data subjects. These laws are not consistent, and compliance in the event of a widespread data breach is costly and burdensome.

In many jurisdictions, enforcement actions and consequences for non-compliance with protection, privacy and information security laws and regulations are rising. In the EU and the UK, data protection authorities may impose large penalties for violations of the data protection laws, including potential fines of up to €20 million (£17.5 million in the UK) or 4% of annual global revenue, whichever is greater. The authorities have shown a willingness to impose significant fines and issue orders preventing the processing of personal data on non-compliant businesses. Data subjects also have a private right of action, as do consumer associations, to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of applicable data protection laws.

The risk of our being found in violation of these laws is increased by the fact that the in interpretation and enforcement of them is not entirely clear. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance and/or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

Compliance with data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. It could also require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business. Failure by us or our collaborators and third-party providers to comply with data protection laws and regulations could result in government enforcement actions (which could include civil or criminal penalties and orders preventing us from processing personal data), private litigation and result in significant fines and penalties against us. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend, could result in adverse publicity and could have a material adverse effect on our business, financial condition, results of operations and prospects.

Healthcare reform measures in the U.S., as well as the general tightening of drug reimbursement pathways and levels of reimbursement globally, are expected to add additional pressure to achieve financial expectations for our product candidates, if approved.

The U.S. and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that may affect our ability to profitably sell our product candidates, if approved. The U.S. government, state legislatures and foreign governments also have shown significant interest in implementing cost-containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs.

The Affordable Care Act was intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. See the section titled, "Item 1. Business – Healthcare Reform."

Further changes to and under the Affordable Care Act remain possible. It is unknown what form any such changes or any law proposed to replace the Affordable Care Act would take, and how or whether it may affect our business in the future. We expect that changes to the Affordable Care Act, the Medicare and Medicaid programs, changes allowing the federal government to directly negotiate

drug prices and changes stemming from other healthcare reform measures, especially with regard to healthcare access, financing or other legislation in individual states, could have a material adverse effect on the healthcare industry.

Any reduction in reimbursement from Medicare, Medicaid, or other government programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain and maintain profitability of our product and product candidates, if approved. The Inflation Reduction Act of 2022 contains substantial drug pricing reforms, including the establishment of a drug price negotiation program within the U.S. Department of Health and Human Services that would require manufacturers to charge a negotiated "maximum fair price" for certain selected drugs or pay an excise tax for noncompliance, the establishment of rebate payment requirements on manufacturers of certain drugs payable under Medicare Parts B and D to penalize price increases that outpace inflation, and requires manufacturers to provide discounts on Part D drugs. Substantial penalties can be assessed for noncompliance with the drug pricing provisions in the Inflation Reduction Act of 2022. The Inflation Reduction Act of 2022 could have the effect of reducing the prices we can charge and reimbursement we receive for our product candidates, if approved, thereby reducing our profitability, and could have a material adverse effect on our financial condition, results of operations and growth prospects. The effect of Inflation Reduction Act of 2022 on our business and the pharmaceutical industry in general is not yet known.

Our international operations subject us to additional regulatory oversight in foreign jurisdictions, as well as economic, social, and political uncertainties, which could cause a material adverse effect on our business, financial position, and operating results.

We are subject to certain risks associated with having assets, both physical and intangible, and operations located in Taiwan. Our activity in Taiwan is subject to regulatory agencies, such as the Taiwan Food and Drug Administration. Our operations in foreign jurisdictions are conducted by our subsidiary, CVie Therapeutics, Taiwan, which also owns a substantial portion of our intellectual property. Our international operations may be adversely affected by general economic conditions and economic and fiscal policy, including changes in exchange rates and controls, interest rates and taxation policies, and increased government regulation, which could have a material adverse effect on our business, financial position, and operating results. In addition, the impacts of political unrest, including as a result geopolitical tension, such as a deterioration in the relationship between the U.S. and China, including any potential resulting sanctions, export controls, or other restrictive actions that may be imposed by the U.S. and/or other countries against governmental or other entities in, for example, China or Taiwan, also could have an adverse impact on our international operations.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates, if approved.

We face an inherent risk of product liability as a result of the clinical trials of our product candidates and will face an even greater risk if we commercialize our product candidates if we receive approval. For example, we may be sued if our product candidates allegedly cause injury or are found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product candidate, negligence, strict liability and a breach of warranties. Claims may be brought against us by clinical trial participants, patients or others using, administering or selling products that may be approved in the future. Claims could also be asserted under state consumer protection acts.

If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit or cease the commercialization of our product candidates, if approved. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our product candidates, if approved;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management's time, attention and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- significant negative financial impact;
- the inability to commercialize our product candidates, if approved; and
- a decline in our stock price.

We currently hold product liability insurance coverage at a level we believe to be consistent with our activities. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates, if approved. Insurance coverage is increasingly expensive.

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of our product candidates, if approved. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies will also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

Our employees and independent contractors, including principal investigators, CROs, consultants and vendors, may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees and independent contractors, including principal investigators, CROs, consultants and vendors may engage in misconduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violate: (i) the laws and regulations of the FDA and other similar regulatory requirements, including those laws that require the reporting of true, complete and accurate information to such authorities, (ii) manufacturing standards, including cGMP requirements, (iii) federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations in the U.S. and abroad or (iv) laws that require the true, complete and accurate reporting of financial information or data. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, the creation of fraudulent data in our preclinical studies or clinical trials, or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. In addition, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and financial results, including, without limitation, the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, individual imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

We are subject to anti-bribery, anti-corruption, and anti-money laundering laws, including the U.S. Foreign Corrupt Practices Act, in which violations of these laws could result in substantial penalties and prosecution.

We are exposed to trade and economic sanctions and other restrictions imposed by the U.S. and other governments and organizations. The U.S. Departments of Justice, Commerce, State and Treasury and other federal agencies and authorities have a broad range of civil and criminal penalties they may seek to impose against corporations and individuals for violations of economic sanctions laws, export control laws, the U.S. Foreign Corrupt Practices Act, or the FCPA, and other federal statutes and regulations, including those established by the Office of Foreign Assets Control. The Department of Justice, or DOJ, also has increased its focus on the enforcement of the FCPA, particularly as it relates to the conduct of pharmaceutical companies.

In addition, the U.K. Bribery Act of 2010, or the Bribery Act, prohibits both domestic and international bribery, as well as bribery across both private and public sectors. An organization that "fails to prevent bribery" by anyone associated with the organization can be charged under the Bribery Act unless the organization can establish the defense of having implemented "adequate procedures" to prevent bribery. Under these laws and regulations, as well as other anti-corruption laws, anti-money laundering laws, export control laws, customs laws, sanctions laws and other laws governing our operations, various government agencies may require export licenses, may seek to impose modifications to business practices, including cessation of business activities in sanctioned countries or with sanctioned persons or entities and modifications to compliance programs, which may increase compliance costs, and may subject us to fines, penalties and other sanctions. A violation of these laws or regulations would negatively affect our business, financial condition and results of operations.

We and any of our third-party manufacturers or suppliers may use potent chemical agents and hazardous materials, and any claims relating to improper handling, storage or disposal of these materials could be time consuming or costly.

We and any of our third-party manufacturers or suppliers will use biological materials, potent chemical agents and may use hazardous materials, including chemicals and biological agents and compounds that could be dangerous to human health and safety of the environment. Our operations and the operations of our third-party manufacturers and suppliers also produce hazardous waste products. Federal, state and local laws and regulations govern the use, generation, manufacture, storage, handling and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our product development efforts. In addition, we cannot eliminate the risk of accidental injury or contamination from these materials or wastes. We carry a limited amount of specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies offer limited coverage for damages and fines arising from biological or hazardous waste exposure or contamination. In the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

Although we maintain workers' compensation insurance for certain costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities.

We maintain a limited amount of insurance for toxic tort claims that may be asserted against us in connection with our storage or disposal of biologic, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations, which have tended to become more stringent over time. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions or liabilities, which could materially adversely affect our business, financial condition, results of operations and prospects.

Risks Related to Intellectual Property Matters

If we cannot protect our intellectual property, others could use our technology in competitive products. Even if we obtain patents to protect our product candidates, those patents may not be sufficiently broad, or they may expire and others could then compete with us.

The patent position of biotechnology companies is highly uncertain and involves complex legal and factual questions for which important legal principles are unresolved. To date, the USPTO has not adopted a consistent policy regarding the breadth of claims that is accorded in biotechnology patents or the degree of protection that these types of patents afford. As a result, there are risks that we may not secure proprietary rights to products or processes that appear to be patentable.

The parties who licensed technologies to us and we have filed various U.S. and foreign patent applications with respect to the products and technologies under our development, and the USPTO and foreign patent offices have issued patents with respect to our products and technologies. These patent applications include international applications filed under the Patent Cooperation Treaty. Our pending patent applications, as well as those we may file in the future or those we may license from third parties, may not result in the USPTO or foreign patent office issuing patents. In addition, if patent rights covering our products are not sufficiently broad, they may not provide us with sufficient proprietary protection or competitive advantages against competitors with similar products and technologies. For example, the core composition of matter patents covering istaroxime have expired. As such, istaroxime relies on data and market exclusivity, as well as method-of-use patents, which may offer a lesser scope of protection than the original core patents. Furthermore, even if the USPTO or foreign patent offices were to issue patents to us or our licensors, others may challenge the patents or circumvent the patents, or the patent office or the courts may invalidate the patents. Thus, any patents we own or license from third parties may not provide us any protection against competitors.

The patents that we own or in-license have a limited life. Patents related to our cardiovascular drug products issued in the U.S., Europe and elsewhere have expired or will expire on various dates between 2028 and 2039. Further, we cannot guarantee that all patent applications related to our cardiovascular drug products that are still pending in U.S., Europe and elsewhere will be granted as patents.

Intellectual property rights of third parties could limit our ability to develop and market our product candidates.

Our success also depends upon our ability to operate our business without infringing the patents or violating the proprietary rights of others. Patent applications in most jurisdictions are not published until 18 months after filing. In certain cases, the USPTO keeps U.S. patent applications confidential for the entire time the applications are pending. As a result, we cannot determine in advance what inventions third parties may claim in their pending patent applications. We may need to defend or enforce our patent and license rights or to determine the scope and validity of the proprietary rights of others through legal proceedings, which would be costly, unpredictable and time consuming. Even in proceedings where the outcome is favorable to us, they would likely divert substantial resources, including management time, from our other activities. Moreover, any adverse determination could subject us to significant liability or require us to seek licenses that third parties might not grant to us or might only grant at rates that diminish or deplete the profitability of our products. An adverse determination could also require us to alter our products or processes or cease altogether any product sales or related research and development activities.

We may need to license intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

We may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we cannot provide any assurances that third-party patents do not exist which might be enforced against our product candidates in the absence of such a license. The licensing and acquisition of third-party intellectual property rights is a competitive practice and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. We may fail to obtain any of these licenses on commercially reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation. Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may not be able to successfully develop and commercialize the affected product candidates, which would have a material adverse effect on our business.

We rely on agreements containing obligations regarding intellectual property, confidentiality and noncompetition provisions that could be breached and may be difficult to enforce.

Although we take what we believe to be reasonable steps to protect our intellectual property, including the use of agreements relating to the non-disclosure of our confidential and proprietary information and trade secrets to third parties, as well as agreements that provide for disclosure and assignment to us of all rights to the ideas, developments, improvements, discoveries and inventions of our employees, consultants, advisors and research collaborators while we employ them, such agreements can be difficult and costly to enforce. We generally seek to enter into these types of agreements with consultants, advisors and research collaborators; however, to the extent that such parties apply or independently develop intellectual property in connection with any of our projects, disputes may arise concerning allocation of the related proprietary rights. Such disputes often involve significant expense and yield unpredictable results.

Moreover, although all employees enter into agreements with us that include non-compete covenants, and our senior executive officers have agreements that include broader non-competition covenants and provide for severance payments that are contingent upon the applicable employee's refraining from competition with us, such non-compete provisions can be difficult and costly to monitor and enforce, such that, if any should resign, we may not be successful in enforcing our noncompetition agreements with them.

Despite the protective measures we employ, we still face the risk that:

- agreements may be breached;
- agreements may not provide adequate remedies for the applicable type of breach;
- our trade secrets or proprietary know-how may otherwise become known;
- our competitors may independently develop similar technology; or
- our competitors may independently discover our proprietary information and trade secrets.

Patents covering our product candidates could be found invalid or unenforceable if challenged in court or before administrative bodies in the U.S. or abroad.

Although an issued patent is presumed valid and enforceable, its issuance is not conclusive as to its validity or its enforceability and it may not provide us with adequate proprietary protection or competitive advantages against competitors with similar product candidates. Competitors could attempt to replicate the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights, design around the relevant patents, or develop and obtain patent protection for more effective technologies, designs or methods. We may be unable to prevent the unauthorized disclosure or use of our technical knowledge or trade secrets by consultants, suppliers, vendors, former employees and current employees. The laws of some non-U.S. countries do not protect our proprietary rights to the same extent as the laws of the U.S., and we may encounter significant problems in protecting our proprietary rights in these countries.

In addition, proceedings to enforce or defend our patents, or patents to which we have ownership rights through licensing agreements, could put those patents at risk of being invalidated, held unenforceable or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of those patents are invalid or otherwise unenforceable. If any of the patents covering our product candidates are invalidated or found unenforceable, or if a court found that valid, enforceable patents held by third parties covered one or more of our product candidates, our competitive position could be harmed or we could be required to incur significant expenses to enforce or defend our rights.

Third parties may assert ownership or commercial rights to inventions we develop.

Third parties may in the future make claims challenging the inventorship or ownership of our intellectual property. In addition, we may face claims by third parties that our agreements with employees, contractors or consultants obligating them to assign intellectual property to us are ineffective or in conflict with prior or competing contractual obligations of assignment, which could result in ownership disputes regarding intellectual property we have developed or will develop and interfere with our ability to capture the commercial value of such intellectual property. Litigation may be necessary to resolve an ownership dispute, and if we are not successful, we may be precluded from using certain intellectual property or may lose our exclusive rights in such intellectual property. Either outcome could harm our business and competitive position.

Litigation or other proceedings or third-party claims of intellectual property infringement could require us to spend significant time and money and could prevent us from selling our product candidates or affect our stock price.

Our commercial success will depend in part on not infringing the patents or violating other proprietary rights of others. Significant litigation regarding patent rights occurs in our industry. Our competitors may have applied for or obtained, or may in the future apply for and obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell our product candidates. We do not always conduct independent reviews of patents issued to third parties. In addition, patent applications in the U.S. and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived, so there may be applications of others now pending or recently revived patents of which we are unaware. Patent applications in the U.S., the EU and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. These applications may later result in issued patents, or the revival of previously abandoned patents, that will prevent, limit or otherwise interfere with our ability to develop and market our product candidates. Third parties may assert claims that we are employing their proprietary technology without authorization, including claims from competitors or from nonpracticing entities that have no relevant product revenue and against whom our own patent portfolio may have no deterrent effect.

As we attempt to commercialize our product candidates in their current or updated forms, launch new product candidates and enter new markets, we expect competitors may claim that one or more of our product candidates infringe their intellectual property rights as a strategy to impede our commercialization and entry into new markets. The large number of patents, the rapid rate of new patent applications and issuances, the complexities of the technologies involved, and the uncertainty of litigation may increase the risk of business resources and management's attention being diverted to patent litigation. We may in the future receive, letters or other threats or claims from third parties inviting us to take licenses under, or alleging that we infringe, their patents.

Moreover, we may become party to adversarial proceedings regarding our or third-party patent portfolios. Such proceedings could include supplemental examination or contested post-grant proceedings such as review, reexamination, inter parties review, interference or derivation proceedings before the USPTO and challenges in U.S. District Courts. Patents may be subjected to opposition, post-grant review or comparable proceedings lodged in various foreign, both national and regional, patent offices. The legal threshold for initiating litigation or contested proceedings may be low, so that even lawsuits or proceedings with a low probability of success might be initiated. Litigation and contested proceedings can also be expensive and time-consuming, and our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can. We may also occasionally use these proceedings to challenge the patent rights of others. We cannot be certain that any particular challenge will be successful in limiting or eliminating the challenged patent rights of the third party.

Any lawsuits resulting from such allegations could subject us to significant liability for damages and/ or invalidate our proprietary rights. Any potential intellectual property litigation also could force us to do one or more of the following:

- stop making, selling or using product candidates or technologies that allegedly infringe the asserted intellectual property;
- lose the opportunity to license our technology to others or to collect royalty payments;
- incur significant legal expenses, including, in some cases, the attorney's fees and costs of litigation to the party whose intellectual property rights we may be found to be infringing;
- pay substantial damages (possibly treble damages) or royalties to the party whose intellectual property rights on which we may be found to be infringing;
- redesign product candidates that contain the allegedly infringing intellectual property; and
- attempt to obtain a license to the relevant intellectual property from third parties, which may not be available on reasonable terms or at all.

Any litigation or claim against us, even those without merit, may cause us to incur substantial costs, and could place a significant strain on our financial resources, divert the attention of management from our business and harm our reputation. If we are found to infringe the intellectual property rights of third parties, we could be required to pay substantial damages (which may be increased up to three times of awarded damages) and/or substantial royalties and could be prevented from selling our product candidates unless we obtain a license or are able to redesign our product candidates to avoid infringement. Any such license may not be available on reasonable terms, if at all, and there can be no assurance that we would be able to redesign our product candidates in a technically feasible way that would not infringe the intellectual property rights of others. We could encounter delays while we attempt to develop alternative methods or product candidates. If we fail to obtain any required licenses or make any necessary changes to our product candidates or technologies, we may be unable to commercialize one or more of our product candidates.

Even if we were ultimately to prevail, any of these events could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business. Intellectual property litigation, regardless of its outcome, may cause negative publicity, or prohibit us from manufacturing, importing, marketing or otherwise commercializing our product candidates, services and technology. In addition, if the breadth or strength of protection provided by the patents and patent applications we own or in-license is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. In addition, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

There could also be public announcements of the results of hearings, motions or other interim proceedings or developments, and if securities analysts or investors view these announcements in a negative light, the price of our common stock could be adversely affected.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position could be harmed.

We also rely upon copyright and trade secret protection, as well as non-disclosure agreements and invention assignment agreements with our employees, consultants and third parties, to protect our confidential and proprietary information.

In addition to contractual measures, we try to protect the confidential nature of our proprietary information using commonly accepted physical and technological security measures. Such measures may not provide adequate protection for our proprietary information. Our security measures may not prevent an employee or consultant from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our product candidates that we consider proprietary. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive and time-consuming, and the outcome of any such claim is unpredictable. Trade secret violations are often a matter of state law, and the criteria for protection of trade secrets can vary among different jurisdictions. In addition, trade secrets may be independently developed or reverse engineered by others in a manner that could prevent legal recourse by us. If any of our confidential or proprietary information, such as our trade secrets, were to be disclosed or misappropriated, or if any such information were independently developed by a competitor, our business and competitive position could be harmed.

We may be unable to enforce our intellectual property rights throughout the world.

Filing, prosecuting and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive, and the laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the U.S. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. This could make it difficult for us to stop infringement of our foreign patents, if obtained, or the misappropriation of our other intellectual property rights. For example, some foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, some countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries. Additionally, in the event that our trademarks are successfully challenged, we could be forced to rebrand our product candidates, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe our trademarks, and we may not have adequate resources to enforce our trademarks.

Proceedings to enforce our patent or trademark rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

Third parties may assert that our employees or consultants have wrongfully used or disclosed confidential information or misappropriated trade secrets.

In the future, we may employ individuals who previously worked with other companies, including our competitors. Although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property or personal data, including trade secrets or other proprietary information, of a former employer or other third party. Litigation may be necessary to defend against these claims. If we fail in defending any such claims or settling those claims, in addition to paying monetary damages or a settlement payment, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Changes in U.S. patent laws may limit our ability to obtain, defend and/or enforce our patents.

In 2011, the U.S. enacted and later implemented wide ranging patent reform legislation. The U.S. Supreme Court has ruled on several patent cases since that time, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on actions by the U.S. Congress, the U.S. federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce patents that we have licensed or that we might obtain in the future. Similarly, changes in patent law and regulations in other countries or jurisdictions, changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we have licensed or that we may obtain in the future.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and other patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO and other patent agencies over the lifetime of the patent. While an inadvertent failure to make payment of such fees or to comply with such provisions can in many cases be cured by additional payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance with such provisions will result in the abandonment or lapse of the patent or patent application, and the partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents within prescribed time limits. If we or our licensors fail to maintain the patents and patent applications covering our product or if we or our licensors otherwise allow our patents or patent applications to be abandoned or lapse, it can create opportunities for competitors to enter the market, which would hurt our competitive position and could impair our ability to successfully commercialize our product candidates.

We may be unable to obtain a patent term extension in the U.S. under the Hatch-Waxman Act and in foreign countries under similar legislation.

In the U.S., a patent that covers a drug product approved by the FDA may be eligible for a term extension designed to restore the period of the patent term that is lost during the premarket regulatory review process conducted by the FDA. Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, it is possible, though unlikely, that one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, which permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended, and only one patent may be extended. In the EU, it is possible, though unlikely, that our product candidates may be eligible for term extensions based on similar legislation. However, in either jurisdiction, if we were eligible to apply for patent term extension, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Even if we are granted such extension, the duration of such extension may be less than our request. If we are unable to obtain a patent term extension, or if the term of any such extension is less than our request, the period during which we can enforce our patent rights for that product will be in effect shortened and our competitors may obtain approval to market competing products sooner. The resulting reduction of years of revenue from applicable product candidates could be substantial.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make products that are similar to our product candidates or utilize similar technology but that are not covered by the claims of our patents or that incorporate certain technology in our product candidates that is in the public domain;
- we, or our future licensors or collaborators, might not have been the first to make the inventions covered by the applicable issued patent or pending patent application that we own now or may own or license in the future;
- we, or our future licensors or collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- we may not be able to successfully commercialize our product candidates before our relevant patents we may have, or to which we have ownership rights through licensing agreements, expire;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our current or future pending patent applications will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors or other third parties;
- our competitors or other third parties might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Any of the foregoing could have a material adverse effect on our business, financial condition and results of operations.

Risks Related to the Ownership of our Securities

Our common stock is listed on the Nasdaq Capital Market, or Nasdaq. We can provide no assurance that we will be able to comply with the continued listing requirements over time and that our common stock will continue to be listed on Nasdaq.

In May 2020, we successfully listed our common stock on the Nasdaq Capital Market. However, we can give no assurance that we will be able to satisfy the continued listing requirements of Nasdaq in the future, including but not limited to the corporate governance requirements and the minimum closing bid price requirement or the minimum equity requirement.

On June 3, 2022, we received a deficiency letter from the Nasdaq Listing Qualifications Department, or the Staff, of Nasdaq notifying us that, for 30 consecutive business days, the closing bid price for our common stock was below the minimum $1.00 per share required for continued listing on the Nasdaq Capital Market pursuant to Nasdaq Listing Rule 5550(a)(2), or Rule 5550(a)(2). The Nasdaq deficiency letter had no immediate effect on the listing of our common stock, and our common stock continued to trade on the Nasdaq Capital Market under the symbol "WINT". We were initially given 180 calendar days, or until November 30, 2022, to regain compliance with Rule 5550(a)(2), which was extended by an additional 180 calendar days, or May 29, 2023.

On February 24, 2023, we effected a reverse stock split of our issued and outstanding shares of common stock, par value $0.001 per share, at a ratio of 1 post-split share for every 50 pre-split shares. On March 10, 2023, we received written confirmation from Nasdaq notifying us that we had regained compliance with Nasdaq Listing Rule 5550(a)(2).

On January 22, 2024, we received a deficiency letter from the Staff of Nasdaq notifying us that, for the last 31 consecutive business days, the closing bid price for our common stock has been below the minimum $1.00 per share required for continued listing on the Nasdaq Capital Market pursuant to Rule 5550(a)(2). The Nasdaq deficiency letter has no immediate effect on the listing of our common stock, and our common stock will continue to trade on the Nasdaq Capital Market under the symbol "WINT" at this time. We have been given an initial 180 calendar days, or until July 22, 2024, to regain compliance with Rule 5550(a)(2). If at any time before July 22, 2024, the bid price of our common stock closes at $1.00 per share or more for a minimum of 10 consecutive business days, the Staff will provide written confirmation that we have achieved compliance. If we do not regain compliance with Rule 5550(a)(2) by July 22, 2024, we may be afforded a second 180 calendar day period to regain compliance, if we meet certain other conditions. If we fail to maintain compliance, Nasdaq may take steps to de-list our common stock. If such delisting should occur, it would likely have a negative effect on the price of our common stock and would impair an investor's ability to sell or purchase our common stock when desired. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the Nasdaq minimum bid price requirement, or prevent future non-compliance with Nasdaq's listing requirements.

We effected a reverse stock split on February 24, 2023, and will need to effect a future reverse stock split to regain compliance with the Nasdaq Capital Market listing rules, which may adversely impact the market price of our common stock.

We effected a reverse stock split of our outstanding common stock at a ratio of 1-for-50 shares, which was effected at 12:01 a.m. Eastern Time on February 24, 2023. Additionally, at a special meeting of stockholders held on April 10, 2024, our stockholders approved a proposal to amend our Amended and Restated Certificate of Incorporation, or Certificate of Incorporation, to effect a reverse stock split of our outstanding shares of common stock, par value $0.001 per share by a ratio of any whole number between 1-for-5 and 1-for-25, the implementation and timing of which is subject to the discretion of our Board of Directors.

The impact of any future reverse stock split, once effective, upon the market price of our common stock cannot be predicted with certainty and there is no assurance that our common stock will trade at a price consistent with such reverse stock split. Accordingly, it is possible that the market price of our common stock following the reverse stock split will decline, possibly more than would occur in the absence of a reverse stock split.

The effective increase in the number of shares of our common stock available for issuance as a result of our reverse stock split could result in further dilution to our existing stockholders and have antitakeover implications.

The February 2023 reverse stock split alone had no effect on our authorized capital stock, and the total number of authorized shares remains the same as before the reverse stock split. The reverse stock split of our issued and outstanding shares increased the number of shares of our common stock (or securities convertible or exchangeable for our common stock) available for issuance by decreasing the number of shares of our common stock issued and outstanding. The additional available shares are available for issuance from time to time at the discretion of our Board of Directors when opportunities arise, without further stockholder action or the related delays and expenses, except as may be required for a particular transaction by law, the rules of any exchange on which our securities may then be listed, or other agreements or restrictions. Any issuance of additional shares of our common stock would increase the number of outstanding shares of our common stock and (unless such issuance was pro-rata among existing stockholders) the percentage ownership of existing stockholders would be diluted accordingly. In addition, any such issuance of additional shares of our common stock could have the effect of diluting the earnings per share and book value per share of outstanding shares of our common stock.

Additionally, the effective increase in the number of shares available for issuance could, under certain circumstances, have anti-takeover implications. For example, the additional shares of common stock that have become available for issuance could be used by us to oppose a hostile takeover attempt or to delay or prevent changes in control or our management. Although our reverse stock split is prompted by other considerations and not by the threat of any hostile takeover attempt, stockholders should be aware that our reverse

stock split could facilitate future efforts by us to deter or prevent changes in control, including transactions in which our stockholders might otherwise receive a premium for their shares over then-current market prices.

The market price of our common stock may be highly volatile, and investors may not be able to resell their shares at or above the price at which they purchase them.

The market price of our common stock, like that of many other development stage pharmaceutical or biotechnology companies, has been and is likely to be volatile. In addition to general economic, political and market conditions, the price and trading volume of our stock could fluctuate widely in response to many factors, including:

- our ability to execute our planned clinical trials on a timely basis consistent with timelines established;
- results of our clinical trials and preclinical studies, and the results of trials of our competitors or those of other companies in our market sector;
- regulatory approval of our product candidates, or limitations to specific label indications or patient populations for its use, or changes or delays in the regulatory review process;
- regulatory developments in the U.S. and foreign countries;
- changes in the structure of healthcare payment systems, especially in light of current reforms to the U.S. healthcare system;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates, along with any product modifications and improvements;
- the success or failure of our efforts to acquire, license or develop additional product candidates;
- innovations or new products developed by us or our competitors;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;
- manufacturing, supply or distribution delays or shortages;
- any changes to our relationship with any manufacturers, suppliers, licensors, future collaborators or other strategic partners;
- our expectations regarding the potential market size and the size of the patient populations for our product candidates;
- the implementation of our business model and strategic plans for our business and technology;
- achievement of expected product sales and profitability;
- variations in our financial results or those of companies that are perceived to be similar to us;
- market conditions in the biopharmaceutical sector and issuance of securities analysts' reports or recommendations;
- trading volume of our common stock;
- an inability to obtain additional funding;
- sales of our stock by insiders and stockholders;
- general economic, industry and market conditions other events or factors, including as a result of inflation, liquidity constraints or banking stability, many of which are beyond our control;
- our commercialization, marketing and manufacturing prospects and capabilities;
- additions or departures of key personnel; and
- intellectual property, product liability or other litigation against us.

In addition, the stock markets in general, and the markets for biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that may have been unrelated to the operating performance of the issuer. These broad market fluctuations may adversely affect the market price or liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have sometimes instituted securities class action litigation against the issuer. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our management would be diverted from the operation of our business.

The sale and issuance of our common stock or rights to purchase our common stock, stock incentive plans and upon the exercise of outstanding securities exercisable for shares of our common stock, could result in substantial additional dilution of our stockholders, cause our stock price to fall and adversely affect our ability to raise capital.

We will require additional capital to continue to execute our business plan and advance our research and development efforts. To the extent that we raise additional capital through the issuance of additional equity securities and through the exercise of outstanding warrants, our stockholders may experience substantial dilution. We may sell shares of preferred stock or common stock in one or more transactions at prices that may be at a discount to the then-current market value of our common stock and on such other terms and

conditions as we may determine from time to time. Any such transaction could result in substantial dilution of our existing stockholders. If we sell shares of our common stock in more than one transaction, stockholders who purchase our common stock may be materially diluted by subsequent sales. Such sales could also cause a drop in the market price of our common stock. The issuance of shares of our common stock in connection with a public or private financing, in connection with our compensation programs, and upon exercise of outstanding warrants will have a dilutive impact on our other stockholders and the issuance, or even potential issuance, of such shares could have a negative effect on the market price of our common stock.

The exercise of stock options and other securities could also cause our stockholders to experience substantial dilution. Moreover, holders of our stock options and warrants are likely to exercise them, if ever, at a time when we otherwise could obtain a price for the sale of our securities that is higher than the exercise price per security of the options or warrants. Such exercises, or the possibility of such exercises, may impede our efforts to obtain additional financing through the sale of additional securities or make such financing more costly. It may also reduce the price of our common stock.

The Certificate of Designation for the Series B Preferred Stock and the Notes, each contain anti-dilution provisions that may result in the reduction of the conversion price of the Series B Preferred Stock and the Notes. These features may increase the number of shares of our common stock being issuable upon conversion of the Series B Preferred Stock and the Notes.

The Certificate of Designation, or the Series B Certificate of Designation, authorizes a total of 5,500 Series B Preferred Stock, with an initial conversion price of $0.3603, the Preferred Conversion Price. Similarly, our 10% senior convertible notes, or the Notes, have an initial conversion price of $0.3603, the Notes Conversion Price. Both the Preferred Conversion Price and the Notes Conversion Price are subject to adjustment upon the occurrence of specified events to no lower than $0.0721, subject to any stock split, stock dividend, stock combination, recapitalization or other similar transaction involving our common stock at a price below the then-applicable Preferred Conversion Price or Notes Conversion Price, as applicable, each as described in further detail in the Certificate of Designation or the Notes, respectively.

If in the future, while any of our Series B Preferred Stock or Notes are outstanding, we grant, issue or sell any shares of our common stock for a consideration per share of our common stock, the New Issuance Price, less than a price equal to the Preferred Conversion Price or Notes Conversion Price, respectively, as then in effect immediately prior to such granting, issuance or sale, we will be required, subject to certain limitations and adjustments (as provided in the Series B Certificate of Designation or the Note) to reduce the Preferred Conversion Price or the Notes Conversion Price, as applicable, to be equal to the New Issuance Price, which will result in a greater number of shares of our common stock being issuable upon conversion, which in turn will increase the dilutive effect of such conversion on existing holders of our common stock. It is possible that we will not have a sufficient number of shares available to satisfy the conversion of the Series B Preferred Stock and/or the Notes if we enter into a future transaction that reduces the applicable Preferred Conversion Price or Notes Conversion Price. If we do not have a sufficient number of available shares for the conversion of any Series B Preferred Stock or Notes, we may need to seek shareholder approval to increase the number of authorized shares of our common stock, which may not be possible and will be time consuming and expensive. The potential for such additional issuances may depress the price of our common stock regardless of our business performance and may make it difficult for us to raise additional equity capital while any of our Series B Preferred Stock or Notes are outstanding.

The Series B Preferred Stock have a liquidation preference senior to our common stock.

Subject to certain exceptions, in accordance with the Series B Certificate of Designation, shares of our capital stock are junior in rank to the Series B Preferred Stock with respect to the preferences as to dividends, distributions and payments upon our liquidation, dissolution and winding up. The payment of the liquidation preferences could result in common stockholders and warrant holders not receiving any consideration if we were to liquidate, dissolve or wind up, either voluntarily or involuntarily. This liquidation preference may increase over time based on the payment of dividends.

The existence of the liquidation preferences may reduce the value of our common stock, make it harder for us to sell shares of common stock in offerings in the future, or prevent or delay a change of control.

Under the terms of the Notes, we are subject to certain restrictive covenants that may make it difficult to procure additional financing.

On April 2, 2024, we entered into a Securities Purchase Agreement, or the Purchase Agreement, with the buyers named therein. The Purchase Agreement, pursuant to which we issued the Notes, contains the restrictive covenants, subject to certain exceptions. For example, without the consent of the holders holding at least a majority of the certain registrable securities for the period commencing on April 2, 2024 and ending on the date immediately following the 90th trading day after the Applicable Date (as defined in the Purchase Agreement), or the Restricted Period, neither we nor any of our subsidiaries will directly or indirectly issue, offer, sell, grant any option or right to purchase, or otherwise dispose of (or announce any issuance, offer, sale, grant of any option or right to purchase or other disposition of) any equity security or any equity-linked or related security (including, without limitation, any “equity security” (as that term is defined under Rule 405 promulgated under the Securities Act of 1933, as amended), any Convertible Securities (as defined in the Purchase Agreement), any debt, any preferred stock or any purchase rights), or a Subsequent Placement.

Subject to the limitations described in the Purchase Agreement, for so long as the Notes are outstanding, we are prohibited from effecting or entering into an agreement to effect any Subsequent Placement involving a Variable Rate Transaction (as defined in the Purchase Agreement).

Additionally, the Purchase Agreement contains a participation right, which provides that, subject to certain exceptions, at any time on or prior to April 2, 2028, neither we nor our subsidiaries shall, directly or indirectly, effect any Subsequent Placement unless we comply with certain notice procedures as outlined in the Purchase Agreement with respect to each buyer, providing the opportunity for such buyer to participate in such Subsequent Placement on a pro rata basis as described in the Purchase Agreement.

Any of these restrictions on our ability to operate our business in our discretion could adversely affect our business by, among other things, limiting our ability to adapt to changing economic, financial, or industry conditions and to take advantage of corporate opportunities, including opportunities to obtain debt financing, repurchase stock, refinance or pay principal on our outstanding debt, or complete acquisitions for cash or debt. If we require additional funding while these restrictive covenants remain in effect, we may be unable to effect a financing transaction while remaining in compliance with the terms of the Purchase Agreement, or we may be forced to seek a waiver from the buyers party to the Purchase Agreement.

Provisions of our Certificate of Incorporation, our Amended and Restated By-Laws, or By-Laws, and Delaware law could deter a change of our management and thereby discourage or delay offers to acquire us.

Provisions of our Certificate of Incorporation, our By-Laws and Delaware law may make it more difficult for someone to acquire control of us or for our stockholders to remove existing management and might discourage a third party from offering to acquire us, even if a change of control or in management would be beneficial to our stockholders. Such provisions may make it costlier for a potential acquirer to engage in a business combination transaction with us. Provisions that have the effect of discouraging, delaying or preventing a change of control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock and could also affect the price that some investors are willing to pay for our common stock.

Our Certificate of Incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to file in a different judicial forum to resolve disputes with us or our directors, officers or employees.

Our Certificate of Incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our Certificate of Incorporation or our By-Laws, or any action asserting a claim against us that is governed by the internal affairs doctrine; provided, that, this provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act. These choice of forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

We are a "smaller reporting company," and the reduced disclosure requirements applicable to smaller reporting companies may make our common stock less attractive to investors.

We are a "smaller reporting company" as defined in the Exchange Act and have elected to take advantage of certain of the scaled disclosures available to smaller reporting companies, which include, among other things, audited financial statements and Management Discussion and Analysis for two years instead of three years, an update of the general development of the business for such period that is material to an understanding of the company, simplified executive compensation disclosures, and exemption from the provisions of Section 404(b) of the Sarbanes-Oxley Act requiring that an independent registered accounting firm provide an attestation report on the effectiveness of internal control over financial reporting. We cannot predict whether investors will find our common stock less attractive because of our reliance on any of these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

ITEM 1B. UNRESOLVED STAFF COMMENTS.

None.

ITEM 1C. CYBERSECURITY.

We use, store, and process data for and about our employees and suppliers. We have implemented a cybersecurity risk management program that is designed to identify, assess, and mitigate risks from cybersecurity threats to this data and our systems.

Risk Management Oversight and Governance

Under the ultimate direction of our Chief Executive Officer, or CEO, and executive management team, our Chief Operating Officer, or COO, has primary responsibility for overseeing our management of cybersecurity risks. Our COO reports directly to our CEO. Our COO has primary responsibility for assessing and managing our cybersecurity threat management program. He has more than 20 years of professional experience and is responsible for our corporate strategy, pipeline development plan, and business development.

The Board of Directors has delegated oversight of the Company's cybersecurity program to the Audit Committee of the Board of Directors. As provided in the Audit Committee Charter, the Audit Committee is responsible for reviewing reports on data management and security initiatives and significant existing and emerging cybersecurity risks, including cybersecurity incidents, the impact on us and our stockholders of any significant cybersecurity incident and any disclosure obligations arising from any such incidents. The COO reports to the Audit Committee about cybersecurity and cyber risk management on a periodic basis.

Processes for the Identification of Cybersecurity Threats

Our Information Security team is responsible for monitoring our information systems for vulnerabilities and mitigating any issues. It works with other groups in the company to understand the severity of the potential consequences of a cybersecurity incident and to make decisions about how to prioritize mitigation and other initiatives based on, among other things, materiality to the business. The Information Security team has processes designed to keep the company apprised of the different threats in the cybersecurity landscape – this includes interacting with intelligence networks, discussions with peers at other companies, monitoring social media, reviewing government alerts and other news items, and attending security conferences.

We have an employee education program that is designed to raise awareness of cybersecurity threats to reduce our vulnerability as well as to encourage consideration of cybersecurity risks across functions. As part of the assessment of the protections we have in place to mitigate risks from cybersecurity threats, we engage our third-party information technology provider to conduct risk assessments on our systems. To assess the effectiveness of our program, we also have engaged our information technology provider to conduct penetration testing and other vulnerability analyses.

Before purchasing third-party technology or other solutions that involve exposure to our assets and electronic information, our information technology provider conducts an evaluation of the company and software prior to authorizing it for installation.

We have not identified any cybersecurity incidents or threats that have materially affected us or are reasonably likely to materially affect us, including our business strategy, results of operations, or financial condition. However, like other companies in our industry, we and our third-party vendors have from time to time experienced threats that could affect our information or systems. For more information, see the section titled, "Item 1A – Risk Factors."

ITEM 2. PROPERTIES.

We maintain our principal executive offices at 2600 Kelly Road, Suite 100, Warrington, Pennsylvania 18976-3622. Our premises include corporate administration, research and drug development, clinical operations, regulatory affairs, and quality.

We also maintain a location in Taipei, Taiwan consisting of approximately 1,317 square feet of office space, where we oversee certain manufacturing development and preclinical activities occurring at a university in Taiwan related to our cardiovascular drug product candidates. We believe our current facilities are adequate for our needs in 2024.

ITEM 3. LEGAL PROCEEDINGS.

We are not aware of any pending legal actions that would, if determined adversely to us, have a material adverse effect on our business and operations.

We may be subject to other legal proceedings and claims in the ordinary course of business. We cannot predict the results of any such disputes, and despite the potential outcomes, the existence thereof may have an adverse material impact on us due to diversion of management time and attention as well as the financial costs related to resolving such disputes.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES.

Market Information

Our common stock is quoted on The Nasdaq Capital Market, or Nasdaq, operated by The Nasdaq Stock Market LLC under the symbol "WINT."

Holders of Our Common Stock

As of April 16, 2024, we had 38 holders of record of shares of our common stock, and there were 9,183,220 shares of our common stock outstanding. The actual number of holders of our common stock is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers or held by other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

We have not paid any dividends and we do not anticipate paying any cash dividends in the foreseeable future and we intend to retain all of our earnings, if any, to finance our growth and operations and to fund the expansion of our business. Payment of any dividends will be made in the discretion of our Board of Directors, or the Board, after our taking into account various factors, including our financial condition, operating results, current and anticipated cash needs and plans for expansion.

Recent Sales of Unregistered Securities

During the period covered by this Annual Report on Form 10-K, there were no sales by us of unregistered securities that were not previously reported by us in a Quarterly Report on Form 10-Q or Current Report on Form 8-K.

Securities Authorized for Issuance Under Equity Compensation Plans

Information about our equity compensation plans is incorporated herein by reference to Part III, Item 12 of this Annual Report on Form 10-K.

Share Repurchase

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

ITEM 6. [Reserved].

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS.

INTRODUCTION

Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing activities, includes forward-looking statements that involve risks and uncertainties. You should review the Forward-Looking Statements and Risk Factors sections of this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis or elsewhere in the Annual Report on Form 10-K.

Management's discussion and analysis of the financial condition and results of operations, or MD&A, is provided as a supplement to the accompanying consolidated financial statements and footnotes to help provide an understanding of our financial condition, the changes in our financial condition and our results of operations. This item should be read in connection with our Consolidated Financial Statements for the year ending December 31, 2023 and notes thereto, or Notes, included in this Annual Report on Form 10-K. See the section titled, "Item 8 – Financial Statements and Supplementary Data."

Information concerning the shares of our common stock and related share prices in this MD&A has been adjusted to reflect the 1-for-50 reverse split of our common stock that was made effective on February 24, 2023. (See the section titled, "Item 8 – Notes to consolidated financial statements – Note 2 – Basis of Presentation").

OVERVEW

We are a biotechnology company focused on advancing early and late-stage innovative therapies for critical conditions and diseases. Our portfolio of product candidates includes istaroxime, a Phase 2 candidate with sarco endoplasmic reticulum Ca2+ -ATPase 2a, or SERCA2a, activating properties for acute heart failure and associated cardiogenic shock, preclinical SERCA2a activators for heart failure, rostafuroxin for the treatment of hypertension in patients with a specific genetic profile, and a preclinical atypical protein kinase C iota, or aPKCi, inhibitor (topical and oral formulations), being developed for potential application in rare and broad oncology indications. We also have a licensing business model with partnership out-licenses currently in place.

Our lead product candidate, istaroxime, is a first-in-class, dual-acting agent being developed to increase blood pressure and improve cardiac function in patients with cardiogenic shock and to improve cardiac function in patients with acute heart failure, or AHF, and reverse the hypotension and hypoperfusion associated with heart failure that deteriorates to cardiogenic shock. Istaroxime demonstrated significant improvement in both systolic and diastolic aspects of cardiac function and was generally well tolerated in three Phase 2 clinical trials. Istaroxime has been granted Fast Track designation for the treatment of AHF by the U.S. Food and Drug Administration, or FDA. Based on the profile observed in our Phase 2 clinical studies in AHF, where istaroxime significantly improved cardiac function and systolic blood pressure, or SBP, in acute decompensated heart failure patients and had a favorable renal profile, we initiated a Phase 2 global clinical study, or the SEISMiC Study, to evaluate istaroxime for the treatment of early cardiogenic shock (Society for Cardiovascular Angiography and Interventions, or SCAI, Stage B shock), a severe form of AHF characterized by very low blood pressure and risk for hypoperfusion to critical organs and mortality. In April 2022, we announced our observations in the SEISMiC Study that istaroxime rapidly and significantly increased SBP while also improving cardiac function and preserving renal function. We believe that istaroxime has the potential to fulfill an unmet need in early and potentially more severe cardiogenic shock. We further believe that the data from the SEISMiC Study supports continued development in both cardiogenic shock and AHF. In the fourth quarter of 2023, we initiated an extension to the SEISMiC Study, or the SEISMiC Extension, to evaluate a longer dosing period and to continue to characterize the effects of istaroxime, including activation of SERCA2a. The SEISMiC Extension study is expected to enroll up to 30 subjects with SCAI Stage B cardiogenic shock with data anticipated in the second half of 2024. Additionally, we have recently initiated a small study in more severe SCAI Stage C cardiogenic shock, or SEISMiC C, to evaluate the safety and efficacy of istaroxime in cardiogenic shock patients who are also receiving standard of care rescue therapy for shock. The SEISMiC C study is expected to enroll up to 20 subjects with SCAI Stage C cardiogenic shock with enrollment anticipated to be completed in late 2024. Our ability to complete both of these studies with their intended sample size is dependent upon us securing adequate resourcing for the program through financing efforts or business development activities.

Our heart failure cardiovascular portfolio also includes SERCA2a activators. This research program is evaluating these preclinical product candidates, including oral and intravenous SERCA2a activator heart failure compounds. These candidates would potentially be developed for both acute decompensated and chronic out-patient heart failure. In addition, our cardiovascular drug product candidates include rostafuroxin, a novel product candidate for the treatment of hypertension in patients with a specific genetic profile. We are pursuing potential licensing arrangements and/or other strategic partnerships and do not intend to advance rostafuroxin without securing such an arrangement or partnership.

Our cardiovascular assets and programs are associated with a regional licensed partnership with Lee's Pharmaceutical (HK) Ltd., or Lee's (HK), for the development and commercialization of our product candidate, istaroxime, in Greater China. In addition to istaroxime, the agreement also licenses our preclinical next-generation SERCA2a activators, known as dual mechanism SERCA2a activators, and rostafuroxin, a Phase 2 product candidate for hypertension associated with specific genotypes. In addition, we are supporting the efforts of Lee's (HK) in starting a Phase 3 trial in AHF with istaroxime. Further, we are engaged in discussions regarding potential global licensing partnerships outside of Lee's (HK) territory.

On April 2, 2024, we entered into an Asset Purchase Agreement, or the Asset Purchase Agreement, with Varian Biopharmaceuticals, Inc., or Varian. Pursuant to the Asset Purchase Agreement, we purchased all of the assets of Varian's business associated with a Licence Agreement, dated as of July 5, 2019, by and between Varian and Cancer Research Technology Limited, or the Licence Agreement, including the Licence Agreement, all rights in molecules and compounds subject to the Licence Agreement, know-how and inventory of drug substance, or the Transferred Assets. The Transferred Assets include a novel, potential high-potency, specific, aPKCi with possible broad use in oncology as well as certain rare malignant diseases. The asset platform includes two formulations (topical and oral) of an aPKCi inhibitor. We plan to advance investigational new drug, or IND, enabling activities and are in the process of determining the expected clinical development plan for the platform.

We have incurred operating losses since our incorporation on November 6, 1992. For the years ended December 31, 2023 and 2022, we had operating losses of $20.6 million and $41.3 million, respectively. As of December 31, 2023, we had an accumulated deficit of $844.8 million. To date, we have financed our operations primarily through private placements and public offerings of our common and preferred stock and borrowings from investors and financial institutions. As of December 31, 2023, we had cash and cash equivalents of $4.3 million and current liabilities of $4.0 million. In April 2024, we entered into a Securities Purchase Agreement, or the Purchase Agreement, with the buyers named therein, or the Buyers, pursuant to which we agreed to sell senior convertible notes, or the Notes, for $1.5 million of gross proceeds. As a result, we believe that we have sufficient resources available to fund our business operations through April 2024.

We expect to continue to incur significant research and clinical development, regulatory and other expenses as we (i) continue to develop our product candidates; (ii) seek regulatory clearances or approvals for our product candidates; (iii) conduct clinical trials on our product candidates; and (iv) manufacture, market and sell any product candidates for which we may obtain regulatory approval.

Our ability to advance our development programs is dependent upon our ability to secure additional capital in both the near and long-term, through public or private securities offerings; convertible debt financings; and/or potential strategic opportunities, including licensing agreements, drug product development, and marketing collaboration arrangements, pharmaceutical research cooperation arrangements, and/or other similar transactions in geographic markets, including the U.S., and/or through potential grants and other funding commitments from U.S. government agencies, in each case, if available. We have engaged with potential counterparties in various markets and will continue to pursue non-dilutive sources of capital as well as potential private and public securities offerings. There can be no assurance, however, that we will be able to identify and enter into public or private securities offerings on acceptable terms and in amounts sufficient to meet our needs or qualify for non-dilutive funding opportunities under any grant programs sponsored by U.S. government agencies, private foundations, and/or leading academic institutions, or identify and enter into any strategic transactions that will provide the additional capital that we will require. If none of these alternatives is available, or if available and we are unable to raise sufficient capital through such transactions, we potentially could be forced to limit or cease our development activities, which would have a material adverse effect on our business, financial condition, and results of operations (See the section titled, "Liquidity and Capital Resources").

REVERSE STOCK SPLIT

On February 22, 2023, we filed an amendment to our Amended and Restated Certificate of Incorporation to implement a 1-for-50 reverse split stock of our issued and outstanding common stock. The reverse stock split of our outstanding common stock was effected at a ratio of 1 post-split share for every 50 pre-split shares as of 12:01 a.m. Eastern Time on February 24, 2023. The reverse stock split correspondingly adjusted the per share exercise price and the number of shares issuable upon the exercise of all outstanding options and the per share exercise price of all outstanding options and all shares underlying any of our outstanding warrants by reducing the conversion ratio for each outstanding warrant and increasing the applicable exercise price or conversion price in accordance with the terms of each outstanding warrant and based on the reverse stock split ratio. No fractional shares were issued in connection with the reverse stock split. The number of shares of common stock authorized under our Amended and Restated Certificate of Incorporation is unchanged at 120 million shares. The accompanying consolidated financial statements reflect the 1-for-50 reverse split of our common stock. All share and per share information data herein that relates to our common stock prior to the effective date has been retroactively restated to reflect the reverse stock split.

RECENT DEVELOPMENTS

Asset Purchase Agreement

On April 2, 2024, we entered into the Asset Purchase Agreement with Varian. Pursuant to the Asset Purchase Agreement, we purchased all of the assets of Varian's business associated with the Licence Agreement, including the Licence Agreement, all rights in molecules and compounds subject to the Licence Agreement, know-how and inventory of drug substance, or the Transferred Assets. We also assumed all liabilities arising on or after April 2, 2024, relating to the research, development, manufacturing, registration, commercialization, use, handling, supply, storage, import, export or other disposition or exploitation of any and all products associated with the Transferred Assets.

In consideration of the purchase of the Transferred Assets, (i) on April 2, 2024, we issued a total of 5,500 shares of our Series B Convertible Preferred Stock, par value $0.001 per share, or the Series B Preferred Stock, to certain creditors of Varian and (ii) agreed to pay up to $2.3 million in milestone payments upon the achievement of certain regulatory and clinical development milestones with our option to pay such milestone payments either in cash or our common stock.

For additional details on the terms of the Series B Preferred Stock, see the section titled, "Liquidity and Capital Resources – Series B Preferred Stock."

Securities Purchase Agreement and Convertible Notes

On April 2, 2024, we entered into the Purchase Agreement with the Buyers. Pursuant to the Purchase Agreement, we agreed to sell the Notes for $1.5 million of gross proceeds. The Notes have an initial conversion price of $0.3603, which is subject to adjustment upon the occurrence of specified events to no lower than $0.0721, subject to any stock split, stock dividend, stock combination, recapitalization or other similar transaction involving our common stock.

For additional details on the terms of the Notes, see the section titled, "Liquidity and Capital Resources – Convertible Notes."

Nasdaq Compliance

At a special meeting of stockholders held on April 10, 2024, our stockholders approved a proposal to amend our Amended and Restated Certificate of Incorporation, or Certificate of Incorporation, to effect a reverse stock split of our outstanding shares of common stock, par value $0.001 per share by a ratio of any whole number between 1-for-5 and 1-for-25, the implementation and timing of which is subject to the discretion of our Board of Directors. Given that the reverse stock split is not yet effective, the share and per share information reflected in this Annual Report on Form 10-K have not yet been adjusted to reflect the reverse stock split.

RESULTS OF OPERATIONS

Comparison of Years Ended December 31, 2023 and 2022

(in thousands)	Year Ended December 31, 2023	2022	Change
Expenses:			
Research and development	$ 8,341	$ 11,099	$ (2,758)
General and administrative	9,198	10,790	(1,592)
Loss on impairment of goodwill	3,058	12,624	(9,566)
Loss on impairment of intangible assets	-	6,820	(6,820)
Total operating expenses	20,597	41,333	(20,736)
Operating loss	(20,597)	(41,333)	20,736
Other income (expense):			
Interest income	325	109	216
Interest expense	(50)	(53)	3
Other income, net	31	702	(671)
Total other income, net	306	758	(452)
Loss before income taxes	(20,291)	(40,575)	20,284
Deferred income tax benefit	-	1,367	(1,367)
Net loss	$ (20,291)	$ (39,208)	$ 18,917

Net Loss

Our net loss was $20.3 million and $39.2 million, respectively, for the years ended December 31, 2023 and 2022. Included in our net loss for the year ended December 31, 2023 is a non-cash loss on impairment of goodwill of $3.1 million. Included in our net loss for the year ended December 31, 2022 are a non-cash loss on impairment of goodwill of $12.6 million, a non-cash loss on impairment of intangible assets related to rostafuroxin of $6.8 million and a related $1.4 million deferred income tax benefit.

Research and Development Expenses

Our research and development expenses are charged to operations as incurred and we incur both direct and indirect expenses for each of our programs. We track direct research and development expenses by preclinical and clinical programs, which include third-party costs such as CROs, CMOs, contract laboratories, consulting, and clinical trial costs. We do not allocate indirect research and development expenses, which include product development and manufacturing expenses and clinical, medical, and regulatory operations expenses, to specific programs. We also account for research and development and report annually by major expense category as follows: (i) contracted services; (ii) salaries and benefits; (iii) rents and utilities; (iv) stock-based compensation; (v) depreciation; and (vi) other. We expect that our research and development expenses related to istaroxime – cardiogenic shock program will continue to increase to the extent that we continue the SEISMiC Extension trial of istaroxime for the treatment of early cardiogenic shock and start-up procedures for a small study in more severe SCAI Stage C cardiogenic shock. We currently do not have sufficient capital to fully complete these clinical trials. At this time, we cannot reasonably estimate or know the nature, timing, and estimated costs of the efforts that will be necessary to complete the development of our product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from sales of our product candidates.

Research and development expenses for the years ended December 31, 2023 and 2022 are as follows:

(in thousands)	Year Ended December 31, 2023	2022	Increase (Decrease)
Istaroxime - cardiogenic shock program	$ 3,731	$ 3,318	$ 413
Istaroxime - AHF	71	764	(693)
KL4 surfactant	(61)	300	(361)
Total direct clinical and preclinical programs	3,741	4,382	(641)
Product development and manufacturing	960	2,480	(1,520)
Clinical, medical, and regulatory operations	3,640	4,237	(597)
Total research and development expenses	$ 8,341	$ 11,099	$ (2,758)

Research and development expenses include non-cash charges associated with stock-based compensation and depreciation of $0.4 million and $1.2 million, respectively, for 2023 and 2022.

Direct Clinical and Preclinical Programs

Direct clinical and preclinical programs include: (i) activities associated with conducting clinical trials, including patient enrollment costs, clinical site costs, clinical drug supply, and related external costs, such as consultant fees and expenses; and (ii) development activities, toxicology studies, and other preclinical studies.

Total direct clinical and preclinical programs expenses decreased $0.6 million from 2022 to 2023 primarily due to decreases in expenses in our istaroxime – AHF costs and KL4 surfactant costs, partially offset by an increase in istaroxime – cardiogenic shock program costs as described below.

Istaroxime – cardiogenic shock program costs increased $0.4 million from 2022 to 2023 due to (i) the start-up procedures for the small study in more severe SCAI Stage C cardiogenic shock, which began in the second quarter of 2023; and (ii) the trial execution costs for the SEISMiC Extension study, which was initiated during the third quarter of 2023, and in which the first patient was enrolled in the fourth quarter of 2023; partially offset by (iii) the SEISMiC study, which was completed in mid-2022.

Istaroxime – AHF costs decreased $0.7 million from 2022 to 2023 due to focusing our resources on the start-up and initiation of the SEISMiC Extension study.

KL4 surfactant costs decreased $0.4 million from 2022 to 2023 due to the completion of enrollment in January 2022 of our Phase 2b study of lucinactant for patients with severe COVID-19 associated acute respiratory distress syndrome. Costs related to the KL4 surfactant platform are expected to continue to decrease as we complete close-out activities on prior KL4 surfactant platform clinical trials and focus our resources on the development of our istaroxime pipeline.

Product Development and Manufacturing

Product development and manufacturing includes (i) manufacturing operations, with our CMO, validation activities, quality assurance; and (ii) pharmaceutical and manufacturing development activities of our drug product candidates, including development of istaroxime. These costs include employee expenses, facility-related costs, depreciation, costs of drug substances (including raw materials), supplies, quality assurance activities, and expert consultants and outside services to support pharmaceutical development activities.

Product development and manufacturing expenses decreased $1.5 million from 2022 to 2023 due to (i) headcount reductions of $0.5 million; (ii) a decrease of $0.5 million related to our decision in January 2022 to begin reducing costs associated with the KL4 surfactant platform including analytical testing and support; (iii) $0.4 million in accelerated depreciation following the abandonment and decommissioning of certain manufacturing and laboratory equipment assets related to the KL4 surfactant platform during the first quarter of 2022; and (iv) a decrease of $0.1 million in non-cash stock-based compensation expense.

Clinical, Medical, and Regulatory Operations

Clinical, medical, and regulatory operations include medical, scientific, preclinical and clinical, regulatory, data management, and biostatistics activities in support of our research and development programs. These costs include personnel, expert consultants, outside services to support regulatory and data management, symposiums at key medical meetings, facilities-related costs, and other costs for the management of clinical trials.

Clinical, medical, and regulatory operations expenses decreased $0.6 million from 2022 to 2023 due to (i) a decrease of $1.4 million in personnel costs related to reductions in headcount for the KL4 surfactant platform; and (ii) a decrease of $0.3 million in non-cash stock-based compensation expense related to headcount reductions as well as the timing of the stock-based compensation grants that were granted in the first quarter of 2022 compared to the third quarter of 2023; partially offset by (iii) a $1.1 million change in royalty expense relating to $0.9 million in accrued payments to Philip Morris USA Inc., or PMUSA, and Philip Morris Products S.A., or PMPSA, in 2023 related to amendments to our license agreements and a reversal of royalty expense in 2022 after entering into an outlicensing agreement under which the licensee had agreed to assume certain of our obligations under the PMUSA and PMPSA license agreements (See the section titled, “Note 9 – Other Current Liabilities”).

Research and Development Expense by Major Expense Category

We also account for our research and development expense by major expense category as shown in the following table:

(in thousands)	Year Ended December 31, 2023	2022	Increase (Decrease)
Contracted services	$ 3,904	$ 5,252	$ (1,348)
Salaries and benefits	2,450	3,985	(1,535)
Royalties	900	(200)	1,100
Rents and utilities	445	478	(33)
Stock-based compensation	383	807	(424)
Depreciation	30	457	(427)
Other	229	320	(91)
Total research and development expenses	$ 8,341	$ 11,099	$ (2,758)

Contracted services include third-party costs of preclinical studies, clinical trial activities, quality control and analytical stability and release testing of our drug products, and consulting services. The decrease of $1.3 million from 2022 to 2023 is primarily due to (i) a decrease in consulting services related to clinical operations as a part of our cost reduction initiatives; (ii) a decrease in costs related to analytical and technical support laboratories, both in-house and external, that previously supported the KL4 surfactant platform; and (iii) a decrease in outside services related to the SEISMiC study which was completed in mid-2022.

The $1.5 million decrease in salaries and benefits expense from 2022 to 2023 is primarily due to reductions in headcount that previously supported the KL4 surfactant platform as well as certain other headcount reductions.

Historically, royalties represented minimum royalties in connection with licensing agreements with PMUSA and PMPSA. In 2023, we accrued payments of $0.9 million to PMUSA and PMPSA related to amendments to our license agreements. In 2022, we reversed $0.2 million in royalty expense after entering into an outlicensing agreement under which the licensee had agreed to assume certain of our obligations under the PMUSA and PMPSA license agreements (See the section titled, “Note 9 – Other Current Liabilities”).

The $0.4 million decrease in stock-based compensation expense from 2022 to 2023 is related to implementing certain reductions in headcount in 2023. The decrease is also due to the timing of the stock-based compensation grants that were granted in the first quarter of 2022 compared to the third quarter of 2023.

The $0.4 million decrease in depreciation expense from 2022 to 2023 is primarily due to $0.4 million of accelerated depreciation expense in 2022 related to the abandonment and decommissioning of certain manufacturing and laboratory equipment assets related to the KL4 surfactant platform.

Other consists primarily of ongoing research and development costs such as insurance, taxes, education and training, and software licenses.

Research and Development Projects

A substantial portion of our cumulative losses to date relate to investments in our research and development projects, for which we incurred $19.4 million in expenses during the two-year period ended December 31, 2023. Due to the significant risks and uncertainties inherent in the clinical development and regulatory approval processes, the nature, timing and costs of the efforts necessary to complete individual projects in development are not reasonably estimable. With every phase of a development project, there are unknowns that may significantly affect cost projections and timelines. In view of the number and nature of these factors, many of which are outside our control, the success, timing of completion and ultimate cost of development of any of our product candidates are highly uncertain and cannot be estimated with any degree of certainty. In addition to the risks and uncertainties affecting our research and development projects discussed in this MD&A (See the section titled, “Item 1A – Risk Factors”), other risks could arise that we may not foresee that could affect our ability to estimate projections and timelines.

Ultimately, if we do not successfully develop and gain marketing approval for our drug product candidates, in the U.S. or elsewhere, we will not be able to commercialize, or generate any revenues from the sale of our products and the value of our company and our financial condition and results of operations will be substantially harmed.

General and Administrative Expenses

General and administrative expenses consist of costs for executive management, business development, intellectual property, finance and accounting, legal, insurance, human resources, information technology, facilities, and other administrative costs.

General and administrative expenses include non-cash charges associated with stock-based compensation of $0.9 million and $2.3 million, respectively, for the years ended December 31, 2023 and 2022. General and administrative expenses decreased $1.6 million from 2022 to 2023 due to (i) a decrease of $1.4 million in non-cash stock-based compensation expense related to implementing certain headcount reductions in 2023 as well as the timing of the stock-based compensation grants that were granted in the first quarter of 2022 compared to the third quarter of 2023; (ii) a decrease of $0.6 million in personnel costs due to headcount reductions; and (iii) a decrease of $0.4 million in insurance costs; partially offset by (iv) an increase of $0.4 million in professional fees; and (v) an increase of $0.4 million in severance expense related to a former executive.

Other Income (Expense), Net

Interest income relates to income on our money market funds.

Interest expense consists of interest expense associated with loans payable.

Other income, net in 2022 primarily consists of $0.7 million in gains on foreign currency translation.

LIQUIDITY AND CAPITAL RESOURCES

We are subject to risks common to companies in the biotechnology industry, including but not limited to, the need for additional capital, risks of failure of preclinical and clinical studies, the need to obtain marketing approval and reimbursement for any drug product candidate that we may identify and develop, the need to successfully commercialize and gain market acceptance of our product candidates, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development of technological innovations by competitors, and risks associated with our international operations in Taiwan and activities abroad, including but not limited to having foreign suppliers, manufacturers, and clinical sites in support of our development activities.

We have incurred net losses since inception. Our net loss was $20.3 million and $39.2 million, respectively, for the years ended December 31, 2023 and 2022. Included in our net loss for the year ended December 31, 2023 is a non-cash loss on impairment of goodwill of $3.1 million. Included in our net loss for the year ended December 31, 2022 are a non-cash loss on impairment of goodwill of $12.6 million, a non-cash loss on impairment of intangible assets related to rostafuroxin of $6.8 million and a related $1.4 million deferred income tax benefit (See the section titled, "Note 4 – Accounting Policies"). We expect to continue to incur operating losses for at least the next several years. As of December 31, 2023, we had an accumulated deficit of $844.8 million. Our future success is dependent on our ability to fund and develop our product candidates, and ultimately upon our ability to attain profitable operations. We have devoted substantially all of our financial resources and efforts to research and development and general and administrative expense to support such research and development. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital, and accordingly, our ability to execute our future operating plans.

On November 9, 2023, we entered into an At-The-Market Offering Agreement with Ladenburg Thalmann & Co. Inc., or Ladenburg, pursuant to which we may offer and sell, from time to time at our sole discretion, shares of our common stock through Ladenburg as agent and/or principal (subject to the limitations of General Instruction I.B.6 of Form S-3) through an at-the-market program, or the 2023 ATM Program (See the section titled, "Note 11 – Mezzanine Equity and Stockholders' Equity").

The shares of common stock we may issue or sell under the 2023 ATM Program are registered under our Registration Statement on Form S-3 (File No. 333-261878), which was declared effective by the SEC on January 3, 2022. We are currently subject to the limitations contained in General Instruction I.B.6 of Form S-3. As a result, we are limited to selling no more than one-third of the aggregate market value of the equity held by non-affiliates, or the public float, during any 12-month period, and, as of April 16, 2024, we had sold substantially all we are permitted to sell under the Form S-3 pursuant to General Instruction I.B.6. If our public float increases, we will have additional availability under such limitations, and if our public float increases to $75 million or more, we will no longer be subject to such limitations. There can be no assurance that our public float will increase or that we will no longer be subject to such limitations.

During the fourth quarter of 2023, we sold 848,367 shares of our common stock under the 2023 ATM Program resulting in aggregate gross and net proceeds to us of approximately $0.8 million. During the first quarter of 2024, we sold 2,576,153 shares of our common stock under the 2023 ATM Program resulting in aggregate gross and net proceeds to us of approximately $1.4 million.

As of December 31, 2023, we had cash and cash equivalents of $4.3 million and current liabilities of $4.0 million. In April 2024, we entered into the Purchase Agreement pursuant to which we agreed to sell the Notes for $1.5 million of gross proceeds. As a result, we believe that we have sufficient resources available to fund our business operations through April 2024. We do not have sufficient cash and cash equivalents as of the date of this Annual Report on Form 10-K to support our operations for at least the 12 months following the date that the financial statements are issued. These conditions raise substantial doubt about our ability to continue as a going concern.

To alleviate the conditions that raise substantial doubt about our ability to continue as a going concern, management plans to secure additional capital, potentially through a combination of public or private securities offerings, convertible debt financings, and/or strategic transactions, including potential licensing arrangements, alliances, and drug product collaborations focused on specified geographic markets; however, none of these alternatives are committed at this time. There can be no assurance that we will be successful in obtaining sufficient funding on terms acceptable to us to fund continuing operations, if at all, or identify and enter into any strategic transactions that will provide the capital that we will require. The failure to obtain sufficient additional capital on acceptable terms when needed would have a material adverse effect on our business, results of operations, and financial condition. Accordingly, management has concluded that substantial doubt exists with respect to our ability to continue as a going concern for at least 12 months after the issuance of the accompanying financial statements.

The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the normal course of business, and do not include any adjustments relating to recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might be necessary should we be unable to continue as a going concern.

Series B Preferred Stock

The terms of the Series B Preferred Stock are as set forth in the Series B Certificate of Designation of Series B Preferred Stock, as filed with the Delaware Secretary of State and effective on April 3, 2024. The Series B Preferred Stock has an initial conversion price of $0.3603, or the Preferred Conversion Price, which is subject to adjustment as provided in the Series B Certificate of Designation to no lower than $0.0721. The Series B Preferred Stock has a stated value of $1,000 per share, or the Stated Value, which equal to an aggregate Stated Value of $5,500,000 as of April 2, 2024. Each share of Series B Preferred Stock is initially convertible into 15,265 shares of our common stock, subject to adjustment as provided in the Series B Certificate of Designation. No fractional shares will be issued upon conversion; rather any fractional share will be rounded up to the nearest whole share.

From and after April 2, 2024, each holder of a share of Series B Preferred Stock is entitled to receive dividends, or Dividends, which are computed on the basis of a 360-day year and twelve 30-day months and will increase the Stated Value of the Series B Preferred Stock on each dividend date (as defined in the Series B Certificate of Designation).

Dividends on the Series B Preferred Stock will accrue at 10.0% per annum, or the Dividend Rate, and be payable by way of inclusion of the Dividends in the Conversion Amount (as defined in the Series B Certificate of Designation) on each Conversion Date (as defined in the Series B Certificate of Designation) in accordance with the Series B Certificate of Designation or upon any redemption in accordance with the Series B Certificate of Designation or upon any required payment upon any Bankruptcy Triggering Event (as defined in the Series B Certificate of Designation). From and after the occurrence and during the continuance of any Triggering Event (as defined in the Series B Certificate of Designation), the Dividend Rate will automatically be increased to 18.0% per annum.

The Preferred Conversion Price is subject to adjustment upon the occurrence of specified events and subject to price-based adjustment in the event of any stock split, stock dividend, stock combination, recapitalization or other similar transaction involving our common stock at a price below the then-applicable Preferred Conversion Price, as described in further detail in the Series B Certificate of Designation.

Convertible Notes

On April 2, 2024, we entered into the Purchase Agreement with the Buyers. Pursuant to the Purchase Agreement, we agreed to sell the Notes for $1.5 million of gross proceeds. The Notes have an initial conversion price of $0.3603, which is subject to adjustment upon the occurrence of specified events to no lower than $0.0721, subject to any stock split, stock dividend, stock combination, recapitalization or other similar transaction involving our common stock.

The Notes will be senior obligations of the Company. The Notes will accrue interest at a rate of 10.0% per annum, payable in arrears on the first calendar day of each calendar month, beginning on May 2, 2024, unless an event of default has occurred, upon which interest will accrue at 18.0% per annum. The Notes mature on January 2, 2025 unless earlier converted or redeemed (upon the satisfaction of certain conditions).

We may, subject to certain conditions, redeem all, but not less than all, of the amount then remaining under the Notes in cash at a premium of 20% of the greater of (i) the amount then outstanding under the Notes, and (ii) the equity value of our common stock underlying the Notes, which is calculated using the greatest closing sale price of our common stock on any trading day during the period commencing on the date of notice of such redemption and ending on the date we make the entire payment required pursuant to the Purchase Agreement. The Notes can also be redeemed by us under various other circumstances, such as a change of control, events of default, or at the option of the Buyer under limited circumstances, with any such redemption subject to the terms and conditions as set forth in the Notes.

The Notes contain certain conversion limitations, providing that no conversion may be made if, after giving effect to the conversion, the holder, together with any of its affiliates, would own in excess of 4.99% of our outstanding shares of common stock.

The Notes contain certain customary affirmative and negative covenants regarding the incurrence of indebtedness, the existence of liens, the repayment of indebtedness, the payment of cash in respect of dividends, distributions or redemptions and the transfer of assets, among other matters. The Notes also contain certain customary events of default, including, among other things, the failure to file and maintain an effective registration statement covering the certain registrable securities, subject to certain exceptions.

We agreed to seek stockholder approval for the issuance of all of the shares of common stock issuable upon conversion of the Notes and the Series B Preferred Stock in accordance with the rules and regulations of the Nasdaq Stock Market.

We additionally agreed that, subject to certain exceptions, without the consent of the holders holding at least a majority of our common stock underlying the Series B Preferred Stock and our common stock underlying the Notes for the Restricted Period, neither we nor our subsidiaries shall directly or indirectly issue, offer, sell, grant any option or right to purchase, or otherwise dispose of (or announce any issuance, offer, sale, grant of any option or right to purchase or other disposition of) any equity security or any equity-linked or related security (including, without limitation, any equity security (as that term is defined under Rule 405 promulgated under the Securities Act of 1933, as amended), any Convertible Securities (as defined in the Purchase Agreement), any debt, any preferred stock or any purchase rights) (any such issuance, offer, sale, grant, disposition or announcement (whether occurring during the Restricted Period or at any time thereafter) is referred to as a Subsequent Placement).

Subject to the limitations described in the Purchase Agreement, for so long as the Notes are outstanding, we will be prohibited from effecting or entering into an agreement to effect any Subsequent Placement involving a Variable Rate Transaction (as defined in the Purchase Agreement). Additionally, the Purchase Agreement contains a participation right, which provides that, subject to certain exceptions, at any time on or prior to the fourth anniversary of April 2, 2024, neither we nor our subsidiaries shall, directly or indirectly, effect any Subsequent Placement unless we comply with the notice procedures as outlined in the Purchase Agreement with respect to each Buyer, providing the opportunity for such Buyer to participate in such Subsequent Placement on a pro rata basis as described in the Purchase Agreement.

Cash Flows

Cash flows for the years ended December 31, 2023 and 2022

Net cash outflows for 2023 consist of $13.4 million net cash used in operating activities and $11.6 million of net cash provided by financing activities. Net cash outflows for 2022 consist of $19.5 million net cash used in operating activities, $0.2 million of net cash provided by investing activities, and $3.1 million of net cash provided by financing activities.

Operating Activities

Net cash used in operating activities was $13.4 million for the year ended December 31, 2023 and consisted primarily of (i) a net loss of $20.3 million; partially offset by (ii) a non-cash loss on impairment of goodwill of $3.1 million; (iii) a non-cash stock-based compensation expense of $1.3 million; (iv) changes in operating assets and liabilities of $2.0 million; (v) a non-cash lease expense of $0.4 million; and (vi) depreciation and amortization of $0.1 million. Changes in prepaid expenses and other current assets, accounts payable, accrued expenses, and operating lease liabilities result from timing differences between the receipt and payment of cash and when the transactions are recognized in our results of operations.

Net cash used in operating activities was $19.5 million for the year ended December 31, 2022 and consisted primarily of (i) a net loss of $39.2 million; (ii) changes in operating assets and liabilities of $1.8 million; (iii) a non-cash deferred income tax benefit of $1.4 million; and (iv) an unrealized gain on foreign exchange rate changes of $0.7 million; partially offset by (v) a non-cash loss on impairment of goodwill of $12.6 million; (vi) a non-cash loss on impairment of intangible assets of $6.8 million; (vii) a non-cash stock-based compensation expense of $3.1 million; (viii) depreciation and amortization of $0.5 million; and (ix) a non-cash lease expense of $0.5 million. Changes in prepaid expenses and other current assets, accounts payable, accrued expenses, and operating lease liabilities result from timing differences between the receipt and payment of cash and when the transactions are recognized in our results of operations.

Investing Activities

Net cash provided by investing activities was $0.2 million for the year ended December 31, 2022 and primarily includes proceeds from sale of property and equipment related to the decommissioning and sale of certain manufacturing and laboratory equipment assets previously used for the KL4 surfactant platform. There was a de minimis amount of net cash used in investing activities for the year ended December 31, 2023.

Financing Activities

Net cash provided by financing activities was $11.6 million and $3.1 million for the years ended December 31, 2023 and 2022, respectively, summarized as follows:

(in thousands)	Year Ended December 31, 2023	2022
Proceeds from issuance of common stock and warrants, net of issuance costs	$ 10,794	$ -
Proceeds from exercise of common stock warrants, net of expenses	843	-
Proceeds from ATM Program, net of issuance costs	755	4,253
Principal payments on loans payable	(797)	(1,174)
Net cash provided by financing activities	$ 11,595	$ 3,079

The following sections provide a more detailed discussion of our available financing facilities.

Common Stock Offerings

Historically, we have funded, and expect that we will continue to fund, our business operations through various sources, including financings in the form of common stock offerings.

April 2023 Public Offering

On April 20, 2023, we entered into an underwriting agreement with Ladenburg as the sole underwriter relating to a public offering, or the April 2023 Offering, of an aggregate of 3,686,006 units with each unit consisting of one share of common stock and a warrant, or the April 2023 Warrants. The April 2023 Warrants were immediately exercisable for shares of common stock at a price of $2.93 per share and expire five years from the date of issuance. The shares of common stock and the April 2023 Warrants were immediately separable and were issued separately in the April 2023 Offering.

In addition, Ladenburg exercised in full a 45-day option, or the Overallotment Option, to purchase up to 552,900 additional shares of common stock and/or warrants to purchase up to 552,900 additional shares of common stock.

The closing of the April 2023 Offering occurred on April 24, 2023, inclusive of the Overallotment Option. The offering price to the public was $2.93 per unit resulting in gross proceeds to us of approximately $12.4 million. After deducting underwriting discounts and commissions and other estimated offering expenses payable by us, and excluding the proceeds, if any, from the exercise of the April 2023 Warrants issued pursuant to this April 2023 Offering, the net proceeds to us were approximately $10.8 million.

At-The-Market Program

On September 17, 2020, we entered into an At-The-Market Offering Agreement with Ladenburg, or the 2020 ATM Program, pursuant to which we were able to offer and sell, from time to time at our sole discretion, up to a maximum of $10.0 million of shares of our common stock through Ladenburg as agent and/or principal through the 2020 ATM Program. For the year ended December 31, 2022, we sold 206,824 shares of our common stock under the 2020 ATM Program resulting in aggregate gross proceeds to us of approximately $4.4 million and net proceeds of approximately $4.3 million.

The shares of common stock issued and sold under the 2020 ATM Program were registered under our Registration Statement on Form S-3 (File No. 333-248874), which was declared effective by the SEC on September 29, 2020 and expired on September 29, 2023. The 2020 ATM Program was terminated by us and Ladenburg on November 9, 2023.

On November 9, 2023, we entered into an At-The-Market Offering Agreement with Ladenburg pursuant to which we may offer and sell, from time to time at our sole discretion, shares of our common stock through Ladenburg as agent and/or principal (subject to the limitations of General Instruction I.B.6 of Form S-3) through an at-the-market program, or the 2023 ATM Program. During the fourth quarter of 2023, we sold 848,367 shares of our common stock under the 2023 ATM Program resulting in aggregate gross and net proceeds to us of approximately $0.8 million (See the section titled, “Note 11 – Mezzanine Equity and Stockholders’ Equity”).

During the first quarter of 2024, we sold 2,576,153 shares of our common stock under the 2023 ATM Program resulting in aggregate gross and net proceeds to us of approximately $1.4 million.

Loans Payable

In June 2023, we entered into an insurance premium financing and security agreement with IPFS Corporation. Under the agreement, we financed $0.8 million of certain premiums at a 7.24% fixed annual interest rate. Payments of approximately $126,000 are due monthly from July 2023 through April 2024. As of December 31, 2023, the outstanding principal of the loan was $0.2 million.

In June 2022, we entered into an insurance premium financing and security agreement with Bank Direct Capital Finance. Under the agreement, we financed $1.1 million of certain premiums at a 3.90% fixed annual interest rate. Payments of approximately $126,000 were due monthly from July 2022 through March 2023. As of December 31, 2022, the outstanding principal of the loan was $0.3 million. The balance of the loan was repaid during the first quarter of 2023.

Restructured Debt Liability

On October 27, 2017, we and Deerfield Management Company, L.P., or Deerfield, entered into the Exchange and Termination Agreement, or the Milestone Agreement, pursuant to which (i) promissory notes evidencing a loan with affiliates of Deerfield in the aggregate principal amount of $25.0 million and (ii) warrants to purchase up to 167 shares of our common stock at an exercise price of $118,020.00 per share held by Deerfield were cancelled in consideration for (x) a cash payment in the aggregate amount of $2.5 million, (y) 474 shares of common stock, representing 2% of fully-diluted shares outstanding (as defined in the Milestone Agreement) on the closing date, and (z) the right to receive certain milestone payments, or Milestone Payments, based on achievement of specified AEROSURF development and commercial milestones, which, if achieved, could potentially total up to $15.0 million. In addition, a related security agreement, pursuant to which Deerfield held a security interest in substantially all of our assets, was terminated. We established a $15.0 million long-term liability for the contingent milestone payments potentially due to Deerfield under the Milestone Agreement (See the section titled, “Note 4 – Accounting Policies”). The liability has been recorded at the full value of the contingent milestones and will continue to be carried at full value until the milestones are achieved and paid or the milestones are not achieved and the liability is written off as a gain on debt restructuring.

As of December 31, 2023 and 2022, the restructured debt liability balance was $15.0 million.

On January 24, 2024, we and affiliates of Deerfield entered into an Exchange and Termination Agreement wherein Deerfield agreed to terminate its rights to receive the Milestone Payments and all related rights and obligations in respect of such Milestone Payments in exchange for (i) cash in the aggregate amount of $200,000, $100,000 of which was paid on January 24, 2024 and $100,000 of which will be paid no later than the earlier to occur of (a) January 24, 2025 and (b) us receiving a specified amount of gross proceeds from debt or equity financings occurring on or after January 24, 2024, and (ii) an aggregate of 608,272 shares of our common stock (See the section titled, “Note 18 – Subsequent Events”).

CRITICAL ACCOUNTING POLICIES AND ESTIMATES

The preceding discussion and analysis of financial condition and results of operations are based upon our Consolidated Financial Statements, which have been prepared in conformity with U.S. generally accepted accounting principles, or GAAP. Preparing financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses. Estimates are based on our historical operations, our future business plans and projected financial results, the terms of existing contracts, our observance of trends in the industry, and information available from other outside sources, as appropriate. These estimates and assumptions are affected by the application of our accounting policies. Critical accounting policies and practices are both important to the portrayal of a company's financial condition and results of operations, and require management's most difficult, subjective or complex judgments, often as a result of the need to make estimates about the effects of matters that are inherently uncertain. Actual results could differ from such estimates due to changes in economic factors or other conditions that are outside the control of management. A summary of our significant accounting policies is described in Note 4 of the Audited Consolidated Financial Statements contained in this Annual Report on Form 10-K. Of those policies, we believe that the following accounting policy is critical to aid our stockholders in fully understanding and evaluating our reported financial results.

Intangible Assets and Goodwill

We record acquired intangible assets and goodwill based on estimated fair value. The identifiable intangible assets resulting from the CVie Therapeutics acquisition in December 2018 relate to in-process research and development, or IPR&D, of istaroxime and rostafuroxin. The IPR&D assets are considered indefinite-lived intangible assets until completion or abandonment of the associated research and development efforts. IPR&D is not amortized but reviewed for impairment at least annually, or when events or changes in the business environment indicate the carrying value may be impaired.

When testing our indefinite-lived intangible assets and goodwill for impairment, we can elect to perform a qualitative assessment to determine if it is more likely than not that the fair values of our indefinite-lived intangible assets and our reporting unit are less than their respective carrying values. Such qualitative factors can include, among others, industry and market conditions, overall financial performance, and relevant entity-specific events. If we conclude based on our qualitative assessment that it is more likely than not that the fair value of our indefinite-lived intangible assets or reporting unit are less than their respective carrying values, we perform a quantitative assessment. When conducting our annual impairment test of indefinite-lived intangible assets and goodwill as of December 1, 2023 and 2022, we elected to perform a quantitative assessment.

When performing the quantitative impairment assessment for our indefinite-lived IPR&D intangible assets, we estimate the fair values of the assets using the multi-period excess earnings method, or MPEEM. MPEEM is a variation of the income approach which estimates the fair value of an intangible asset based on the present value of the incremental after-tax cash flows attributable to the intangible asset. Significant factors considered in the calculation of IPR&D intangible assets include the risks inherent in the development process, including the likelihood of achieving commercial success and the cost and related time to complete the remaining development. Future cash flows for each project were estimated based on forecasted revenue and costs, taking into account the expected product life cycles, market penetration, and growth rates. Other significant estimates and assumptions inherent in this approach include (i) the amount and timing of the projected net cash flows associated with the IPR&D assets, (ii) the discount rate, which seeks to reflect the various risks inherent in the projected cash flows; and (iii) the tax rate, which considers geographic diversity of the projected cash flows. While we use the best available information to prepare our cash flows and discount rate assumptions, actual future cash flows could differ significantly based on the commercial success of the related drug candidates and market conditions which could result in future impairment charges related to our indefinite-lived intangible asset balances.

Based on our annual quantitative impairment assessment of our indefinite-lived IPR&D intangible assets as of December 1, 2023, we concluded that the assets were not impaired.

As part of our annual quantitative impairment assessment of indefinite-lived IPR&D intangible assets as of December 1, 2022, we reassessed certain assumptions related to our rostafuroxin drug candidate due to the continued difficulties in current macroeconomic conditions which have continued to make it more challenging to secure the funding needed to conduct the additional Phase 2 clinical trial and have therefore further delayed our intended development of rostafuroxin. As a result, we concluded that the fair value of the IPR&D related to our rostafuroxin drug candidate was less than its carrying value. We estimated the fair value of the asset using MPEEM and determined that the fair value as of December 1, 2022 was approximately $2.9 million. We then compared this fair value to the carrying value of approximately $9.7 million, and recorded an additional loss on impairment of intangible assets of $6.8 million related to the IPR&D of our rostafuroxin drug candidate. We also reassessed the assumptions related to the fair value of the IPR&D related to our istaroxime drug candidate. The estimated fair value exceeded the carrying value of that asset. As a result, no impairment charge was recognized related to the IPR&D of our istaroxime drug candidate.

Goodwill represents the excess of the purchase price over the fair value of assets acquired and liabilities assumed in a business combination and is not amortized. It is reviewed for impairment at least annually or when events or changes in the business environment indicate that its carrying value may be impaired. Our company consists of one reporting unit. In order to perform the quantitative goodwill impairment test, we compare the estimated fair value of our reporting unit to its carrying value. If the fair value exceeds the carrying value, no further evaluation is required, and no impairment exists. If the carrying value exceeds the fair value, the difference between the carrying value and the fair value is recorded as an impairment loss, the amount of which may not exceed the total amount of goodwill. When performing a goodwill impairment assessment, we estimate the fair value of our reporting unit, including the use of the quoted market price and related market capitalization of our common stock, adjusted for an estimated control premium based on transactions completed by comparable companies.

In accordance with applicable accounting standards, we are required to review intangible assets and goodwill for impairment on an annual basis, or more frequently where there is an indication of impairment. Throughout the year, we consider whether any events or changes in the business environment have occurred which indicate that goodwill may be impaired. For example, a significant decline in the closing share price of our common stock and market capitalization may suggest that the fair value of our reporting unit has fallen below its carrying value, indicating that an interim goodwill impairment test is required. Accordingly, we monitor changes in our share price during interim periods between annual impairment tests and consider overall stock market conditions, the underlying reasons for the decline in our share price, the significance of the decline, and the duration of time that our securities have been trading at a lower value.

Since early 2022, we have experienced a declining trend in the closing share price of our common stock, on a split-adjusted basis. As a result, we performed the required interim goodwill impairment test in the second and third quarters of 2022 as well as the annual goodwill quantitative test as of December 1, 2022 and determined that the fair value of our reporting unit was more likely than not less than its carrying value. For the year ended December 31, 2022, we recorded an aggregate loss on goodwill of $12.6 million within operating expenses in our consolidated statement of operations.

During each of the first and second quarters of 2023, the continued declining trend in the closing share price of our common stock, on a split-adjusted basis, suggested that the fair value of our reporting unit was more likely than not less than its carrying value. As a result, in each quarter, we performed the required interim goodwill impairment test consistent with the methodology described above and determined that the fair value of our reporting unit was more likely than not less than its carrying value. We recorded a loss on impairment of goodwill of $0.5 million in the first quarter of 2023 and an additional loss of $2.6 million, representing the remaining balance of goodwill, in the second quarter of 2023. For the year ended December 31, 2023, the aggregate loss on impairment of goodwill was $3.1 million, recognized within operating expenses in our consolidated statement of operations. As of December 31, 2023, goodwill was zero on our consolidated balance sheet.

The following table represents identifiable intangible assets and goodwill as of December 31, 2023 and 2022:

(in thousands)	December 31, 2023	December 31, 2022
Istaroxime drug candidate	$ 22,340	$ 22,340
Rostafuroxin drug candidate	2,910	2,910
Intangible assets	25,250	25,250
Goodwill	$ -	$ 3,058

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing quotations and contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses are related to expenses incurred with respect to CROs, CMOs, clinical trial sites, and other vendors supporting our research and development and manufacturing activities.

We base our expenses related to CROs, CMOs, and clinical trial sites on our estimates of services received and efforts expended under quotations and contracts with those vendors that conduct research and development and manufacturing activities on our behalf. The financial terms of these agreements are negotiated, vary from contract to contract and may result in uneven payment flows. At times, payments made to our vendors may exceed the level of services provided and result in a prepayment of the applicable research and development or manufacturing expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in us reporting amounts that are too high or too low in any particular period. There have been no material changes in estimates for the periods presented.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK.

Not applicable.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA.

The information required by this Item is set forth in the financial statements and notes thereto beginning at page F-1 of this Annual Report on Form 10-K.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE.

Not applicable.

ITEM 9A. CONTROLS AND PROCEDURES.

(a) Evaluation of Disclosure Controls and Procedures

Our management, including our President and Chief Executive Officer (principal executive officer and principal financial officer), does not expect that our disclosure controls or our internal control over financial reporting will prevent all error and all fraud. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, have been detected. These inherent limitations include the realities that judgments in decision-making can be faulty and that breakdowns can occur because of simple error or mistake. Controls can also be circumvented by the individual acts of some persons, by collusion of two or more people, or by management override of the controls. The design of any system of controls is based in part on certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions. Over time, controls may become inadequate because of changes in conditions or deterioration in the degree of compliance with policies or procedures. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected. In designing and evaluating the disclosure controls and procedures, our management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives and our management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Our President and Chief Executive Officer has evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rule 13a-15(e) and Rule 15d-15(e) of the Exchange Act) as of the end of the period covered by this Annual Report on Form 10-K. Based on this evaluation, our President and Chief Executive Officer concluded that, as of the end of the period covered by this report, our disclosure controls and procedures were effective to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is accumulated and communicated to our management, including our President and Chief Executive Officer, to allow for timely decisions regarding required disclosures, and recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms.

(b) Management's Report on Internal Control over Financial Reporting

Our management, including our President and Chief Executive Officer, is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) promulgated under the Exchange Act. Our internal control system is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. All internal control systems, no matter how well designed, have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation.

Under the supervision and with the participation of our management, including our President and Chief Executive Officer, our management conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2023. In making this assessment, our management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control-Integrated 2013 Framework. Based on our assessment, our management believes that our internal control over financial reporting is effective based on those criteria, as of December 31, 2023.

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm regarding internal control over financial reporting. Management's report was not subject to attestation by our registered public accounting firm pursuant to rules of the Securities and Exchange Commission, or the SEC, that permit us to provide only management's report in this Annual Report on Form 10-K.

(c) Changes in Internal Control

There were no changes in our internal control over financial reporting identified in connection with the evaluation described above that occurred during the quarter ended December 31, 2023 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION.

None.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS.

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The following table sets forth information regarding our executive officers and directors, including their ages as of April 16, 2024:

NAME	AGE	POSITION(S)
Executive Officers		
Craig E. Fraser	59	President and Chief Executive Officer, Board Chair
Eric Curtis	56	Senior Vice President and Chief Operating Officer
Steven G. Simonson, M.D.	65	Senior Vice President and Chief Medical Officer
Non-Employee Directors		
Daniel E. Geffken	67	Director
Robert Scott, M.D.	70	Director
Mark Strobeck, Ph.D.	53	Director
Leslie J. Williams	64	Director

Information about our Executive Officers

Craig E. Fraser. Mr. Fraser has served as President and Chief Executive Officer, or CEO, and a member of the Board of Directors, or the Board, since February 1, 2016. In June 2023, Mr. Fraser was appointed to serve as Chair of the Board. He brings over 30 years of experience as a leader in drug development, fundraising, business development and commercial operations in building biopharmaceutical and device businesses for startups as well as larger companies. Prior to joining us, Mr. Fraser held executive positions at several biopharmaceutical companies, including Novelion as President and Chief Operating Officer from 2014 to 2015 and, prior to that, positions of increasing responsibility; as Vice President of Global Disease Areas at Pfizer from 2009 to 2011 and Vice President and Global Business Manager at Wyeth Pharmaceuticals from 2007 to 2009. Previously, Mr. Fraser served as Vice President, Sales & Marketing and Commercial Operations and as Vice President, Oncology Global Strategic Marketing at Johnson & Johnson; and as Gastroenterology Franchise Lead, National Sales Director - Immunology and Acute Cardiovasculars, and Marketing Director - Cardiovasculars and Diagnostics at Centocor and various sales and sales management positions prior to marketing roles. Mr. Fraser is a veteran of both the U.S. Marine Corps and the U.S. Army. Mr. Fraser does not serve on any other public company boards. Mr. Fraser received his B.S. degree in Public Administration from Slippery Rock University of Pennsylvania.

Mr. Fraser's knowledge of our business as well as his extensive leadership and biopharmaceutical industry experience provide him with the qualifications and skills to serve on our Board.

Eric Curtis. Mr. Curtis has served as our Senior Vice President and Chief Operating Officer, or COO, since March 2020. Prior to joining us, he served as Chief Executive Officer and President of Centurion BioPharma, a biopharmaceutical research and development focused company and a private subsidiary of CytRx Corporation, from June 2018 to November 2019. Mr. Curtis was primarily responsible for the company's corporate strategy, pipeline development plan and business development. Prior to that role, he was President and Chief Operating Officer of CytRx Corporation, a biopharmaceutical company focused in oncology, from February 2018 to March 2020. Mr. Curtis' responsibilities included corporate strategy, pipeline development and investor relations. Before that, Mr. Curtis was principal of Curtis Biopharm Consulting where he led his consulting business to work with the chief executive officers of several biopharmaceutical companies on refining their company's strategic product development, commercialization effectiveness and focusing resources from 2016 to February 2018. Before that, Mr. Curtis served as President, US Commercial of Aegerion Pharmaceuticals, a biopharmaceutical company from 2014 to 2016. He led the commercial organization for US, represented commercial for global business development and was the lead of commercial for investor relations strategy and execution. Mr. Curtis earned his MBA from Pennsylvania State University, and his B.S. in Business and Psychology from the University of Pittsburgh.

Steven G. Simonson, M.D. Dr. Simonson has served as our Senior Vice President and Chief Medical Officer, or CMO, since April 2017, having previously served as our Senior Vice President and Chief Development Officer from October 2014 to April 2017, and our Vice President, Clinical Development, upon joining the Company in May of 2014. Dr. Simonson brings to us over 25 years of medical practice and pharmaceutical industry clinical trial experience with a significant background in drug development, including preclinical, first time into human and phases 1-4, and IND, NDA, and sNDA experience. Dr. Simonson spent 15 years at AstraZeneca Pharmaceuticals in areas of medical and clinical leadership primarily in the pulmonary, cardiovascular, and critical care therapeutic areas. He has been involved in or led several successful IND and NDA filings. He spent the next two years as Vice President of Clinical Development at Agennix, Inc., a biopharmaceutical company primarily focused in oncology and sepsis. Dr. Simonson was also an Executive Director in the Molecule Development Group at Covance, a biopharmaceutical development services company, where he applied his experience to developing clinical development programs for small and mid-size biotech and pharmaceutical companies. Dr. Simonson completed training in internal medicine followed by a fellowship in pulmonary and critical care medicine at Duke University Medical Center. He then held several faculty appointments at Duke in the departments of Anesthesiology and Medicine, including the divisions of Pulmonary and Critical Care Medicine. He is a Fellow of the American College of Chest Physicians, and author or co-author of multiple peer reviewed publications, abstracts, posters and chapters. Dr. Simonson received his medical degree from the Medical College of Wisconsin, and his Master of Health Sciences degree in Biometry from the Duke University School of Medicine.

Non-Employee Directors

Daniel E. Geffken. Mr. Geffken has served as a member of our Board since April 24, 2019 and was also appointed Chair of the Audit Committee and as a member of the Compensation Committee. Since 2011, Mr. Geffken has been serving as the Founding Managing Partner of Danforth Advisors, a leading financial and strategy consulting firm to the life sciences industry. He has served as chief financial officer and strategic consultant to numerous companies, including Apellis Pharmaceuticals, Cidara Therapeutics, Cabaletta Bio, Homology Medicines, Stealth BioTherapeutics and Transkaryotic Therapies. Mr. Geffken has served on the Board of Elicio Bio, Alcobra Ltd. and Arcturus Inc., after its merger with Alcobra. Mr. Geffken earned his MBA from Harvard Business School, and his B.S. in Economics from the Wharton School.

Mr. Geffken's deep understanding of the industry in which we operate, in corporate financial management, and his overall business acumen and insights provide him with the qualifications and skills to serve on our Board.

Robert Scott, M.D. Dr. Scott has served as a member of our Board since February 2021. He has held leadership positions for over 30 years in the world's leading biopharma companies, including J&J, Pfizer, Amgen and AbbVie. During that time, Dr. Scott has led development teams responsible for highly successful brands such as Norvasc®, Lipitor®, Repatha®, Humira®, Skyrizi® and Rinvoq™. Prior to his recent retirement as Chief Medical Officer and Head of Development for AbbVie, a research-based global biopharmaceutical company, in April 2020, Dr. Scott was responsible for a team of over 4,000 individuals across 52 countries, a budget of nearly US$3 billion and programs involving more than 40 new molecular entities since joining in April 2016. Prior to joining AbbVie, Dr. Scott served as Vice President of Global Development for Amgen from October 2010 to February 2016, where he conducted, among other programs, heart failure development. From 2002 until 2007, he was the Chief Medical Officer and Executive Vice President of Research and Development at AtheroGenics. While there he designed and implemented the first large cardiovascular outcomes study to be wholly performed by a small biotech. Dr. Scott also worked for Pfizer, one of the world's premier biopharmaceutical companies, from 1992 to 2002. While there, he was intimately involved in many cardiovascular clinical trials. He also was integral in developing the cholesterol drug Lipitor® and Norvasc®, a drug used to treat high blood pressure. Dr. Scott has served on many committees and boards, including as a member of the FDA Cardiac and Renal Drug Advisory Committee from 2012 until 2016, the Board of Transcelerate, and as a member of the PhRMA Research and Development Leadership Forum. Dr. Scott currently serves as a director for Redx Pharma, ArisGlobal, Confo Therapeutics, Oncospherix Inc. and Draupnir Bio, where he also sits on the Remuneration Committee. Dr. Scott received his BSc in Microbiology and Biochemistry and MbChB in Medicine from the University of Cape Town.

Dr. Scott's extensive experience leading large biopharmaceutical companies through several successful product developments provides him with the qualifications and skills to serve on our Board.

Mark Strobeck, Ph.D. Dr. Strobeck has served as a member of our Board since June 2023. Dr. Strobeck has served as the President and Chief Executive Officer, and as a member of the board of directors, of Rockwell Medical, Inc., a biopharmaceutical company, since July 2022. Dr. Strobeck served as Managing Director of Aquilo Partners, LP, a life sciences investment bank, from May 2021 to June 2022. He previously served as Executive Vice President and Chief Operating Officer of Assertio Holdings, Inc., a pharmaceutical company, from May 2020 to December 2020. Prior to that, Dr. Strobeck was Executive Vice President and Chief Operating Officer of Zyla Life Sciences, a pharmaceutical company, from September 2015 through its merger with Assertio Holdings, Inc. in May 2020, and previously served as Zyla's Chief Business Officer from January 2014 to September 2015. Before his employment at Zyla, he served as Zyla's advisor from June 2012 to December 2013. From January 2012 to December 2013, he served as President and Chief Executive Officer and as a director of Corridor Pharmaceuticals, Inc., a pharmaceuticals company, which was acquired by AstraZeneca plc in 2014. From December 2010 to October 2011, Dr. Strobeck served as Chief Business Officer of Topaz Pharmaceuticals Inc., a specialty pharmaceutical company acquired by Sanofi Pasteur in 2011. From June 2010 to November 2010 and October 2011 to January 2012, Dr. Strobeck worked as a consultant. From January 2008 to May 2010, Dr. Strobeck served as Chief Business Officer of Trevena, Inc., a pharmaceutical company. Prior to joining Trevena, Dr. Strobeck held management roles at GlaxoSmithKline plc, a pharmaceuticals company, and venture capital firms SR One Limited and EuclidSR Partners, L.P. Dr. Strobeck currently serves on the board of directors of Horse Power For Life, a nonprofit organization dedicated to improving the quality of life for individuals diagnosed with cancer, a position he has held since 2012. Dr. Strobeck received his B.S. in Biology from St. Lawrence University in 1993 and his Ph.D. in Pharmacology and Biophysics from the University of Cincinnati in 1999 and completed his post-doctoral fellowship in Cardiovascular Gene Regulation at the University of Pennsylvania School of Medicine in 2001.

Dr. Strobeck's experience within the biopharmaceutical industry and his public company experience provide him with the qualifications and skills to serve on our Board.

Leslie J. Williams. Ms. Williams has served as a member of our Board since February 2021. She is a 25-year biopharmaceutical veteran and is an experienced biotech chief executive officer and board of directors' member. She has experience in healthcare, management, commercial product development and marketing. In 2021, she founded hC Bioscience, Inc., a discovery stage biotech company, and serves as Director, President and Chief Executive Officer. Prior to this, she spent 10 years at ImmusanT, Inc., a clinical stage biotechnology company, and she served as Director, President & Chief Executive Officer of ImmusanT until 2019. Prior to that, she was President and Chief Executive Officer of Ventaira Pharmaceuticals since 2004 and under her leadership the company became a significant player in the pulmonary drug-delivery market until it was sold at the end of 2007. Prior to Ventaira, Ms. Williams was director of marketing for INO Therapeutics, Inc. and additional experience includes commercial positions at Merck and GSK, and drug-delivery and -monitoring experience at Datex-Ohmeda (formerly Ohmeda, Inc.). She was a venture partner at Battelle Ventures where she sourced and evaluated deals and assisted early-stage technology companies with strategy, management, business development and M&A. She has served on several private, public and non-profit boards. In addition to serving as Chief Executive Officer at hC Bioscience, she serves on the Board of Ocular Therapeutix since 2019, Life Science Leader since 2011, CSCRI since 2018, and Life Science Cares since 2017. Ms. Williams holds an MBA from Washington University, John Olin School of Business, and a B.S. degree with honors in nursing from the University of Iowa. Before entering industry, she was a critical-care nurse at Duke University, Medical College of Virginia and at the University of Iowa.

Ms. Williams' insight into the biotechnology industry and experience and familiarity with public life science company boards provide her with the qualifications and skills to serve on our Board.

Family Relationships

There are no family relationships among our directors and executive officers.

Board Leadership Structure

Our Board is currently composed of four members. In accordance with our Amended and Restated By-Laws, or By-Laws, each director is elected at our Annual Meeting of Stockholders. Each director holds office until our next Annual Meeting of Stockholders and until his or her successors have been duly elected and qualified, or until such director's death, or until such director shall have resigned, or have been removed.

We believe that the Board should remain free to configure the leadership of the Board and the Company in a way that best serves the interests of the Company and its stockholders at the time and, accordingly, has no fixed policy with respect to combining or separating the offices of the Chairman of the Board and the CEO.

Role of Board in Risk Oversight

One of the key functions of our Board is to oversee our risk management process. Our Board does not have a standing risk management committee, but rather administers this oversight function directly through our Board as a whole, as well as through various standing committees of our Board that address the risks inherent in their respective areas of oversight. In particular, our Board is responsible for monitoring and assessing strategic risk exposure and our Audit Committee has the responsibility to consider and discuss our major financial risk exposures and the steps our management has taken to monitor and control these exposures, including guidelines and policies to govern the process by which risk assessment and management is undertaken. While our Board maintains the ultimate oversight responsibility for the risk management process, its committees oversee risk in certain specified areas. For example:

- Our Audit Committee oversees management of financial reporting, compliance and litigation risks, including risks related to our insurance, information technology, human resources and regulatory matters, as well as the steps management has taken to monitor and control such exposures.

- Our Compensation Committee is responsible for overseeing the management of risks relating to our executive compensation policies, plans and arrangements and the extent to which those policies or practices increase or decrease risks for our company.

- Our Nominating and Corporate Governance Committee manages risks associated with the independence of our Board, potential conflicts of interest and the effectiveness of our Board.

Director Independence

Our Board has undertaken a review of its composition, the composition of its committees and the independence of each director. Based upon information provided by each director, our Board has determined that each of our directors, and directors whom have served on our Board since the beginning of the 2023 fiscal year, with the exception of Mr. Fraser, does or did not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and is independent under the listing rules of Nasdaq. In making these determinations, our Board considered the current and prior relationships that each non-employee director has with our company and all other facts and circumstances our Board deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director, and the transactions involving them described in "Item 13—Certain Relationships and Related Party Transactions."

Board Committees

Our Board has established an Audit Committee, a Compensation Committee and a Nominating and Corporate Governance Committee. The composition and responsibilities of each of the committees of our Board is described below. Members will serve on these committees until their resignation or until as otherwise determined by our Board.

Audit Committee

Our Audit Committee consists of Mr. Geffken, Ms. Williams, and Dr. Strobeck, with Mr. Geffken serving as Chair of our Audit Committee.

The primary purpose of the Audit Committee is to assist the Board in fulfilling its oversight responsibilities relating to our accounting, reporting and financial practices, and our compliance with all related legal and regulatory requirements, including, but not limited to, oversight of:

- the appointment, retention and compensation of the Company's independent auditor;
- the maintenance by management of the reliability and integrity of the Company's accounting policies, financial reporting and disclosure practices, and tax compliance;
- the establishment and maintenance by management of processes to ensure that an adequate system of internal control is functioning within the Company; and
- the establishment and maintenance by management of processes to ensure compliance by the Company with all applicable laws, regulations and Company policy.

In addition, the Audit Committee is responsible for, among other things, the appointment, compensation and oversight of the work of our independent auditor or any registered public accounting firm engaged (including resolution of disagreements between management and the auditor regarding financial reporting), reviewing the range and cost of audit and non-audit services performed by our independent auditor, reviewing the adequacy of our systems of internal control, and reviewing all related party transactions. In discharging its role, the Audit Committee is empowered to investigate any matter brought to its attention and has full access to all the Company's books, records, facilities and personnel. The Audit Committee also has the power to retain such legal, accounting and other advisors as it deems necessary to carry out its duties.

The Board has adopted a written Audit Committee Charter. The composition and responsibilities of the Audit Committee and the attributes of its members, as reflected in its Charter, are intended to be in accordance with certain listing requirements of Nasdaq and the rules of the SEC for corporate audit committees. The Audit Committee Charter may be found on our website at www.windtreetx.com. All members of our Audit Committee are "independent" as defined in Rule 5605(a)(2) of the Nasdaq Listing Rules and the financial sophistication requirements of the SEC rules. The Board has determined that Mr. Geffken is an "audit committee financial expert" as defined under SEC rules.

Compensation Committee

Our Compensation Committee consists of Mr. Geffken, Dr. Scott, and Dr. Strobeck, with Dr. Scott serving as Chair of our Compensation Committee. Each member of the Compensation Committee (i) meets the requirements for independence under the current Nasdaq Listing Rules, and (ii) is a non-employee director, as defined by Rule 16b-3 promulgated under the Securities Exchange Act of 1934, as amended, or the Exchange Act.

The Compensation Committee is responsible for, among other things:

- reviewing management of the Company's policies regarding compensation policies relating to executive and general compensation;
- reviewing and approving corporate goals and objectives relating to the composition of our CEO, executive officers, and other senior officers, evaluate performance of executive officers and other senior officers and determine the CEO's and other executive officers' compensation level based on the Compensation Committee's evaluation;
- reviewing, approving, and establishing guidelines for the Board; and
- overseeing the key employee benefits programs, policies and plans relating to the compensation, benefits and equity incentives of the Company's executives and, where deemed appropriate by the Compensation Committee, those programs, policies and plans relating to the Company's other employees.

The Board has adopted a written Compensation Committee Charter. The composition and responsibilities of the Compensation Committee, as reflected in its Charter, satisfy the applicable rules of the SEC and the listing requirements of Nasdaq. The Compensation Committee Charter may be found on our website at www.windtreetx.com.

In the past, our Compensation Committee has delegated authority to our CEO to grant options or other stock awards, in accordance with guidelines established by the Compensation Committee in consultation with our compensation consultant, to certain non-executive officers. Our Compensation Committee also has the authority to form and delegate authority to one or more subcommittees as it deems appropriate from time to time under the circumstances.

Our CEO annually reviews the performance of each of the other executive officers, including the other named executive officers. He then recommends annual merit salary adjustments and any changes in annual or long-term incentive opportunities for other executives. The Compensation Committee considers our CEO's recommendations in addition to data and recommendations presented by our executive compensation consultant, if any.

AON Consulting, Inc., or AON, served as our executive compensation consultant from 2022 to 2023. Through this assignment, AON has provided various executive compensation services to the Compensation Committee, including advising the Compensation Committee on the principal aspects of our executive compensation program and evolving industry practices and providing market information and analysis regarding the competitiveness of our program design and our award values in relation to performance. Upon request by the Compensation Committee, a representative of AON attended certain Compensation Committee meetings. AON does not provide services to us other than with regard to its advice to the Compensation Committee on executive and director compensation matters. The Compensation Committee determined AON to be independent under the Nasdaq and SEC regulations.

Nominating and Corporate Governance Committee

Our Nominating and Corporate Governance Committee consists of Dr. Scott and Ms. Williams, with Ms. Williams serving as Chair of our Nominating and Corporate Governance Committee. Each member of the Nominating and Corporate Governance Committee meets the requirements for independence under the listing requirements of Nasdaq.

The Nominating and Corporate Governance Committee is responsible for, among other things:

- identifying, evaluating and approving a slate of nominees for election to the Board at the Annual Meeting of Stockholders or any other meetings of stockholders and reviewing the qualifications, experience and fitness for service on the Board of any potential directors;
- determining the criteria for selection by the Board of the Chairman of the Board, the individual directors and the members of the committees of the Board;
- reviewing, evaluating and approving candidates submitted by stockholders to the Company and the timeliness of the submission therefor and recommending to the Board appropriate action on each such candidates; and
- reviewing annually the performance of the Board.

The Board has adopted a written Nominating and Corporate Governance Committee Charter. The composition and responsibilities of the Nominating and Corporate Governance Committee, as reflected in its Charter, satisfy the applicable rules of the SEC and the listing requirements of Nasdaq. The Nominating and Corporate Governance Committee Charter may be found on our website at www.windtreetx.com.

Code of Business Conduct and Ethics

We have adopted a Code of Business Conduct and Ethics that applies to our officers, including our principal executive, financial and accounting officers, and our directors and employees. We have posted the Code of Business Conduct and Ethics on our Internet website at "http://www.windtreetx.com" under the "*Investors—Corporate Governance*" tab. We intend to make all required disclosures on our website concerning any amendments to, or waivers from, our Code of Business Conduct and Ethics with respect to our executive officers and directors.

Delinquent Section 16(a) Reports

Section 16 of the Exchange Act requires our directors, certain officers, and beneficial owners of more than ten percent of our common stock to file reports with the SEC indicating their holdings of and transactions in our equity securities, and to provide copies of such reports to us. Based solely on a review of our records, publicly available information, and written representations by the persons required to file such reports, all filing requirements of Section 16(a) were satisfied with respect to the 2023 fiscal year by our directors and officers.

ITEM 11. EXECUTIVE COMPENSATION

Named Executive Officers

Our named executive officers, or NEOs, for the year ended December 31, 2023, which consists of (i) our principal executive officer, (ii) our two other most highly compensated executive officers who were serving as executive officers on December 31, 2023 and (iii) one additional individual who would have been in prong but for the fact that such individual was not serving as an executive officer on December 31, 2023, are:

consists of our principal executive officer and our three other most highly compensated executive officers, are:

- Craig E. Fraser, our President and CEO;
- Steven G. Simonson, M.D., our Senior Vice President and CMO;
- Eric Curtis, our Senior Vice President and COO; and
- Diane Carman, our Former Senior Vice President and General Counsel.

This section discusses the material components of the executive compensation program for our NEOs.

The following table presents summary information regarding the total compensation that was awarded to, earned by or paid to our NEOs for services rendered during the years ended December 31, 2023 and 2022.

2023 Summary Compensation Table

Name and Principal Position	Year	Salary ($)	Stock Awards ($)(1)	Option Awards ($)(2)	All Other Compensation ($)(3)	Total ($)
Craig E. Fraser	2023	$ 557,300	$ 55,499	$ 70,926	$ 9,900	$ 693,625
President and CEO	2022	544,600	170,238	216,922	9,150	940,910
Steven G. Simonson, M.D.	2023	438,100	19,199	24,535	9,900	491,734
Senior Vice President and CMO	2022	434,952	67,626	86,283	9,150	598,011
Eric Curtis (4)	2023	401,400	17,747	22,680	9,900	451,727
Senior Vice President and COO						
Diane Carman (5)	2023	220,935	-	-	439,617	660,552
Former Senior Vice President and General Counsel						

(1) Represents the aggregate grant date fair value of restricted stock unit awards, or RSUs, computed in accordance with Financial Accounting Standards Board Accounting Standards Codification, or ASC, Topic 718, Stock Compensation, or ASC Topic 718, and does not take into account estimated forfeitures related to service-based vesting conditions, if any. The valuation assumptions used in calculating these values are discussed in the section titled, "Note 12 – Stock Options and Stock-based Employee Compensation." These amounts do not represent actual amounts paid or to be realized. Amounts shown are not necessarily indicative of values to be achieved, which may be more or less than the amounts shown as awards are subject to time-based vesting.

(2) Represents the aggregate grant date fair value of option awards computed in accordance with ASC Topic 718 and does not take into account estimated forfeitures related to service-based vesting conditions, if any. The valuation assumptions used in calculating these values are discussed in the section titled, "Note 12 – Stock Options and Stock-based Employee Compensation." These amounts do not represent actual amounts paid or to be realized. Amounts shown are not necessarily indicative of values to be achieved, which may be more or less than the amounts shown as awards are subject to time-based vesting.

(3) Messrs. Fraser and Curtis and Dr. Simonson received $9,900 and $9,150 in 2023 and 2022, respectively, for matching contributions under our 401(k) Plan. Ms. Carman received $4,950 in 2023 for matching contributions under our 401(k) Plan. Ms. Carman received severance in connection with her departure in the amount of $434,667 comprised of $394,100 of continued base salary payments and $40,567 in company-subsidized COBRA premiums as part of her separation agreement (as described below in Ms. Carman's Separation Agreement).

(4) Mr. Curtis was not a NEO for 2022.

(5) Ms. Carman's separation date was July 21, 2023. Ms. Carman was not a NEO for 2022.

Narrative Disclosure to Summary Compensation Table

Elements of Compensation

The compensation of our NEOs generally consists of base salary, annual cash bonus opportunities, long term incentive compensation in the form of equity awards and other benefits, as described below.

Base Salary

The base salary payable to each NEO is intended to provide a fixed component of compensation reflecting the NEO's skill set, experience, role, responsibilities, and contributions. As of January 1, 2023, the annual base salaries for Mr. Fraser, Dr. Simonson, Mr. Curtis, and Ms. Carman were $557,300, $438,100, $401,400, and $394,100 respectively. There were no increases to the base salaries of our NEOs in 2023.

Annual Cash Bonus Opportunities

The performance-based cash bonus opportunity for each of our NEOs is expressed as a percentage of the applicable NEO's base salary that can be achieved at a target level by meeting predetermined corporate and individual performance objectives. Each executive's target bonus for the year is set forth in their employment agreements, as may be amended by the Compensation Committee from time to time. For 2023, our Compensation Committee and Board determined that each NEO's performance bonus should be based principally on contribution towards the achievement of corporate goals. These goals primarily included research and development, financial, and positioning and awareness objectives. The Compensation Committee recommended, and the Board established that the 2023 annual target bonus amount for Mr. Fraser be targeted at 50% of his base salary, and the Compensation Committee determined that the annual target bonus amounts for Dr. Simonson, Mr. Curtis, and Ms. Carman be targeted at 40% of their respective base salaries. No bonus payments were made for the 2022 or 2023 performance year.

Equity-Based Incentive Awards

Our equity-based incentive awards are designed to align our interests and the interests of our stockholders with those of our employees and consultants, including our NEOs. Our Board or Compensation Committee approves equity grants in its discretion, which have historically been in the form of stock options or RSUs.

On August 23, 2023, the Compensation Committee approved grants of stock options to Messrs. Fraser and Curtis and Dr. Simonson to purchase 68,800, 22,000 and 23,800 shares of our common stock, respectively, each with a per share exercise price of $1.21. All options vest in equal annual installments on each of the first three anniversaries of the date of grant, subject to the NEO's continuous service through the relevant vesting dates; provided, however, that such stock options may be eligible to fully accelerate in vesting in connection with a termination of employment as further described in the section titled "*Executive Employment Agreements*" below. See "*Executive Compensation—Outstanding Equity Awards at Fiscal Year-End*" for more information regarding equity awards made to our NEOs.

Other Benefits

We currently provide health and welfare benefits that are available to all of our employees, including our NEOs, including health, dental, life, vision and disability insurance.

In addition, we maintain, and the NEOs participate in, our 401(k) Plan that is intended to be qualified under Section 401(a) of the Code and that provides eligible employees with an opportunity to save for retirement on a tax advantaged basis and under which we are permitted to make discretionary employer contributions. The 401(k) Plan also includes a discretionary company match in an amount per participant equal to 50% of each participant's contribution (up to a maximum of 6% of the participant's base salary). Matching contributions were made in 2022 to 2023.

We do not maintain any defined benefit pension plans or nonqualified deferred compensation plans.

Executive Employment Agreements

We are party to executive employment agreements, or the Executive Agreements, as amended from time to time, with each of our NEOs, the key terms of which are described below.

Mr. Fraser's Employment Agreement

We entered into an employment agreement with Mr. Fraser, effective February 1, 2016, which was subsequently amended. Mr. Fraser's employment agreement provides for an annual base salary, which in 2023 was $557,300, and eligibility to receive an annual incentive-based cash bonus, which may be awarded at the discretion of the Compensation Committee, with a target amount equal to 50% of his base salary.

If Mr. Fraser's employment is terminated due to death or Disability (as such term is defined in the employment agreement), all equity awards held by Mr. Fraser shall become fully vested and all stock options shall continue to be exercisable for the remainder of their stated term.

If Mr. Fraser's employment is terminated by us without Cause or by Mr. Fraser for Good Reason prior to a Change of Control (as such terms are defined in the employment agreement) or after the 2nd anniversary of a Change of Control, Mr. Fraser will be eligible to receive the following, in addition to any amounts or benefits that are due under any of our vested plans or other policies, and on the condition that he enters into a separation agreement containing a final and effective plenary release of claims in a form acceptable to us, provided that all of our obligations shall cease if Mr. Fraser engages in a material breach of the employment agreement, or his restrictive covenant obligations, and fails to cure such breach within five business days after receipt from us of notice of such breach:

- A pro rata bonus equal to a percentage of Mr. Fraser's target bonus amount determined by dividing the total actual bonuses paid to other contract executives for the year in which the termination occurs by the aggregate of such other contract executives' total target bonuses for that year, and further prorated for the number of days Mr. Fraser was employed in the year of termination, payable at the time that other contract executives are paid bonuses with respect to the year of termination;

- A severance amount equal to the sum of Mr. Fraser's base salary then in effect (determined without regard to any reduction constituting Good Reason) and the target bonus amount, payable in equal installments in accordance with our regular payroll schedule from the date of termination to the date that is 12 months after the date of termination, or the Severance Period;

- All vested stock options and other similar equity awards held by Mr. Fraser shall continue to be exercisable during the Severance Period; and

- During the Severance Period, if Mr. Fraser elects to continue medical benefits through the Consolidated Omnibus Budget Reconciliation Act of 1985, or COBRA, we will continue to pay our costs of Mr. Fraser's and his dependents' benefits as in effect on the date of termination as such benefits are provided to active employees, which obligation terminates in the event substantially similar coverage (determined on a benefit-by-benefit basis) is provided by a subsequent employer.

If Mr. Fraser's employment is terminated by us without Cause or by Mr. Fraser for Good Reason prior to but in connection with a Change of Control or prior to the 2nd anniversary of a Change of Control, Mr. Fraser will be eligible to receive the following, in addition to any amounts or benefits that are due under any of our vested plans or other policies, and on the condition that he enters into a separation agreement containing a final and effective plenary release of claims in a form acceptable to us, provided that all of our obligations shall cease if Mr. Fraser engages in a material breach of the employment agreement, or his restrictive covenant obligations, and fails to cure such breach within five business days after receipt from us of notice of such breach:

- A pro rata bonus equal to Mr. Fraser's target bonus amount and prorated for the number of days Mr. Fraser was employed in the year of termination, payable in a lump sum within 10 days after the date of termination;

- A severance amount equal to 1.5 times the sum of Mr. Fraser's base salary then in effect (determined without regard to any reduction constituting Good Reason) and the target bonus amount, payable in a lump sum within 10 days after the date of termination except in certain limited circumstances;

- All equity awards held by Mr. Fraser shall accelerate and become fully vested and all stock options shall continue to be exercisable for the remainder of their stated terms; and

- For a period of 18 months following the termination date, if Mr. Fraser elects to continue medical benefits through COBRA, we will continue to pay our costs of Mr. Fraser and his dependents' benefits as in effect on the date of termination as such benefits are provided to active employees, which obligation terminates in the event substantially similar coverage (determined on a benefit-by-benefit basis) is provided by a subsequent employer.

In addition, upon a Change of Control, for a period of 24 months after the date of the Change of Control and provided that Mr. Fraser is employed on the last day of a fiscal year ending in that period, Mr. Fraser will be entitled to an annual bonus at least equal to Mr. Fraser's target bonus amount, payable no later than March 15 in the next succeeding fiscal year.

Mr. Fraser's employment agreement includes 12-month post-employment non-competition and non-solicitation covenants and provides for confidentiality and the assignment to us of all intellectual property.

Dr. Simonson's Employment Agreement

We are a party to an employment agreement with Dr. Simonson, which was effective December 19, 2014, as subsequently amended on December 29, 2014 and March 13, 2018. Dr. Simonson's employment agreement provides for an annual base salary, which in 2023 was $438,100, and an annual incentive-based cash bonus, which may be awarded at the discretion of the Compensation Committee, with a target amount equal to 40% of his annual base salary.

The employment agreement provides for Dr. Simonson to receive severance upon termination without Cause or by Dr. Simonson with Good Reason (as such terms are defined in the employment agreement) of (a) continued payment of base salary and subsidized COBRA benefits for 12 months following termination, which obligation terminates in the event substantially similar coverage (determined on a benefit-by-benefit basis) is provided by a subsequent employer, (b) a pro rata bonus equal to a percentage of Dr. Simonson's target bonus amount determined by dividing the total actual bonuses paid to other contract executives for the year in which the termination occurs by the aggregate of such other contract executives' total target bonuses for that year, and further prorated for the number of days Dr. Simonson was employed in the year of termination, payable at the time that other contract executives are paid bonuses with respect to the year of termination, and, (d) during the 12-month period following termination, all vested stock options and similar equity awards held by Dr. Simonson shall continue to be exercisable (such benefits, the Simonson Severance Benefits).

If Dr. Simonson is terminated by us without Cause or Dr. Simonson terminates his employment with Good Reason within 24 months of a Change of Control (as defined in the employment agreement), or in certain specific circumstances prior to, but in connection with or anticipation of, a Change of Control (as defined in the employment agreement), the employment agreement further provides Dr. Simonson with severance, or the Simonson Change of Control Severance Benefits, consisting of a lump sum equal to 1.5 times Dr. Simonson's base salary and annual bonus amount paid in a lump sum within 10 days after the date of termination, a pro rata bonus equal to Dr. Simonson's target bonus amount prorated for the number of days Dr. Simonson was employed in the year of termination, payable in a lump sum within 10 days after the date of termination, 18 months of COBRA benefits, which obligation terminates in the event substantially similar coverage (determined on a benefit-by-benefit basis) is provided by a subsequent employer, full vesting and acceleration of Dr. Simonson's equity awards upon the date of Dr. Simonson's termination and the continued exercisability of Dr. Simonson's equity awards for the remainder of their stated terms.

Dr. Simonson's receipt of the Simonson Severance Benefits, or the Simonson Change of Control Severance Benefits, as applicable, is conditioned on his execution of a separation and release agreement in a form acceptable to us. In the case of a termination of Dr. Simonson's employment due to death or disability, all shares of stock and all options shall become fully vested and any earned but unpaid annual bonus for the fiscal year preceding the termination date would be paid.

Mr. Curtis's Employment Agreement

We are a party to an employment agreement with Mr. Curtis, which was effective March 1, 2020. Mr. Curtis's employment agreement provides for an annual base salary, which in 2023 was $401,400, and an annual incentive-based cash bonus, which may be awarded at the discretion of the Compensation Committee, with a target amount equal to 40% of his annual base salary.

The employment agreement provides for Mr. Curtis to receive severance upon termination without Cause or by Mr. Curtis with Good Reason (as such terms are defined in the employment agreement) or in certain specific circumstances prior to, but in connection with or anticipation of, a Change of Control (as defined in the employment agreement) of (a) continued payment of base salary and subsidized COBRA benefits for 12 months following termination, (b) any earned but unpaid annual bonus for the fiscal year preceding Mr. Curtis's date of termination and a pro rata bonus equal to the annual bonus Mr. Curtis would have earned absent his separation (as defined in the employment agreement) which amount shall be paid when our other executives are paid, and (c) during the 12-month period following termination, all vested stock options and similar equity awards held by Mr. Curtis shall continue to be exercisable (such benefits the Curtis Severance Benefits).

If Mr. Curtis is terminated by us without Cause or Mr. Curtis terminates his employment with Good Reason within 24 months after a Change of Control (as defined in the employment agreement), the employment agreement further provides Mr. Curtis with severance, or the Curtis Change of Control Severance Benefits, consisting of any earned but unpaid annual bonus for the fiscal year preceding the date of Mr. Curtis's termination, a lump sum equal to 1.5 times Mr. Curtis's base salary and annual bonus amount paid in a lump sum within 10 days after the date of termination, 18 months of COBRA benefits (which obligation terminates in the event he becomes eligible for group health plan benefits under a subsequent employer's or a spouse's employer's plan), full vesting and acceleration of Mr. Curtis's equity awards upon the date of Mr. Curtis's termination and the continued exercisability of Mr. Curtis's equity awards for the remainder of their stated terms.

Mr. Curtis's receipt of the Curtis Severance Benefits, or the Curtis Change of Control Severance Benefits, as applicable, is conditioned on his execution of a separation and release agreement in a form acceptable to us. The employment agreement further provides that in the event of a Change of Control transaction, all of Mr. Curtis's outstanding equity incentive awards will become fully vested so long as Mr. Curtis is actively employed by us at the time of such transaction. In the case of a termination of Mr. Curtis's employment due to death or disability, all shares of stock and all options shall become fully vested and any earned but unpaid annual bonus for the fiscal year preceding the termination date would be paid.

Ms. Carman's Separation Agreement

In connection with Ms. Carman's termination without cause, we entered into a separation agreement dated as of August 18, 2023, providing her with the following benefits in exchange for a release of claims in favor of us and further subject to Ms. Carman's continued compliance with the terms of our restrictive covenant agreement entered into with her: twelve months of continued base salary payments, and company-subsidized COBRA continuation payments for up to 12 months.

Clawback Policy

In accordance with the requirements of the SEC and Nasdaq listing rules, the Board has adopted a compensation recovery policy, effective as of October 2, 2023. The compensation recovery policy provides that in the event we are required to prepare a restatement of financial statements due to material noncompliance with any financial reporting requirement under securities laws, we will seek to recover any incentive-based compensation that was based upon the attainment of a financial reporting measure and that was received by any current or former executive officer during the three-year period preceding the date that the restatement was required if such compensation exceeds the amount that the executive officers would have received based on the restated financial statements.

Outstanding Equity Awards at Fiscal Year-End

The following table summarizes the number of shares of common stock underlying outstanding equity incentive plan awards for each NEO as of December 31, 2023.

		Option Awards				Stock Awards	
Name	Grant Date	Number of Securities Underlying Unexercised Options (#) - Exercisable (1)	Number of Securities Underlying Unexercised Options (#) - Unexercisable (1)	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)(2)	Market Value of Shares or Units of Stock That Have Not Vested ($)(3)
Craig E. Fraser	02/02/16	68		6,990.00	02/02/26		
	07/28/16	13		5,310.00	07/28/26		
	03/01/17	33		3,690.00	03/01/27		
	12/24/18	8,438		633.00	12/24/28		
	03/19/19	667		645.00	03/19/29		
	01/22/21	4,775	955	272.00	01/22/31		
	03/04/22	2,924	2,085	51.00	03/04/32	2,225	$ 1,602
	08/23/23	-	68,800	1.21	08/23/33	45,867	$ 33,024
Steven G. Simonson, M.D.	05/19/14	3		71,400.00	05/19/24		
	03/27/15	7		49,140.00	03/27/25		
	02/02/16	12		6,990.00	02/02/26		
	07/28/16	9		5,310.00	07/28/26		
	03/01/17	18		3,690.00	03/01/27		
	12/24/18	4,923		633.00	12/24/28		
	03/19/19	333		645.00	03/19/29		
	01/22/21	1,852	400	272.00	01/22/31		
	03/04/22	1,165	827	51.00	03/04/32	884	$ 636
	08/23/23	-	23,800	1.21	08/23/33	15,867	$ 11,424
Eric Curtis	07/29/20	4,109	-	382.50	07/29/30		
	01/22/21	801	399	272.00	01/22/31		
	03/04/22	1,165	827	51.00	03/04/32	884	$ 636
	08/23/23	-	22,000	1.21	08/23/33	14,667	$ 10,560
Diane Carman	07/01/21	2,000	-	113.50	07/01/31		
	03/04/22	832	-	51.00	03/04/32	-	$ -

(1) Options granted prior to 2022 and options granted in 2023 vest and become exercisable in equal installments on each of the first three anniversaries of the applicable grant date, assuming that the NEO continues to be employed with us through each vesting date. Options granted in 2022 vest and become exercisable with respect to one-twelfth of the total number of shares subject to the options on a quarterly basis (every three months) following the applicable grant date, provided that the NEO remains in continuous service on each vesting date.

(2) The RSUs represent a contingent right to receive the equivalent number of shares of common stock. These RSUs shall vest with respect to one-third of the total number of shares subject to the RSUs on an annual basis (every 12 months) following the applicable grant date, provided that the NEO remains in continuous service on each vesting date.

(3) The market value of the unvested RSUs is calculated based on the number of RSUs at December 31, 2023 and the closing market price of our common stock on December 29, 2023, the last trading day of 2023, of $0.72 per share.

Director Compensation

Directors who are also employees are not compensated separately for serving on the Board or any of its committees. Each of our non-employee directors receives cash compensation for his or her services. The Compensation Committee periodically conducts reviews of peer company director compensation practices, including before considering changes to our director compensation policy and amounts. In addition, to better align the interests of our Board with our stockholders, the Compensation Committee considers and recommends to the Board long-term equity compensation.

Pursuant to our Non-Employee Director Compensation Policy in place during 2023, our directors received annual cash retainers, paid on a quarterly basis, as set forth in the table below.

Non-Employee Director Compensation Policy

CASH	**Quarterly Retainer ($)**
Board Member Cash Retainer	$ 10,000
Additional Board Chair Cash Retainer	6,250
	Additional Quarterly Retainers
Audit Committee	
Chair	3,750
Member	1,750
Compensation Committee	
Chair	2,500
Member	1,250
Nominating and Corporate Governance Committee	
Chair	1,875
Member	1,000

EQUITY	
Initial Equity Grant	Option to purchase shares of common stock, vesting in three equal annual installments, beginning on the first anniversary of the grant date and subject to the director's continued service on the Board
Annual Equity Grant	Option to purchase shares of common stock, vesting in three equal annual installments, beginning on the first anniversary of the grant date and subject to the director's continued service on the Board

Cash fees are paid quarterly and are typically pro-rated for non-employee directors who do not serve a full quarter. Our non-employee directors are also reimbursed for their business-related expenses incurred in connection with attendance at Board and committee meetings and related activities. Our only employee director, Mr. Fraser, receives no separate compensation for his service in such capacity. The compensation paid to Mr. Fraser is reported in the "Executive Compensation—2023 Summary Compensation Table" above.

The following table summarizes information concerning the compensation awarded to, earned by, or paid for services rendered in all capacities by our non-employee directors during the year ended December 31, 2023.

Name of Non-Employee Director	**Fee Earned or Paid in Cash ($)**	**Stock Awards ($)[1]**	**Option Awards ($)[2]**	**Total ($)**
Daniel E. Geffken	60,000	2,460	3,144	65,604
Robert Scott, M.D.	57,500	2,460	3,144	63,104
Leslie J. Williams	56,250	2,460	3,144	61,854
Mark Strobeck, Ph.D.	26,000	2,783	3,557	32,340
James Huang[3]	19,464	-	-	19,464

(1) Represents the aggregate grant date fair value of RSUs computed in accordance with ASC Topic 718 and does not take into account estimated forfeitures related to service-based vesting conditions, if any. The valuation assumptions used in calculating these values are discussed in the section titled, "Note 12 – Stock Options and Stock-based Employee Compensation." These amounts do not represent actual amounts paid or to be realized. Amounts shown are not necessarily indicative of values to be achieved, which may be more or less than the amounts shown as awards are subject to time-based vesting. As of December 31, 2023, (i) Messrs. Geffken, Dr. Scott, and Ms. Williams each held RSUs to receive 2,033 shares of our common stock; and (ii) Dr. Strobeck held RSUs to receive 2,300 shares of our common stock. Further, as of December 31, 2023, Mr. Huang did not have any RSUs.

(2) Represents the aggregate grant date fair value of option awards computed in accordance with ASC Topic 718 and does not take into account estimated forfeitures related to service-based vesting conditions, if any. The valuation assumptions used in calculating these values are discussed in the section titled, "Note 12 – Stock Options and Stock-based Employee Compensation." These amounts do not represent actual amounts paid or to be realized. Amounts shown are not necessarily indicative of values to be achieved, which may be more or less than the amounts shown as awards are subject to time-based vesting. As of December 31, 2023, (i) Mr. Huang held options to purchase 1,150 shares of our common stock; (ii) Mr. Geffken held options to purchase 4,200 shares of our common stock; (iii) Dr. Scott and Ms. Williams each held options to purchase 3,800 shares of our common stock; and (iv) Dr. Strobeck held options to purchase 3,450 shares of our common stock.

(3) On April 18, 2023, Mr. Huang resigned from our Board.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

Securities Authorized for Issuance Under Equity Compensation Plans

The following table describes as of December 31, 2023 the number of shares of our common stock issuable upon exercise of outstanding awards under our 2020 and 2011 Plans.

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)	Weighted-average exercise price of outstanding options, warrants and rights (b)[1]	Number of securities available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (c)
Equity compensation plans approved by security holders			
2020 Long-Term Incentive Plan [2]	393,469	$ 16.10	338,677
2011 Long-Term Incentive Plan [3]	28,890	643.40	-
Equity compensation plans not approved by security holders [4]			
Inducement Grants [5]	2,068	339.61	-
Total	**424,427**	$ **60.38**	**338,677**

(1) Represents the weighted-average exercise price of outstanding stock options and does not include RSUs.
(2) All shares that were available under the 2020 Plan, including any that are expired, forfeited or otherwise returnable to the 2020 Plan are transferred to and become available for grant under the 2020 Plan. All awards granted under the 2020 Plan continue to be governed by the terms of the 2020 Plan and the award agreements.
(3) The 2011 Plan terminated on the effective date of the 2020 Plan. All shares that were available under the 2011 Plan, including any that are expired, forfeited or otherwise returnable to the 2011 Plan are transferred to and become available for grant under the 2020 Plan. All awards granted under the 2011 Plan continue to be governed by the terms of the 2011 Plan and the award agreements.
(4) Our Board has not established any specific number of shares that could be issued without stockholder approval. Inducement grants to new key employees are determined on a case-by-case basis. Other than possible inducement grants, we expect that all equity awards will be made under stockholder-approved plans
(5) Reflects grants of stock options to purchase 2,068 shares of common stock that were "inducement grants" as defined under Nasdaq Listing Rule 5635(c)(4). For more information, see the section titled, "Note 12 – Stock Options and Stock-based Employee Compensation."

Security Ownership of Certain Beneficial Owners and Management

Based solely upon information made available to us, the following table sets forth information as of April 16, 2024 regarding the beneficial ownership of our common stock by:

- each person known by us to be the beneficial owner of more than 5% of the outstanding shares of our common stock;
- each of our NEOs and directors; and
- all of our executive officers as a group.

The percentage of common stock outstanding is based on 9,183,220 shares of our common stock outstanding as of April 16, 2024. For purposes of the table below, and in accordance with the rules of the SEC, we deem shares of common stock subject to options that are currently exercisable or exercisable within 60 days of April 16, 2024 to be outstanding and to be beneficially owned by the person holding the options for the purpose of computing the percentage ownership of that person, but we do not treat them as outstanding for the purpose of computing the percentage ownership of any other person. Except as otherwise noted, each of the persons or entities in this table has sole voting and investing power with respect to all of the shares of common stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise noted below, the street address of each beneficial owner is c/o Windtree Therapeutics, Inc. 2600 Kelly Road, Suite 100, Warrington, PA 18976.

Name and Address of Beneficial Owner	Shares Beneficially Owned	
	Number of Shares	Percentage
Greater than 5% Stockholder		
Deerfield Entities(1)	608,272	6.62%
Lincoln Park Capital Fund, LLC (2)	614,334	6.47%
Directors and Named Executive Officers		
Daniel E. Geffken (3)	1,232	*
Robert Scott, M.D. (4)	850	*
Mark Strobeck, Ph.D.	-	*
Leslie J. Williams (4)	850	*
Craig E. Fraser (5)	29,130	*
Steven G. Simonson, M.D. (6)	10,009	*
Eric Curtis (7)	7,398	*
Former Officer		
Diane Carman (8)	3,201	*
Executive Officers and Directors as a group (8 persons) (9)	**50,690**	**0.54%**

* Less than 1%

(1) Includes 324,817 shares of common stock issued to Deerfield PDI Financing II, L.P. and 283,455 shares of common stock issued to Deerfield Private Design Fund II, L.P. for a total of 608,272 shares of common stock. Deerfield Mgmt, L.P. is the general partner of Deerfield PDI Financing II, L.P. and Deerfield Private Design Fund II, L.P. (collectively, the Deerfield Entities). Deerfield Management Company, L.P. is the investment manager of the Deerfield Entities. James E. Flynn is the sole member of the general partner of each of Deerfield Mgmt, L.P. and Deerfield Management Company, L.P. Each of Deerfield Mgmt, L.P., Deerfield Management Company, L.P. and Mr. James E. Flynn may be deemed to beneficially own the shares of common stock of our company beneficially owned by the Deerfield Entities. The selling stockholder's address is c/o Deerfield Management Company, L.P., 345 Park Avenue South, 12th Floor, New York, New York 10010.

(2) Includes 307,167 shares of common stock and 307,167 April 2023 Warrants to purchase 307,167 shares of common stock exercisable within 60 days of April 16, 2024. The April 2023 Warrants are subject to a 4.99% ownership cap (or, at the election of each holder prior to the date of issuance, 9.99%). Lincoln Park Capital, LLC, or LPC, is the Managing Member of Lincoln Park Capital Fund, LLC, or LPC Fund. Rockledge Capital Corporation, or RCC, and Alex Noah Investors, Inc., or Alex Noah, are the Managing Members of LPC. Joshua B. Scheinfeld is the president and sole shareholder of RCC, as well as a principal of LPC. Jonathan I. Cope is the president and sole shareholder of Alex Noah, as well as a principal of LPC. As a result of the foregoing, Mr. Scheinfeld and Mr. Cope have shared voting and shared investment power over the shares of common stock held directly by LPC Fund. Pursuant to Section 13(d) of the Act and the rules thereunder, each of LPC, RCC, Mr. Scheinfeld, Alex Noah, and Mr. Cope may be deemed to be a beneficial owner of the shares of Common Stock of the Issuer beneficially owned directly by LPC Fund. Pursuant to Rule 13(d)(4) of the Exchange Act, each of LPC, RCC, Mr. Scheinfeld, Alex Noah, and Mr. Cope disclaims beneficial ownership of the shares of common stock held directly by LPC Fund. The address for LPC Fund, LPC, RCC, Mr. Scheinfeld, Alex Noah, and Mr. Cope is 440 North Wells, Suite 410, Chicago, Illinois 60654.

(3) Includes 141 shares of common stock, 41 May 2020 Warrants to purchase 41 shares of common stock exercisable within 60 days of April 16, 2024 and options to purchase 1,050 shares of common stock exercisable within 60 days of April 16, 2024. The May 2020 Warrants are subject to a 4.99% ownership cap (or, at the election of each holder prior to the date of issuance, 9.99%), except that upon at least sixty-one (61) days' prior notice to us, each holder may increase the ownership cap after exercising such holder's May 2020 Warrants up to 9.99% (or up to 19.99% upon prior written approval by us).

(4) Includes 100 shares of common stock and options to purchase 750 shares of common stock exercisable within 60 days of April 16, 2024.

(5) Includes 10,769 shares of common stock, 41 May 2020 Warrants to purchase 41 shares of common stock exercisable within 60 days of April 16, 2024, 30 March 2021 Warrants to purchase 30 shares of common stock exercisable within 60 days of April 16, 2024, and options to purchase 18,290 shares of common stock exercisable within 60 days of April 16, 2024. The May 2020 Warrants are subject to a 4.99% ownership cap (or, at the election of each holder prior to the date of issuance, 9.99%), except that upon at least sixty-one (61) days' prior notice to us, each holder may increase the ownership cap after exercising such holder's May 2020 Warrants up to 9.99% (or up to 19.99% upon prior written approval by us).

(6) Includes 1,084 shares of common stock, 10 May 2020 Warrants to purchase 10 shares of common stock exercisable within 60 days of April 16, 2024, 30 March 2021 Warrants to purchase 30 shares of common stock exercisable within 60 days of April 16, 2024, and options to purchase 8,888 shares of common stock exercisable within 60 days of April 16, 2024. The May 2020 Warrants are subject to a 4.99% ownership cap (or, at the election of each holder prior to the date of issuance, 9.99%), except that upon at least sixty-one (61) days' prior notice to us, each holder may increase the ownership cap after exercising such holder's May 2020 Warrants up to 9.99% (or up to 19.99% upon prior written approval by us).

(7) Includes 758 shares of common stock and options to purchase 6,640 shares of common stock exercisable within 60 days of April 16, 2024.

(8) Includes 369 shares of common stock and options to purchase 2,832 shares of common stock exercisable within 60 days of April 16, 2024.

(9) This information does not include securities held by Ms. Carman, who is no longer an officer.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

We describe below transactions and series of similar transactions, since January 1, 2022 or currently proposed, to which we were a party or will be a party, in which:

- the amounts involved exceeded $120,000; and
- any of our directors, executive officers or beneficial holders of more than 5% of any class of our capital stock had or will have a direct or indirect material interest.

Other than as described below, there have not been, nor are there any currently proposed, transactions or series of similar transactions meeting this criteria to which we have been or will be a party other than compensation arrangements, which are described where required under the sections titled "Management—Board Leadership Structure" and "Executive Compensation."

Our Board has adopted a written related person transaction policy setting forth the policies and procedures for the review and approval or ratification of related-person transactions. This policy covers any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we were or are to be a participant, where the amount involved exceeds $120,000 and a related person had or will have a direct or indirect material interest. Our management is responsible for determining whether a transaction is a related party transaction subject to our policy, and upon subject determination, is responsible for disclosing the material facts concerning the transaction and the related party's interest in our transaction to our Audit Committee. In reviewing and approving any such transactions, our Audit Committee is tasked to consider all relevant facts and circumstances with respect to the transaction and shall evaluate all available options, including ratification, revision or termination of the transaction. All of the transactions described above either were approved or ratified in compliance with this policy.

Since January 1, 2022, we have engaged in the following transactions with our directors, executive officers, holders of more than 5% of our voting securities, and affiliates or immediate family members of our directors, executive officers, and holders of more than 5% of our voting securities. We believe that all of these transactions were on terms as favorable as could have been obtained from unrelated third parties.

Lee's Pharmaceutical Holdings Limited and Affiliates

We have received substantial support from Lee's Holdings. Lee's Holdings is a company incorporated in the Cayman Islands with limited liability, whose common stock is listed on the Hong Kong Stock Exchange. As of December 31, 2023 and 2022, Lee's Holdings' beneficial ownership of our issued and outstanding shares of common stock was 2% and 13%, respectively.

A&R License Agreement

On August 17, 2022, we entered into an Amended and Restated License, Development and Commercialization Agreement, or the A&R License Agreement, with Lee's (HK), and Zhaoke Pharmaceutical (Hefei) Co. Ltd., or Zhaoke, a company organized under the laws of the People's Republic of China, effective as of August 9, 2022. We refer to Zhaoke and Lee's (HK) together as the "Licensee." The A&R License Agreement amends, restates, and supersedes the Asia License Agreement.

Under the A&R License Agreement, we granted to Licensee an exclusive license, with a right to sublicense, to develop, register, make, use, sell, offer for sale, import, distribute, and otherwise commercialize our KL4 surfactant products, including SURFAXIN®, the lyophilized dosage form of SURFAXIN, and aerosolized KL4 surfactant, in each case for the prevention, mitigation and/or treatment of any respiratory disease, disorder, or condition in humans worldwide, except for Andorra, Greece, and Italy (including the Republic of San Marino and Vatican City), Portugal, and Spain, or the Licensed Territory, which countries are currently exclusively licensed to Laboratorios Del Dr. Esteve, S.A.

We may receive up to $78.9 million in potential clinical, regulatory, and commercial milestone payments under the A&R License Agreement. We are also entitled to receive a low double-digit percentage of Licensee's non-royalty sublicense income. Further, Licensee is solely and exclusively responsible for all costs and activities related to the development, manufacturing, regulatory approval, and commercialization of licensed products in the Licensed Territory, including all royalties payable in respect of third-party intellectual property rights sublicensed by us to Licensee and all intellectual property prosecution, maintenance and defense activities and costs.

Panacea Venture Management Company Ltd.

As of December 31, 2023 and 2022, Panacea Venture Management Company Ltd.'s, or Panacea's, beneficial ownership of our issued and outstanding shares of common stock was 1% and 9%, respectively. James Huang, who in connection with the CVie Acquisition in December 2018 was appointed as a director and Chairman of our Board, is a founding and Managing Partner to Panacea. On April 18, 2023, Mr. Huang resigned as a member of the Board.

February 2023 Warrant Exercise Inducement Offer Letter

On February 21, 2023, we entered into a warrant exercise inducement offer letter with Panacea Venture Healthcare Fund I, L.P., a holder of certain of our: (i) warrants issued in July 2018 to purchase 1,250 shares of common stock with an exercise price of $600.00 per share; (ii) warrants issued in December 2018 to purchase 9,960 shares of common stock with an exercise price of $607.50 per share; (iii) warrants issued in December 2019 to purchase 5,519 shares of common stock with an exercise price of $604.50 per share; and (iv) warrants issued in May 2020 to purchase 5,517 shares of common stock with an exercise price of $398.75 per share (collectively, the February 2023 Existing Warrants).

Pursuant to the terms of the inducement letter, we agreed to amend the February 2023 Existing Warrants by lowering the exercise price of the February 2023 Existing Warrants to $7.06 per share. Additionally, the exercising holder agreed to exercise for cash all of their February 2023 Existing Warrants to purchase an aggregate of 22,246 shares of common stock in exchange for our agreement to issue to such exercising holder new warrants, or the February 2023 New Warrants, to purchase up to an aggregate of 44,492 shares of common stock. We received aggregate gross proceeds of approximately $157,000 from the exercise of the February 2023 Existing Warrants by the exercising holders.

Each February 2023 New Warrant is exercisable into shares of common stock at a price per share of $10.76, will be exercisable six months following its date of issuance, or the initial exercise date, and will expire on the fifth anniversary the initial exercise date. Subject to limited exceptions, Panacea will not have the right to exercise any portion of its February 2023 New Warrants if Panacea (together with Panacea's affiliates, and any persons acting as a group together with Panacea or any of Panacea's affiliates) would beneficially own a number of shares of our common stock in excess of 19.99% of our total shares of common stock outstanding.

Other Transactions

We have granted stock options to our named executive officers and certain of our directors. See "Item 11—Executive Compensation - Outstanding Equity Awards at Fiscal Year-End" for a description of these stock options.

We have entered into change of control and severance agreements with certain of our executive officers that provide for certain severance and change in control benefits. See "Item 11—Executive Compensation - Executive Employment Agreements."

During 2022, we incurred $0.4 million in research and development expenses for services provided by an affiliate of Lee's Holdings to our wholly owned subsidiary, CVie Therapeutics.

Indemnification Agreements

We have entered into indemnification agreements with each of our directors and executive officers. These indemnification agreements, our amended and restated Certificate of Incorporation, as amended, or our Amended and Restated Certificate of Incorporation, and our By-Laws, require us to indemnify directors to the fullest extent permitted by Delaware law.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

Audit Fees, Audit-Related Fees, Non-Audit Fees, Tax Fees and Other Fees

The following table sets forth all fees paid or accrued by us for professional services rendered by EisnerAmper LLP, our independent registered public accounting firm during the year ended December 31, 2023 and by Ernst & Young LLP, our independent registered public accounting firm, during the year ended December 31, 2022:

Service	2023	2022
EisnerAmper LLP		
Audit Fees	$ 368,550	$ 257,250
Tax Fees	-	-
Total	$ 368,550	$ 257,250
Ernst & Young LLP		
Audit Fees	$ -	$ 75,000
Tax Fees	-	-
Total	$ -	$ 75,000
Total fees	$ 368,550	$ 332,250

"Audit fees" include fees incurred for: (i) professional services rendered for the audit of our annual financial statements; (ii) the review of quarterly financial statements, (iii) issuance of consents associated with the filing of registration statements; (iv) delivery of auditor comfort letters, and (v) a statutory audit.

"Tax fees" consisted of all services, except those services specifically related to the audit of the financial statements, performed by the independent registered public accounting firm's tax personnel, including tax compliance and reporting.

The Audit Committee considered whether the provision of all other services by EisnerAmper LLP and Ernst & Young LLP is compatible with maintaining the independence and has concluded that EisnerAmper LLP and Ernst & Young LLP are both independent.

Pre-approval Policies

The Audit Committee pre-approves specified audit and non-audit services prior to the engagement of our independent registered public accounting firm. Our CFO monitors the performance of all services rendered by our independent auditors, determines whether such services are within the list of pre-approved services and informs the Audit Committee on a timely basis of any such services.

On an ongoing basis, our CFO, together with our independent registered public accounting firm, is responsible to submit to the Audit Committee all requests for approval of services that require a specific pre-approval. The Audit Committee reviews these requests and advises management and the independent registered public accounting firm if the Audit Committee pre-approves the engagement of the independent auditors for such projects and services. On a periodic basis, management reports to the Audit Committee the actual spending for such projects and services compared to the approved amounts. The Audit Committee may delegate the ability to pre-approve audit and permitted non-audit services to a sub-committee of the Audit Committee, provided that any such pre-approvals are reported at the next Audit Committee meeting.

All such audit and permissible non-audit services were pre-approved in accordance with this policy during the fiscal year ended December 31, 2023.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES.

(a) Financial Statements.

The consolidated financial statements required to be filed in this Annual Report on Form 10-K are listed on the Index to Consolidated Financial Statements on page F-1 hereof.

(b) Exhibits.

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

Exhibit No.	Description
2.1+	Form of Asset Purchase Agreement by and between Windtree Therapeutics, Inc. and Varian Biopharmaceuticals, Inc., dated April 2, 2024 (incorporated by reference to Exhibit 2.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on April 8, 2024).
3.1*	Amended and Restated Certificate of Incorporation.
3.2	Amended and Restated By-Laws (incorporated by reference to Exhibit 3.1 to Windtree's Quarterly Report on Form 10-Q for the quarter ended June 30, 2022, as filed with the SEC on August 11, 2022).
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).
4.11	Form of Series I Warrant dated December 6, 2019 (incorporated by reference to Exhibit 4.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on December 9, 2019).
4.12	Form of Series F Warrant Amendment No. 1 dated April 24, 2020 (incorporated by reference to Exhibit 4.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on April 29, 2020).
4.13	Form of Series I Warrant Amendment dated May 6, 2020, to the Series I Warrant dated December 6, 2019 (incorporated by reference to Exhibit 4.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on May 7, 2020).

4.14	Form of Warrant issued in the Company's May 2020 underwritten public offering of securities (incorporated by reference to Exhibit 4.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on May 22, 2020).
4.15	Form of Warrant issued in the Company's March 2021 underwritten public offering of securities (incorporated by reference to Exhibit 4.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on March 24, 2021).
4.16	Form of Common Stock Purchase Warrant dated January 24, 2023 (incorporated by reference to Exhibit 4.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on January 26, 2023).
4.17	Form of Common Stock Purchase Warrant dated February 21, 2023 (incorporated by reference to Exhibit 4.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on February 22, 2023).
4.18*	Description of Securities.
4.19	Form of Common Warrant (incorporated by reference to Exhibit 4.19 to Windtree's Registration Statement on Form S-1/A (File No. 333-269775), as filed with the SEC on April 7, 2023).
4.20	Form of Pre-Funded Warrant (incorporated by reference to Exhibit 4.20 to Windtree's Registration Statement on Form S-1/A (File No. 333-269775), as filed with the SEC on April 7, 2023).
4.21	Form of Warrant Agency Agreement (incorporated by reference to Exhibit 4.21 to Windtree's Registration Statement on Form S-1/A (File No. 333-269775), as filed with the SEC on April 7, 2023).
4.22	Warrant Agency Agreement (including form of global Common Warrant), dated April 24, 2023, by and between Windtree and Continental Stock Transfer & Trust Company (incorporated by reference to Exhibit 4.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on April 24, 2023).
4.23	Form of 10% Convertible Note (incorporated by reference to Exhibit 4.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on April 8, 2024).
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*††	Amendment No. 1, effective as of January 17, 2024, to the Amended and Restated License Agreement, between Windtree and Philip Morris USA Inc. dated March 28, 2008.
10.4†	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).
10.5*††	Amendment No. 1, effective as of January 17, 2024, to the License Agreement, between Windtree and Philip Morris Products S.A. dated March 28, 2008.
10.6††	Amended and Restated Sublicense and Collaboration Agreement dated December 3, 2004, by and between Discovery Laboratories, Inc. (predecessor-in-interest to Windtree) and Laboratorios del Dr. Esteve, S.A. (incorporated by reference to Exhibit 10.3 to Windtree's Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, as filed with the SEC on November 16, 2020).
10.7††	Amended and Restated Supply Agreement dated December 3, 2004, by and between Discovery Laboratories, Inc. (predecessor-in-interest to Windtree) and Laboratorios del Dr. Esteve, S.A. (incorporated by reference to Exhibit 10.2 to Windtree's Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, as filed with the SEC on November 16, 2020).

10.8†	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).
10.9†	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).
10.10	Amended and Restated License, Development and Commercialization Agreement, by and among Lee's Pharmaceutical (HK) Ltd., Zhaoke Pharmaceutical (Hefei) Co. Ltd., and Windtree Therapeutics, Inc., effective as of August 9, 2022 (incorporated by reference to Exhibit 10.1 to Windtree's Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, as filed with the SEC on November 14, 2022).
10.11#	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).
10.12#	Windtree's 2020 Equity Incentive Plan (incorporated by reference to Exhibit 10.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on December 31, 2020).
10.13#	Amended and Restated Windtree Therapeutics, Inc. 2020 Equity Incentive Plan (incorporated by reference to Exhibit 10.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on August 16, 2023).
10.14#	Form of Restricted Stock Unit Grant for Employees under Windtree's 2020 Equity Incentive Plan (incorporated by reference to Exhibit 4.5 To Windtree's Registration Statement on Form S-8, as filed with the SEC on February 12, 2021).
10.15#	Form of Stock Option Grant for Employees under Windtree's 2020 Equity Incentive Plan (incorporated by reference to Exhibit 4.6 To Windtree's Registration Statement on Form S-8, as filed with the SEC on February 12, 2021).
10.16#	Form of Inducement Award Agreement (incorporated by reference to Exhibit 4.4 to Windtree's Registration Statement on Form S-8 (File No. 333-253067), as filed with the SEC on February 12, 2021)
10.17#	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).
10.18#	Form of Non-Employee Director Option Agreement under Windtree's 2011 Long-Term Incentive Plan (incorporated by reference to Exhibit 10.10 to Windtree's Form 10-K, as filed with the SEC on April 3, 2020).
10.19#	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).
10.20#	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).
10.21#	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).
10.22#	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).
10.23#	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).
10.24#	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).
10.25#	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).

10.26#	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).
10.27#	At The Market Offering Agreement, dated as of November 9, 2023, by and between Windtree Therapeutics, Inc. and Ladenburg Thalmann & Co. Inc. (incorporated by reference to Exhibit 1.1 to the Windtree's Current Report on Form 8-K, as filed with the SEC on November 9, 2023).
10.28#	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).
10.29#	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).
10.30	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).
10.31	Second Amendment to Lease Agreement dated January 3, 2013 between TR Stone Manor Corp. and Windtree (incorporated by reference to Exhibit 10.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on January 8, 2013).
10.32	Third Amendment to Lease Agreement dated November 24, 2014 between TR Stone Manor Corp. and Windtree (incorporated by reference to Exhibit 10.29 to Windtree's Annual Report on Form 10-K, as filed with the SEC on March 31, 2023).
10.33	Fourth Amendment to Lease Agreement dated April 29, 2016, 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 May 31, 2016).
10.34	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).
10.35†	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).
10.36	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).
10.37	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).
10.38	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).
10.39††	Collaboration Agreement dated as of October 14, 2014, by and between Battelle Memorial Institute and Discovery Laboratories, Inc. (predecessor-in-interest to Windtree) (incorporated by reference to Exhibit 10.1 to Windtree's Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, as filed with the SEC on November 16, 2020).
10.40	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).
10.41	Amendment No. 1 dated March 30, 2020 to Payment Restructuring Agreement, effective December 7, 2018, between Windtree and Lee's Pharmaceutical (HK) LTD (incorporated by reference to Exhibit 10.48 to Windtree's Registration Statement on Form S-1/A (File No. 333-236085), as filed with the SEC on May 6, 2020).
10.42	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).
10.43	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).

10.44	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).
10.45	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).
10.46	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).
10.47	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).
10.48	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).
10.49	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).
10.50	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).
10.51	Loan Agreement dated October 24, 2019 between Windtree and LPH II Investments Ltd. (incorporated by reference to Exhibit 10.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on October 28, 2019).
10.52	Form of Securities Purchase Agreement dated December 6, 2019 by and among Windtree and the purchasers party thereto (incorporated by reference to Exhibit 10.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on December 9, 2019).
10.53	Form of Registration Rights Agreement dated December 6, 2019 by and among Windtree and the purchasers party thereto (incorporated by reference to Exhibit 10.2 to Windtree's Current Report on Form 8-K, as filed with the SEC on December 9, 2019).
10.54#	Employment Agreement dated March 1, 2020, between Windtree and Eric Curtis (incorporated by reference to Exhibit 10.46 to Windtree's Form 10-K, as filed with the SEC on April 3, 2020).
10.55	Amendment to No. 1 dated February 20, 2020 to the Securities Purchase Agreement dated December 6, 2019 by and among Windtree and the purchasers party thereto (incorporated by reference to Exhibit 10.47 to Windtree's Form 10-K, as filed with the SEC on April 3, 2020).
10.56	Project Financing Agreement, dated August 12, 2020, by and between Windtree and Lee's Pharmaceutical (HK) Ltd. (incorporated by reference to Exhibit 10.4 to Windtree's Quarterly Report on Form 10-Q, as filed with the SEC on November 16, 2020).
10.57#	Employment Agreement by and between Windtree and John Hamill, dated as of July 20, 2020 (incorporated by reference to Exhibit 10.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on July 23, 2020).
10.58#	Employment Agreement by and between Windtree and Diane Carman, dated as of July 1, 2021 (incorporated by reference to Exhibit 10.54 to Windtree's Form 10-K, as filed with the SEC on March 31, 2022).
10.59	Form of Inducement Letter dated January 20, 2023 (incorporated by reference to Exhibit 10.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on January 26, 2023).
10.60	Form of Inducement Letter dated February 21, 2023 (incorporated by reference to Exhibit 10.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on February 22, 2023).
10.61*††	License, Development and Commercialization Agreement, by and between the Company and Lee's Pharmaceutical (HK) Ltd., dated January 12, 2024.

10.62††	Exchange and Termination Agreement, by and between the Company and affiliates of Deerfield Management Company, L.P., effective upon January 24, 2024 (incorporated by reference to Exhibit 10.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on January 25, 2024).
10.63	Registration Rights Agreement, by and between the Company and affiliates of Deerfield Management Company, L.P., effective upon January 24, 2024 (incorporated by reference to Exhibit 10.2 to Windtree's Current Report on Form 8-K, as filed with the SEC on January 25, 2024).
10.64+	Form of Securities Purchase Agreement by and between Windtree Therapeutics, Inc. and the Buyers named therein, dated April 2, 2024 (incorporated by reference to Exhibit 10.1 to Windtree's Current Report on Form 8-K, as filed with the SEC on April 8, 2024).
10.65+	Form of Registration Rights Agreement, by and between Windtree Therapeutics, Inc. and the Buyers named therein, dated April 2, 2024 (incorporated by reference to Exhibit 10.2 to Windtree's Current Report on Form 8-K, as filed with the SEC on April 8, 2024).
21.1	Subsidiaries of Windtree (incorporated by reference to Exhibit 21.1 to Windtree's Annual Report on Form 10-K, as filed with the SEC on April 16, 2019).
23.1*	Consent of EisnerAmper LLP, independent registered public accounting firm.
31.1*	Certification of the Principal Executive Officer and Principal Financial Officer, as required by Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*	Certification of the Principal Executive Officer and Principal Financial Officer as required by 18 U.S.C. 1350.
97.1*	Windtree Therapeutics, Inc. Compensation Recovery Policy.
101.INS*	Inline XBRL Instance Document (the Instance Document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document) (1).
101.SCH*	Inline XBRL Taxonomy Extension Schema Document (1).
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document (1).
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document (1).
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document (1).
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document (1).
104	Cover Page Interactive Data File (formatted as Inline XBRL and combined in Exhibit 101.1)

* Filed herewith.

Compensation Related Contract.

† Confidential treatment received for certain portions of this exhibit.

†† Certain confidential portions have been omitted from this exhibit pursuant to Item 601(b)(10)(iv) of Regulation S-K.

+ Schedules and exhibits have been omitted pursuant to Item 601(a)(5) of Regulation S-K. A copy of any omitted schedule and/or exhibit will be furnished to the SEC upon request.

(1) These Interactive Data Files shall not be deemed filed for purposes of Section 11 or 12 of the Securities Act of 1933, as amended, or Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to liability under those sections.

SIGNATURES

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

WINDTREE THERAPEUTICS, INC.

Date: April 16, 2024

By: /s/ Craig E. Fraser
Craig E. Fraser
Director, President, and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	**Title**	**Date**
/s/ Craig E. Fraser Craig E. Fraser	Director, President, and Chief Executive Officer (Principal Executive Officer and Principal Financial Officer) (Chairman of the Board)	April 16, 2024
/s/ Daniel E. Geffken Daniel E. Geffken	Director	April 16, 2024
/s/ Robert Scott, M.D. Robert Scott, M.D.	Director	April 16, 2024
/s/ Leslie J. Williams Leslie J. Williams	Director	April 16, 2024
/s/ Mark Strobeck, Ph.D. Mark Strobeck Ph.D.	Director	April 16, 2024

WINDTREE THERAPEUTICS, INC. AND SUBSIDIARIES

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WINDTREE THERAPEUTICS, INC. AND SUBSIDIARIES

Report Of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of
Windtree Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Windtree Therapeutics, Inc. and Subsidiaries (the "Company") as of December 31, 2023 and 2022, and the related consolidated statements of operations, changes in mezzanine equity and stockholders' equity, and cash flows for the years then ended, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the consolidated financial position of the Company as of December 31, 2023 and 2022, and the consolidated results of their operations and their cash flows for the years then ended, in conformity with accounting principles generally accepted in the United States of America.

Going Concern

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 3 to the financial statements, the Company has suffered recurring losses from operations and expects to incur losses for the foreseeable future, that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 3. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audit also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Fair value of indefinite-lived intangible assets

As reflected in the Company's consolidated financial statements, indefinite-lived intangible assets totaled $25.3 million and consisted of in-process research and development (IPR&D) at December 31, 2023. As discussed in Note 4 to the consolidated financial statements, IPR&D assets are tested by management for impairment at least annually, or when events or changes in the business environment indicate that the fair value of the IPR&D assets are more likely than not less than their carrying value. The interim and annual quantitative impairment tests require that management estimate the fair value of the IPR&D assets in order to determine if the asset is impaired.

Auditing the estimated fair value of the IPR&D assets was complex and involved a high degree of subjectivity due to the significant estimation uncertainty involved in determining the fair value of the IPR&D assets. In particular, the estimated fair value of the IPR&D assets was sensitive to significant assumptions such as the probability of achieving development and commercial success for the products, the size of the addressable patient population, the anticipated pricing for the products, the probability, timing and amount of any upfront or milestone payments from potential partnering agreements, the timing and amount of additional clinical trial costs to be incurred by the Company, and the discount rate.

To test the estimated fair value of the Company's IPR&D assets, we performed audit procedures that included, among others, testing the significant assumptions used to develop the estimate and evaluating the completeness and accuracy of the underlying data used by the Company in its analyses. For example, we compared the probability of achieving development and commercial success for the products to studies published in medical journals evaluating clinical advancement and approval rates for similar products. We compared the estimated size of the addressable patient population to an industry database that tracks healthcare information and we compared the anticipated pricing and upfront/milestone payment assumptions to publicly available data supporting transactions and products of a similar nature. We compared the anticipated future clinical trial costs to actual costs incurred by the Company for past comparable trials. We also involved internal valuation specialists to assist in our evaluation of the discount rate used by the Company.

/s/ EisnerAmper LLP

We have served as the Company's auditor since 2022.

EISNERAMPER LLP
Philadelphia, Pennsylvania
April 16, 2024

WINDTREE THERAPEUTICS, INC. AND SUBSIDIARIES
Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31, 2023	December 31, 2022
ASSETS		
Current Assets:		
Cash and cash equivalents	$ 4,319	$ 6,172
Prepaid expenses and other current assets	1,060	1,205
Total current assets	5,379	7,377
Property and equipment, net	183	262
Restricted cash	150	154
Operating lease right-of-use assets	1,444	1,853
Intangible assets	25,250	25,250
Goodwill	-	3,058
Total assets	$ 32,406	$ 37,954
LIABILITIES, MEZZANINE EQUITY & STOCKHOLDERS' EQUITY		
Current Liabilities:		
Accounts payable	$ 809	$ 249
Accrued expenses	1,618	1,552
Operating lease liabilities - current portion	436	404
Loans payable - current portion	233	252
Other current liabilities	900	-
Total current liabilities	3,996	2,457
Operating lease liabilities - non-current portion	1,161	1,624
Restructured debt liability - contingent milestone payments	15,000	15,000
Other liabilities	3,800	3,800
Deferred tax liabilities	5,058	5,061
Total liabilities	29,015	27,942
Mezzanine Equity:		
Series A redeemable preferred stock, $0.001 par value; 0 and 40,000 shares authorized; 0 and 38,610.119 shares issued and outstanding at 2023 and 2022, respectively	-	-
Stockholders' Equity:		
Preferred stock, $0.001 par value; 5,000,000 and 4,960,000 shares authorized; 0 shares issued and outstanding at 2023 and 2022, respectively	-	-
Common stock, $0.001 par value; 120,000,000 shares authorized; 5,996,587 and 772,203 shares issued at 2023 and 2022, respectively; 5,996,586 and 772,202 shares outstanding at 2023 and 2022, respectively	6	-
Additional paid-in capital	851,262	837,598
Accumulated deficit	(844,823)	(824,532)
Treasury stock (at cost); 1 share	(3,054)	(3,054)
Total stockholders' equity	3,391	10,012
Total liabilities, mezzanine equity & stockholders' equity	$ 32,406	$ 37,954

See notes to consolidated financial statements

WINDTREE THERAPEUTICS, INC. AND SUBSIDIARIES
Consolidated Statements of Operations
(in thousands, except per share data)

	Year Ended December 31,	
	2023	**2022**
Expenses:		
Research and development	$ 8,341	$ 11,099
General and administrative	9,198	10,790
Loss on impairment of goodwill	3,058	12,624
Loss on impairment of intangible assets	-	6,820
Total operating expenses	20,597	41,333
Operating loss	(20,597)	(41,333)
Other income (expense):		
Interest income	325	109
Interest expense	(50)	(53)
Other income, net	31	702
Total other income, net	306	758
Loss before income taxes	(20,291)	(40,575)
Deferred income tax benefit	-	1,367
Net loss	$ (20,291)	$ (39,208)
Net loss per common share		
Basic and diluted	$ (5.24)	$ (62.23)
Weighted average number of common shares outstanding		
Basic and diluted	3,876	630

See notes to consolidated financial statements

WINDTREE THERAPEUTICS, INC. AND SUBSIDIARIES
Consolidated Statements of Changes in Mezzanine Equity and Stockholders' Equity
(in thousands)

	Mezzanine Equity		Stockholders' Equity						
	Series A Preferred Stock		Common Stock				Treasury Stock		
	Shares	Amount	Shares	Amount	Additional Paid-in Capital	Accumulated Deficit	Shares	Amount	Total
Balance - December 31, 2021	**-**	**$ -**	**565**	**$ -**	**$ 830,259**	**$ (785,324)**	**-**	**$ (3,054)**	**$ 41,881**
Net loss	-	-	-	-	-	(39,208)	-	-	(39,208)
Issuance of Series A Preferred Stock	39	-	-	-	-	-	-	-	-
Issuance of common stock, ATM Program, net of issuance costs of $131	-	-	207	-	4,253	-	-	-	4,253
Stock-based compensation expense	-	-	-	-	3,086	-	-	-	3,086
Balance - December 31, 2022	**39**	**$ -**	**772**	**$ -**	**$ 837,598**	**$ (824,532)**	**-**	**$ (3,054)**	**$ 10,012**
Net loss	-	-	-	-	-	(20,291)	-	-	(20,291)
Redemption of Series A Preferred Stock	(39)	-	-	-	-	-	-	-	-
Vesting of restricted stock units	-	-	2	-	-	-	-	-	-
Exercise of common stock warrants, net of expenses of $276	-	-	118	1	842	-	-	-	843
Reverse split adjustments - fractional share round ups	-	-	17	-	-	-	-	-	-
Issuance of common stock and common stock warrants, net of issuance costs of $1,630	-	-	4,239	4	10,790	-	-	-	10,794
Issuance of common stock, ATM Program, net of issuance costs of $23	-	-	849	1	754	-	-	-	755
Stock-based compensation expense	-	-	-	-	1,278	-	-	-	1,278
Balance - December 31, 2023	**-**	**$ -**	**5,997**	**$ 6**	**$ 851,262**	**$ (844,823)**	**-**	**$ (3,054)**	**$ 3,391**

See notes to consolidated financial statements

WINDTREE THERAPEUTICS, INC. AND SUBSIDIARIES
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,	
	2023	**2022**
Cash flows from operating activities:		
Net loss	$ (20,291)	$ (39,208)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	82	533
Stock-based compensation	1,278	3,086
Non-cash lease expense	409	528
Loss on impairment of goodwill	3,058	12,624
Loss on impairment of intangible assets	-	6,820
Loss on sale and disposal of property and equipment	12	19
Deferred income tax benefit	-	(1,367)
Unrealized gain on foreign exchange rate changes	(3)	(710)
Changes in assets and liabilities:		
Prepaid expenses and other current assets	923	1,076
Accounts payable	560	(444)
Accrued expenses	66	(1,838)
Operating lease liabilities	(431)	(571)
Other current liabilities	900	-
Net cash used in operating activities	(13,437)	(19,452)
Cash flows from investing activities:		
Proceeds from sale of property and equipment	-	210
Purchase of property and equipment	(15)	(13)
Net cash (used in) provided by investing activities	(15)	197
Cash flows from financing activities:		
Proceeds from issuance of common stock and warrants, net of issuance costs	10,794	-
Proceeds from exercise of common stock warrants, net of expenses	843	-
Proceeds from ATM Program, net of issuance costs	755	4,253
Principal payments on loans payable	(797)	(1,174)
Net cash provided by financing activities	11,595	3,079
Net decrease in cash, cash equivalents, and restricted cash	(1,857)	(16,176)
Cash, cash equivalents, and restricted cash - beginning of year	6,326	22,502
Cash, cash equivalents, and restricted cash - end of year	$ 4,469	$ 6,326
Supplementary disclosure of non-cash activity:		
Fair value of January 2023 warrant modifications related to the January 2023 warrant exercise inducement	$ 1,238	$ -
Fair value of February 2023 warrant modifications related to the February 2023 warrant exercise inducement	274	-
Prepayment of insurance through third-party financing	778	1,132

See notes to consolidated financial statements

WINDTREE THERAPEUTICS, INC. AND SUBSIDIARIES

Note 1 – The Company and Description of Business

We are a biotechnology company focused on advancing early and late-stage innovative therapies for critical conditions and diseases. Our portfolio of product candidates includes istaroxime, a Phase 2 candidate with sarco endoplasmic reticulum Ca2+ -ATPase 2a, or SERCA2a, activating properties for acute heart failure and associated cardiogenic shock, preclinical SERCA2a activators for heart failure, rostafuroxin for the treatment of hypertension in patients with a specific genetic profile, and a preclinical atypical protein kinase C iota, or aPKCi, inhibitor (topical and oral formulations), being developed for potential application in rare and broad oncology indications. We also have a licensing business model with partnership out-licenses currently in place.

Our lead product candidate, istaroxime, is a first-in-class, dual-acting agent being developed to increase blood pressure and improve cardiac function in patients with cardiogenic shock and to improve cardiac function in patients with acute heart failure, or AHF, and reverse the hypotension and hypoperfusion associated with heart failure that deteriorates to cardiogenic shock. Istaroxime demonstrated significant improvement in both systolic and diastolic aspects of cardiac function and was generally well tolerated in three Phase 2 clinical trials. Istaroxime has been granted Fast Track designation for the treatment of AHF by the U.S. Food and Drug Administration, or FDA. Based on the profile observed in our Phase 2 clinical studies in AHF, where istaroxime significantly improved cardiac function and systolic blood pressure, or SBP, in acute decompensated heart failure patients and had a favorable renal profile, we initiated a Phase 2 global clinical study, or the SEISMiC Study, to evaluate istaroxime for the treatment of early cardiogenic shock (Society for Cardiovascular Angiography and Interventions, or SCAI, Stage B shock), a severe form of AHF characterized by very low blood pressure and risk for hypoperfusion to critical organs and mortality. In April 2022, we announced our observations in the SEISMiC Study that istaroxime rapidly and significantly increased SBP while also improving cardiac function and preserving renal function. We believe that istaroxime has the potential to fulfill an unmet need in early and potentially more severe cardiogenic shock. We further believe that the data from the SEISMiC Study supports continued development in both cardiogenic shock and AHF. In the fourth quarter of 2023, we initiated an extension to the SEISMiC Study, or the SEISMiC Extension, to evaluate a longer dosing period and to continue to characterize the effects of istaroxime, including activation of SERCA2a. The SEISMiC Extension study is expected to enroll up to 30 subjects with SCAI Stage B cardiogenic shock with data anticipated in the second half of 2024. Additionally, we have recently initiated a small study in more severe SCAI Stage C cardiogenic shock, or SEISMiC C, to evaluate the safety and efficacy of istaroxime in cardiogenic shock patients who are also receiving standard of care rescue therapy for shock. The SEISMiC C study is expected to enroll up to 20 subjects with SCAI Stage C cardiogenic shock with enrollment anticipated to be completed in late 2024. Our ability to complete both of these studies with their intended sample size is dependent upon us securing adequate resourcing for the program through financing efforts or business development activities.

Our heart failure cardiovascular portfolio also includes SERCA2a activators. This research program is evaluating these preclinical product candidates, including oral and intravenous SERCA2a activator heart failure compounds. These candidates would potentially be developed for both acute decompensated and chronic out-patient heart failure. In addition, our cardiovascular drug product candidates include rostafuroxin, a novel product candidate for the treatment of hypertension in patients with a specific genetic profile. We are pursuing potential licensing arrangements and/or other strategic partnerships and do not intend to advance rostafuroxin without securing such an arrangement or partnership.

Our cardiovascular assets and programs are associated with a regional licensed partnership with Lee's Pharmaceutical (HK) Ltd., or Lee's (HK), for the development and commercialization of our product candidate, istaroxime, in Greater China. In addition to istaroxime, the agreement also licenses our preclinical next-generation SERCA2a activators, known as dual mechanism SERCA2a activators, and rostafuroxin, a Phase 2 product candidate for hypertension associated with specific genotypes. In addition, we are supporting the efforts of Lee's (HK) in starting a Phase 3 trial in AHF with istaroxime. Further, we are engaged in discussions regarding potential global licensing partnerships outside of Lee's (HK) territory.

On April 2, 2024, we entered into an Asset Purchase Agreement, or the Asset Purchase Agreement, with Varian Biopharmaceuticals, Inc., or Varian. Pursuant to the Asset Purchase Agreement, we purchased all of the assets of Varian's business associated with a Licence Agreement, dated as of July 5, 2019, by and between Varian and Cancer Research Technology Limited, or the Licence Agreement, including the Licence Agreement, all rights in molecules and compounds subject to the Licence Agreement, know-how and inventory of drug substance, or the Transferred Assets. The Transferred Assets include a novel, potential high-potency, specific, aPKCi with possible broad use in oncology as well as certain rare malignant diseases. The asset platform includes two formulations (topical and oral) of an aPKCi inhibitor. We plan to advance investigational new drug, or IND, enabling activities and are in the process of determining the expected clinical development plan for the platform.

Our ability to advance our development programs is dependent upon our ability to secure additional capital in both the near and long-term, through public or private securities offerings; convertible debt financings; and/or potential strategic opportunities, including licensing agreements, drug product development, and marketing collaboration arrangements, pharmaceutical research cooperation arrangements, and/or other similar transactions in geographic markets, including the U.S., and/or through potential grants and other funding commitments from U.S. government agencies, in each case, if available. We have engaged with potential counterparties in various markets and will continue to pursue non-dilutive sources of capital as well as potential private and public securities offerings. There can be no assurance, however, that we will be able to identify and enter into public or private securities offerings on acceptable terms and in amounts sufficient to meet our needs or qualify for non-dilutive funding opportunities under any grant programs sponsored by U.S. government agencies, private foundations, and/or leading academic institutions, or identify and enter into any strategic transactions that will provide the additional capital that we will require. If none of these alternatives is available, or if available and we are unable to raise sufficient capital through such transactions, we potentially could be forced to limit or cease our development activities, which would have a material adverse effect on our business, financial condition, and results of operations.

WINDTREE THERAPEUTICS, INC. AND SUBSIDIARIES

Note 2 – Basis of Presentation

The consolidated financial statements are prepared in accordance with accounting principles generally accepted in the U.S., or US GAAP, and include accounts of Windtree Therapeutics, Inc. and its wholly owned subsidiaries. Intercompany balances and transactions have been eliminated in consolidation. All adjustments (consisting of normally recurring accruals) considered for fair presentation have been included.

The accompanying consolidated financial statements reflect the 1-for-50 reverse split of our common stock that was approved by our Board of Directors and stockholders and made effective on February 24, 2023. All share and per share information herein that relates to our common stock prior to the effective date has been retroactively restated to reflect the reverse stock split.

Note 3 – Going Concern and Management's Plans

We are subject to risks common to companies in the biotechnology industry, including but not limited to, the need for additional capital, risks of failure of preclinical and clinical studies, the need to obtain marketing approval and reimbursement for any drug product candidate that we may identify and develop, the need to successfully commercialize and gain market acceptance of our product candidates, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development of technological innovations by competitors, and risks associated with our international operations in Taiwan and activities abroad, including but not limited to having foreign suppliers, manufacturers, and clinical sites in support of our development activities.

We have incurred net losses since inception. Our net loss was $20.3 million and $39.2 million, respectively, for the years ended December 31, 2023 and 2022. Included in our net loss for the year ended December 31, 2023 is a non-cash loss on impairment of goodwill of $3.1 million. Included in our net loss for the year ended December 31, 2022 are a non-cash loss on impairment of goodwill of $12.6 million, a non-cash loss on impairment of intangible assets related to rostafuroxin of $6.8 million and a related $1.4 million deferred income tax benefit (See the section titled, "Note 4 – Accounting Policies"). We expect to continue to incur operating losses for at least the next several years. As of December 31, 2023, we had an accumulated deficit of $844.8 million. Our future success is dependent on our ability to fund and develop our product candidates, and ultimately upon our ability to attain profitable operations. We have devoted substantially all of our financial resources and efforts to research and development and general and administrative expense to support such research and development. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital, and accordingly, our ability to execute our future operating plans.

On November 9, 2023, we entered into an At-The-Market Offering Agreement with Ladenburg Thalmann & Co. Inc., or Ladenburg, pursuant to which we may offer and sell, from time to time at our sole discretion, shares of our common stock through Ladenburg as agent and/or principal (subject to the limitations of General Instruction I.B.6 of Form S-3) through an at-the-market program, or the 2023 ATM Program (See the section titled, "Note 11 – Mezzanine Equity and Stockholders' Equity").

The shares of common stock we may issue or sell under the 2023 ATM Program are registered under our Registration Statement on Form S-3 (File No. 333-261878), which was declared effective by the SEC on January 3, 2022. We are currently subject to the limitations contained in General Instruction I.B.6 of Form S-3. As a result, we are limited to selling no more than one-third of the aggregate market value of the equity held by non-affiliates, or the public float, during any 12-month period, and, as of April 16, 2024, we had sold substantially all that we are permitted to sell under the Form S-3 pursuant to General Instruction I.B.6. If our public float increases, we will have additional availability under such limitations, and if our public float increases to $75 million or more, we will no longer be subject to such limitations. There can be no assurance that our public float will increase or that we will no longer be subject to such limitations.

During the fourth quarter of 2023, we sold 848,367 shares of our common stock under the 2023 ATM Program resulting in aggregate gross and net proceeds to us of approximately $0.8 million. During the first quarter of 2024, we sold 2,576,153 shares of our common stock under the 2023 ATM Program resulting in aggregate gross and net proceeds to us of approximately $1.4 million.

As of December 31, 2023, we had cash and cash equivalents of $4.3 million and current liabilities of $4.0 million. On April 2, 2024, we entered into a Securities Purchase Agreement, or the Purchase Agreement, with the buyers named therein, or the Buyers. Pursuant to the Purchase Agreement, we agreed to sell senior convertible notes, or the Notes, for $1.5 million of gross proceeds. As a result, we believe that we have sufficient resources available to fund our business operations through April 2024. We do not have sufficient cash and cash equivalents as of the date of this Annual Report on Form 10-K to support our operations for at least the 12 months following the date that the financial statements are issued. These conditions raise substantial doubt about our ability to continue as a going concern.

To alleviate the conditions that raise substantial doubt about our ability to continue as a going concern, management plans to secure additional capital, potentially through a combination of public or private securities offerings, convertible debt financings, and/or strategic transactions, including potential licensing arrangements, alliances, and drug product collaborations focused on specified geographic markets; however, none of these alternatives are committed at this time. There can be no assurance that we will be successful in obtaining sufficient funding on terms acceptable to us to fund continuing operations, if at all, or identify and enter into any strategic transactions that will provide the capital that we will require. The failure to obtain sufficient additional capital on acceptable terms when needed would have a material adverse effect on our business, results of operations, and financial condition. Accordingly, management has concluded that substantial doubt exists with respect to our ability to continue as a going concern for at least 12 months after the issuance of the accompanying financial statements.

The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the normal course of business, and do not include any adjustments relating to recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might be necessary should we be unable to continue as a going concern.

Note 4 – Accounting Policies

Principles of Consolidation

The consolidated financial statements are prepared in accordance with US GAAP and include accounts of Windtree Therapeutics, Inc. and our wholly owned subsidiary, CVie Investments Limited and its wholly owned subsidiary, CVie Therapeutics Limited, or CVie Therapeutics, and a presently inactive subsidiary, Discovery Laboratories, Inc. (formerly known as Acute Therapeutics, Inc.).

Intangible Assets and Goodwill

We record acquired intangible assets and goodwill based on estimated fair value. The identifiable intangible assets resulting from the CVie Therapeutics acquisition in December 2018 relate to in-process research and development, or IPR&D, of istaroxime and rostafuroxin. The IPR&D assets are considered indefinite-lived intangible assets until completion or abandonment of the associated research and development efforts. IPR&D is not amortized but reviewed for impairment at least annually, or when events or changes in the business environment indicate the carrying value may be impaired.

When testing our indefinite-lived intangible assets and goodwill for impairment, we can elect to perform a qualitative assessment to determine if it is more likely than not that the fair values of our indefinite-lived intangible assets and our reporting unit are less than their respective carrying values. Such qualitative factors can include, among others, industry and market conditions, overall financial performance, and relevant entity-specific events. If we conclude based on our qualitative assessment that it is more likely than not that the fair value of our indefinite-lived intangible assets or reporting unit are less than their respective carrying values, we perform a quantitative assessment. When conducting our annual impairment test of indefinite-lived intangible assets and goodwill as of December 1, 2023 and 2022, we elected to perform a quantitative assessment.

When performing the quantitative impairment assessment for our indefinite-lived IPR&D intangible assets, we estimate the fair values of the assets using the multi-period excess earnings method, or MPEEM. MPEEM is a variation of the income approach which estimates the fair value of an intangible asset based on the present value of the incremental after-tax cash flows attributable to the intangible asset. Significant factors considered in the calculation of IPR&D intangible assets include the risks inherent in the development process, including the likelihood of achieving commercial success and the cost and related time to complete the remaining development. Future cash flows for each project were estimated based on forecasted revenue and costs, taking into account the expected product life cycles, market penetration, and growth rates. Other significant estimates and assumptions inherent in this approach include (i) the amount and timing of the projected net cash flows associated with the IPR&D assets, (ii) the discount rate, which seeks to reflect the various risks inherent in the projected cash flows; and (iii) the tax rate, which considers geographic diversity of the projected cash flows. While we use the best available information to prepare our cash flows and discount rate assumptions, actual future cash flows could differ significantly based on the commercial success of the related drug candidates and market conditions which could result in future impairment charges related to our indefinite-lived intangible asset balances.

Based on our annual quantitative impairment assessment of our indefinite-lived IPR&D intangible assets as of December 1, 2023, we concluded that the assets were not impaired.

As part of our annual quantitative impairment assessment of indefinite-lived IPR&D intangible assets as of December 1, 2022, we reassessed certain assumptions related to our rostafuroxin drug candidate due to the continued difficulties in current macroeconomic conditions which have continued to make it more challenging to secure the funding needed to conduct the additional Phase 2 clinical trial and have therefore further delayed our intended development of rostafuroxin. As a result, we concluded that the fair value of the IPR&D related to our rostafuroxin drug candidate was less than its carrying value. We estimated the fair value of the asset using MPEEM and determined that the fair value as of December 1, 2022 was approximately $2.9 million. We then compared this fair value to the carrying value of approximately $9.7 million, and recorded an additional loss on impairment of intangible assets of $6.8 million related to the IPR&D of our rostafuroxin drug candidate. We also reassessed the assumptions related to the fair value of the IPR&D related to our istaroxime drug candidate. The estimated fair value exceeded the carrying value of that asset. As a result, no impairment charge was recognized related to the IPR&D of our istaroxime drug candidate.

Goodwill represents the excess of the purchase price over the fair value of assets acquired and liabilities assumed in a business combination and is not amortized. It is reviewed for impairment at least annually or when events or changes in the business environment indicate that its carrying value may be impaired. Our company consists of one reporting unit. In order to perform the quantitative goodwill impairment test, we compare the estimated fair value of our reporting unit to its carrying value. If the fair value exceeds the carrying value, no further evaluation is required, and no impairment exists. If the carrying value exceeds the fair value, the difference between the carrying value and the fair value is recorded as an impairment loss, the amount of which may not exceed the total amount of goodwill. When performing a goodwill impairment assessment, we estimate the fair value of our reporting unit, including the use of the quoted market price and related market capitalization of our common stock, adjusted for an estimated control premium based on transactions completed by comparable companies.

In accordance with applicable accounting standards, we are required to review intangible assets and goodwill for impairment on an annual basis, or more frequently where there is an indication of impairment. Throughout the year, we consider whether any events or changes in the business environment have occurred which indicate that goodwill may be impaired. For example, a significant decline in the closing share price of our common stock and market capitalization may suggest that the fair value of our reporting unit has fallen below its carrying value, indicating that an interim goodwill impairment test is required. Accordingly, we monitor changes in our share price during interim periods between annual impairment tests and consider overall stock market conditions, the underlying reasons for the decline in our share price, the significance of the decline, and the duration of time that our securities have been trading at a lower value.

Since early 2022, we have experienced a declining trend in the closing share price of our common stock, on a split-adjusted basis. As a result, we performed the required interim goodwill impairment test in the second and third quarters of 2022 as well as the annual goodwill quantitative test as of December 1, 2022 and determined that the fair value of our reporting unit was more likely than not less than its carrying value. For the year ended December 31, 2022, we recorded an aggregate loss on goodwill of $12.6 million within operating expenses in our consolidated statement of operations.

During each of the first and second quarters of 2023, the continued declining trend in the closing share price of our common stock, on a split-adjusted basis, suggested that the fair value of our reporting unit was more likely than not less than its carrying value. As a result, in each quarter, we performed the required interim goodwill impairment test consistent with the methodology described above and determined that the fair value of our reporting unit was more likely than not less than its carrying value. We recorded a loss on impairment of goodwill of $0.5 million in the first quarter of 2023 and an additional loss of $2.6 million, representing the remaining balance of goodwill, in the second quarter of 2023. For the year ended December 31, 2023, the aggregate loss on impairment of goodwill was $3.1 million, recognized within operating expenses in our consolidated statement of operations. As of December 31, 2023, goodwill was zero on our consolidated balance sheet.

The following table represents identifiable intangible assets and goodwill as of December 31, 2023 and 2022:

(in thousands)	December 31, 2023	December 31, 2022
Istaroxime drug candidate	$ 22,340	$ 22,340
Rostafuroxin drug candidate	2,910	2,910
Intangible assets	25,250	25,250
Goodwill	$ -	$ 3,058

Foreign Currency Transactions

The functional currency for our foreign subsidiaries is the US Dollar. We remeasure monetary assets and liabilities that are not denominated in the functional currency at exchange rates in effect at the end of each period. Gains and losses from the remeasurement of foreign currency transactions are recognized in Total other income, net. Foreign currency transactions resulted in gains of $0.7 million for the year ended December 31, 2022. Foreign currency transactions for the year ended December 31, 2023 are immaterial.

Use of Estimates

The preparation of financial statements in conformity with US GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Cash and Cash Equivalents

Cash and cash equivalents are held at domestic and foreign financial institutions and consist of liquid investments and money market funds that are readily convertible into cash.

Concentration of Credit Risk

Financial instruments, which potentially subject us to credit risk, consist principally of cash and cash equivalents. All cash and cash equivalents are held in U.S. financial institutions and money market funds. At times, we may maintain cash balances in excess of the federally insured amount of $250,000 per depositor, per insured bank, for each account ownership category. Although we currently believe that the financial institutions with whom we do business will be able to fulfill their commitments to us, there is no assurance that those institutions will be able to continue to do so. We have not experienced any credit losses associated with our balances in such accounts.

Fair Value of Financial Instruments

Our financial instruments consist principally of cash and cash equivalents and restricted cash. The fair values of our cash equivalents are based on quoted market prices. The carrying value of cash equivalents is equal to their respective fair values at December 31, 2023 and 2022, respectively. Accounts payable and accrued expenses are carried at cost, which approximates fair value because of their short maturity. The carrying value of loans payable (including current installments) approximates fair value based on a comparison of interest rates on the loan to current market rates considering our credit risk.

Property and Equipment

Property and equipment are recorded at cost and depreciated using the straight-line method over the estimated useful lives of the assets (generally three to ten years). Leasehold improvements are amortized over the shorter of the estimated useful lives or the remaining term of the lease. Repairs and maintenance costs are charged to expense as incurred.

Restricted Cash

Restricted cash consists principally of a $140,000 certificate of deposit held by our bank as collateral for a letter of credit in the same notional amount held by our landlord to secure our obligations under our lease agreement dated May 26, 2004 for our headquarters location in Warrington, Pennsylvania and $10,000 in deposits held by our landlord for our offices in Taipei, Taiwan.

Leases

Leases are accounted for under Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 842, *Leases*, or ASC 842. At the inception of an arrangement, we determine whether an arrangement is, or contains, a lease based on the unique facts and circumstances present in the arrangement. An arrangement is, or contains, a lease if the arrangement conveys the right to control the use of an identified asset for a period of time in exchange for consideration. Leases with a term greater than one year are generally recognized on the balance sheet as operating lease right-of-use assets and current and non-current operating lease liabilities, as applicable. It is our policy not to recognize on the balance sheet leases with terms of 12 months or less. We typically only include the initial lease term in our assessment of a lease arrangement. Options to extend a lease are not included in our assessment unless there is reasonable certainty that we will renew.

Operating lease liabilities and their corresponding operating lease right-of-use assets are recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in our leases is typically not readily determinable. As a result, we utilize our incremental borrowing rate, which reflects the fixed rate at which we could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment.

At the inception of a contract, we assess whether the contract is, or contains, a lease. The assessment is based on: (i) whether the contract involves the use of a distinct identified asset, (ii) whether we obtain the right to substantially all the economic benefit from the use of the asset throughout the period, and (iii) whether we have the right to direct the use of the asset.

We evaluate the classification of our leases as either finance leases or operating leases. A lease is classified as a finance lease if any one of the following criteria are met: the lease transfers ownership of the asset by the end of the lease term, the lease contains an option to purchase the asset that is reasonably certain to be exercised, the lease term is for a major part of the remaining useful life of the asset, the present value of the lease payments equals or exceeds substantially all of the fair value of the asset, or the leased asset is of such a specialized nature that it is expected to have no alternative use to the lessor at the end of the lease. A lease is classified as an operating lease if it does not meet any of these criteria. Currently, all of our leases are classified as operating leases.

Lease cost for our operating leases is recognized on a straight-line basis over the lease term. Included in lease cost are any variable lease payments incurred in the period that are not included in the initial lease liability and lease payments incurred in the period for any leases with an initial term of 12 months or less.

Long-lived Assets

Our long-lived assets, primarily consisting of property and equipment, are reviewed for impairment when events or changes in circumstances indicate that the carrying value of an asset may not be recoverable, or its estimated useful life has changed significantly. When the undiscounted cash flows of an asset are less than its carrying value, an impairment is recorded and the asset is written down to estimated value. No impairment was recorded during the years ended December 31, 2023 and 2022 as management believes there are no circumstances that indicate that the carrying value of the assets will not be recoverable.

Collaborative Arrangements

We account for collaborative arrangements in accordance with applicable accounting guidance provided in ASC Topic 808, *Collaborative Arrangements*. See the section titled, “Note 13 – Collaboration, Licensing and Research Funding Agreements”

Severance

In July 2023, we entered into a separation agreement with an executive, which provides that the former employee will be entitled to receive (i) a severance amount equal to the sum of the employee's base salary then in effect and (ii) subject to certain exceptions, a pro rata bonus commensurate with the bonus awarded to other contract executives for the year 2023, prorated for the number of days of the employee's employment during 2023, and payable at the time that other contract executives are paid bonuses with respect to 2023. The severance amount related to the departure of this executive is approximately $0.5 million, which was recorded in general and administrative expense at the date of the separation, and will be paid ratably through July 2024. As of December 31, 2023, approximately $0.2 million was paid. The remaining liability as of December 31, 2023 is approximately $0.3 million and is included in accrued expenses.

In June 2023, we implemented certain reductions in headcount. The total severance cost for impacted employees is approximately $0.2 million, which was recorded in research and development expense at the date of the separations and will be paid ratably through December 2023. As of December 31, 2023, approximately $0.2 million of severance costs was paid. No further amounts were due as of December 31, 2023.

In January 2022, in order to focus our resources on the development of our istaroxime program, we began to reduce costs related to KL4 surfactant that were not already transferred to our licensee, Lee's Pharmaceutical (HK) Ltd., or Lee's (HK), and Zhaoke Pharmaceutical (Hefei) Co. Ltd., or Zhaoke, under the terms of our License, Development and Commercialization Agreement between us and Lee's (HK) dated as of June 12, 2017, as amended, or the Original License Agreement. These costs included certain reductions in headcount dedicated to KL4 surfactant and the decommissioning of both our analytical and technical support laboratory, which previously conducted release testing of active pharmaceutical ingredients, or APIs, and supportive research for our lyophilized and aerosolized KL4 surfactant, and our medical device development laboratory, which was previously used to conduct development activities and testing for our aerosol delivery system, or ADS, technologies. In February 2022, management communicated its commitment to provide severance payments to impacted employees, provided that they remained employed with us through their expected termination dates. The total severance cost for impacted employees was approximately $0.4 million, which was accrued over the service periods of the employees and was paid ratably through September 2022. All amounts due were paid in 2022.

Restructured Debt Liability – Contingent Milestone Payment

In conjunction with the November 2017 restructuring and retirement of long-term debt (See the section titled, "Note 10 – Restructured Debt Liability"), we have established a $15.0 million long-term liability for contingent milestone payments potentially due under the Exchange and Termination Agreement dated as of October 27, 2017, or the Milestone Agreement, between ourselves and affiliates of Deerfield Management Company L.P., or Deerfield. The liability has been recorded at full value of the contingent milestones and will continue to be carried at full value until the milestones are achieved and paid or milestones are not achieved and the liability is written off as a gain on debt restructuring.

On January 24, 2024, we and affiliates of Deerfield entered into an Exchange and Termination Agreement wherein Deerfield agreed to terminate its rights to receive the milestone payments (See the section titled, "Note 18 – Subsequent Events").

Research and Development

We account for research and development expense by the following categories: (a) product development and manufacturing, (b) clinical, medical, and regulatory operations, and (c) direct clinical and preclinical development programs. Research and development expense includes personnel, facilities, manufacturing and quality operations, pharmaceutical development, research, clinical, regulatory, other preclinical and clinical activities and medical affairs. Research and development costs are charged to operations as incurred in accordance with ASC Topic 730, *Research and Development*.

Stock-based Compensation

Stock-based compensation is accounted for under the fair value recognition provisions of ASC Topic 718, *Stock Compensation*, or ASC Topic 718. See the section titled, "Note 12 – Stock Options and Stock-based Employee Compensation," for a detailed description of our recognition of stock-based compensation expense. The fair value of stock option grants is recognized evenly over the vesting period of the options or over the period between the grant date and the time the option becomes non-forfeitable by the employee, whichever is shorter.

Warrant Accounting

We account for common stock warrants in accordance with applicable accounting guidance provided in ASC Topic 815, *Derivatives and Hedging – Contracts in Entity's Own Equity*, or ASC Topic 815, as either derivative liabilities or equity instruments depending on the specific terms of the warrant agreement.

Income Taxes

We account for income taxes in accordance with ASC Topic 740, *Accounting for Income Taxes*, or ASC Topic 740, which requires the recognition of deferred tax liabilities and assets for the expected future tax consequences of temporary differences between financial statement carrying amounts and the tax basis of assets and liabilities.

We use a recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. Because we have never realized a profit, management has fully reserved the net deferred tax asset since realization is not assured.

For the year ended December 31, 2022, we recorded a deferred income tax benefit of $1.4 million. The deferred income tax benefit recorded relates solely to the reduction of the deferred tax liabilities as a result of the loss on impairment of intangible assets related to rostafuroxin for the year ended December 31, 2022.

Net Loss per Common Share

Basic net loss per common share is computed by dividing net loss by the weighted average number of common shares outstanding for the period. Diluted net loss per common share is computed by giving effect to all potentially dilutive securities outstanding for the period. For the years ended December 31, 2023 and 2022,the number of shares of common stock potentially issuable upon the exercise of certain stock options and warrants, as well as of the vesting of restricted stock units, was 5.4 million and 0.4 million shares, respectively. As of December 31, 2023 and 2022, all potentially dilutive securities were anti-dilutive and therefore have been excluded from the computation of diluted net loss per common share.

We do not have any components of other comprehensive (loss) income.

Concentration of Suppliers

We currently obtain the APIs of our drug products from a single supplier. In addition, our drug products are produced at one contract manufacturer. These single source providers also perform various studies as well as quality control release and stability testing and other activities related to our development and manufacturing activities. At the present time these providers are located outside of the U.S. The loss of either the supplier of our APIs or our drug product contract manufacturer could have a material adverse effect on our operations.

Segment and Geographic Information

We currently operate in one operating segment, which is the research and development of products focused on cardiovascular disease. We are managed and operated as one business. A single management team that reports to the Chief Executive Officer comprehensively manages the entire business. We do not operate separate lines of business with respect to our product candidates. We operate primarily in the U.S. and Asia. Long-lived assets, consisting of intangible assets of $25.3 million, were located outside the U.S. as of December 31, 2023.

Note 5 – Fair Value Measurements

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date.

Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. The fair value hierarchy is based on three levels of inputs, of which the first two are considered observable and the last unobservable, as follows:

- Level 1 - Quoted prices in active markets for identical assets and liabilities.
- Level 2 - Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.
- Level 3 - Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

Fair Value on a Recurring Basis

The tables below categorize assets measured at fair value on a recurring basis as of December 31, 2023 and 2022:

	Fair Value	Fair value measurement using		
(in thousands)	December 31, 2023	Level 1	Level 2	Level 3
Cash equivalents:				
Money market funds	$ 3,532	$ 3,532	$ -	$ -
Total Assets	$ 3,532	$ 3,532	$ -	$ -

	Fair Value	Fair value measurement using		
(in thousands)	December 31, 2022	Level 1	Level 2	Level 3
Cash equivalents:				
Money market funds	$ 4,212	$ 4,212	$ -	$ -
Total Assets	$ 4,212	$ 4,212	$ -	$ -

Fair Value on a Non-Recurring Basis

The table below categorizes assets measured at fair value on a non-recurring basis for the periods presented:

	Fair Value	Fair value measurement using		
(in thousands)	December 31, 2023	Level 1	Level 2	Level 3
Goodwill	$ -	$ -	$ -	$ -

	Fair Value	Fair value measurement using		
(in thousands)	December 31, 2022	Level 1	Level 2	Level 3
Intangible assets:				
Rostafuroxin drug candidate	$ 2,910	$ -	$ -	$ 2,910
Goodwill	$ 3,058	$ -	$ -	$ 3,058

Certain of our assets were measured at fair value on a non-recurring basis during the years ended December 31, 2023 and 2022. The IPR&D intangible asset related to our rostafuroxin drug candidate was recorded at its estimated fair value as a result of the impairment tests performed during 2022. Our goodwill was also recorded at its estimated fair value as a result of the impairment tests performed in 2023 and 2022, which resulted in the goodwill being written down to zero as of June 30, 2023 (See the section titled, “Note 4 – Accounting Policies – Intangible Assets and Goodwill”).

Significant factors considered in estimating the fair value of the IPR&D intangible asset related to our rostafuroxin drug candidate include the risks inherent in the development process, including the likelihood of achieving commercial success and the cost and related time to complete the remaining development. Future cash flows for the IPR&D intangible asset were estimated based on forecasted revenue and costs, taking into account the expected product life cycle, market penetration, and growth rates. Other significant estimates and assumptions inherent in this approach include (i) the amount and timing of the projected net cash flows associated with the IPR&D intangible asset; (ii) the discount rate, which seeks to reflect the various risks inherent in the projected cash flows; and (iii) the tax rate, which considers geographic diversity of the projected cash flows. Quantitative information about the significant unobservable inputs used in the fair value measurement of the IPR&D intangible asset included a discount rate of 20.0% and a tax rate of 30.0% for 2022. While we use the best available information to prepare our cash flows and discount rate assumptions, actual future cash flows could differ significantly based on the commercial success of the related drug candidate and market conditions which could result in future impairment charges related to the indefinite-lived intangible asset balance.

In order to perform the goodwill impairment test, we compare the estimated fair value of our reporting unit to its carrying value. Significant factors considered in estimating the fair value of our reporting unit include the use of the quoted market price and related market capitalization of our common stock, adjusted for an estimated control premium based on transactions completed by comparable companies. Quantitative information about the significant unobservable inputs used in the fair value measurement of the reporting unit included an estimated control premium of 50% for both periods.

Note 6 – Property and Equipment

Property and equipment is comprised of the following:

(in thousands)	December 31, 2023	December 31, 2022
Leasehold improvements	$ 2,664	$ 2,649
Manufacturing, laboratory & office equipment	870	881
Furniture & fixtures	390	390
Subtotal	3,924	3,920
Accumulated depreciation and amortization	(3,741)	(3,658)
Property and equipment, net	$ 183	$ 262

Depreciation expense on property and equipment for the years ended December 31, 2023 and 2022 was $0.1 million and $0.5 million, respectively. During the first quarter of 2022, we determined that certain manufacturing and laboratory equipment assets related to the KL4 surfactant platform would be abandoned by March 31, 2022. We accelerated depreciation of these assets during the first quarter of 2022, resulting in $0.4 million of additional depreciation expense for the three months ended March 31, 2022. During the second quarter of 2022, the abandoned assets and certain other KL4 surfactant platform assets were disposed.

Note 7 – Accrued Expenses

Accrued expenses are comprised of the following:

(in thousands)	December 31, 2023	December 31, 2022
Research and development	$ 574	$ 786
Professional fees	279	459
Severance	261	-
Salaries, bonus and benefits	64	123
Other	440	184
Total accrued expenses	$ 1,618	$ 1,552

Note 8 - Loans Payable

In June 2023, we entered into an insurance premium financing and security agreement with IPFS Corporation. Under the agreement, we financed $0.8 million of certain premiums at a 7.24% fixed annual interest rate. Payments of approximately $126,000 are due monthly from July 2023 through April 2024. As of December 31, 2023, the outstanding principal of the loan was $0.2 million.

In June 2022, we entered into an insurance premium financing and security agreement with Bank Direct Capital Finance. Under the agreement, we financed $1.1 million of certain premiums at a 3.90% fixed annual interest rate. Payments of approximately $126,000 were due monthly from July 2022 through March 2023. As of December 31, 2022, the outstanding principal of the loan was $0.3 million. The balance of the loan was repaid during the first quarter of 2023.

Note 9 - Other Current Liabilities

In 2008, we entered into an Amended and Restated License Agreement with Philip Morris USA, Inc., or PMUSA, with respect to the U.S., or the U.S. License Agreement, and, as PMUSA had assigned its ex-U.S. rights to Philip Morris Products S.A., or PMPSA, effective on the same date and on substantially the same terms and conditions, we entered into a license agreement with PMPSA with respect to rights outside of the U.S., which we refer to, together with the U.S. License Agreement, as the PM License Agreements (See the section titled, "Note 13 – Collaboration, Licensing and Research Funding Agreements – Philip Morris USA Inc. and Philip Morris Products S.A.")

Amendment No. 1 to the Amended and Restated License Agreement with Philip Morris USA for Aerosolization Technology

On January 16, 2024, we entered into Amendment No. 1 to the U.S. License Agreement, effective as of January 17, 2024, or the U.S. License Agreement Amendment, which amended the U.S. License Agreement. The U.S. License Agreement licenses U.S. intellectual property rights to us in respect of our former acute pulmonary care platform that was globally outlicensed to the Licensee in August 2022. Pursuant to the U.S. License Agreement Amendment, we agreed to pay PMUSA (i) $100,000 by January 18, 2024, (ii) $400,000 no later than the earlier of (a) July 1, 2024 or (b) the Company receiving a specified amount of net proceeds from debt or equity financings occurring on or after January 17, 2024 and (iii) up to an aggregate of $1.4 million upon the achievement of certain development and regulatory milestones, which milestone payments are expected to be funded from corresponding milestone payments received from the Licensee. Additionally, under the U.S. License Agreement Amendment, the parties extinguished and released their respective rights, obligations and claims in respect of quarterly payments under Section 7.3 of the U.S. License Agreement as in effect immediately prior to January 17, 2024. The U.S. License Agreement Amendment also grants PMUSA the right to terminate the U.S. License Agreement upon 30 days prior written notice to us if we have not paid a milestone payment to PMUSA by January 1, 2028.

Amendment No. 1 to the License Agreement with Philip Morris Products for Aerosolization Technology

On January 16, 2024, we also entered into Amendment No. 1 to the License Agreement with PMPSA, effective as of January 17, 2024, or the PMPSA License Amendment, which amended the License Agreement, dated March 28, 2008, between us and PMPSA, or the PMPSA License Agreement. The PMPSA License Agreement licenses ex-U.S. intellectual property to us in respect of our former acute pulmonary care platform that was globally outlicensed to the Licensee in August 2022. Pursuant to the PMPSA License Amendment, we agreed to pay PMPSA (i) $75,000 by January 19, 2024, or the Upfront Payment, (ii) $325,000 no later than the earlier of (a) July 1, 2024 or (b) the Company receiving a specified amount of net proceeds from debt or equity financings occurring on or after January 17, 2024 (together with the Upfront Payment, the Fixed Payments) and (iii) up to an aggregate of $1.4 million upon the achievement of certain development and regulatory milestones, which milestone payments are expected to be funded from corresponding milestone payments received from the Licensee. Additionally, but contingent upon our timely payment of the Fixed Payments, the parties extinguished and released their respective rights, obligations and claims in respect of quarterly payments under Section 6.2 of the PMPSA License Agreement as in effect immediately prior to January 17, 2024.

Accounting for the PMUSA and PMPSA Payments

We have accounted for these payments as a recognized subsequent event in accordance with applicable accounting guidance provided in ASC Topic 855, *Subsequent Events.* For the year ended December 31, 2023, we accrued $0.9 million for payments to PMUSA and PMPSA to be paid in 2024.

Note 10 – Restructured Debt Liability

On October 27, 2017, we and Deerfield entered into the Exchange and Termination Agreement, or the Milestone Agreement, pursuant to which (i) promissory notes evidencing a loan with affiliates of Deerfield in the aggregate principal amount of $25.0 million and (ii) warrants to purchase up to 167 shares of our common stock at an exercise price of $118,020.00 per share held by Deerfield were cancelled in consideration for (x) a cash payment in the aggregate amount of $2.5 million, (y) 474 shares of common stock, representing 2% of fully-diluted shares outstanding (as defined in the Milestone Agreement) on the closing date, and (z) the right to receive certain milestone payments based on achievement of specified AEROSURF development and commercial milestones, which, if achieved, could potentially total up to $15.0 million. In addition, a related security agreement, pursuant to which Deerfield held a security interest in substantially all of our assets, was terminated. We established a $15.0 million long-term liability for the contingent milestone payments potentially due to Deerfield under the Milestone Agreement. The liability has been recorded at the full value of the contingent milestones and will continue to be carried at full value until the milestones are achieved and paid or the milestones are not achieved and the liability is written off as a gain on debt restructuring.

As of December 31, 2023 and 2022, the restructured debt liability balance was $15.0 million.

On January 24, 2024, we and affiliates of Deerfield entered into an Exchange and Termination Agreement wherein Deerfield agreed to terminate its rights to receive the milestone payments (See the section titled, "Note 18 – Subsequent Events").

Note 11 – Mezzanine Equity and Stockholders' Equity

April 2023 Public Offering

On April 20, 2023, we commenced the April 2023 Offering for a public offering of an aggregate of 3,686,006 units with each unit consisting of one share of common stock and a warrant, or the April 2023 Warrants. The April 2023 Warrants were immediately exercisable for shares of common stock at a price of $2.93 per share and expire five years from the date of issuance. The shares of common stock and the April 2023 Warrants were immediately separable and were issued separately in the April 2023 Offering.

In addition, Ladenburg exercised in full the Overallotment Option to purchase up to 552,900 additional shares of common stock and/or warrants to purchase up to 552,900 additional shares of common stock.

The closing of the April 2023 Offering occurred on April 24, 2023, inclusive of the Overallotment Option. The offering price to the public was $2.93 per unit resulting in gross proceeds to us of approximately $12.4 million. After deducting underwriting discounts and commissions and other estimated offering expenses payable by us, and excluding the proceeds, if any, from the exercise of the April 2023 Warrants issued pursuant to this April 2023 Offering, the net proceeds to us were approximately $10.8 million.

We have determined that the appropriate accounting treatment under ASC 480, Distinguishing Liabilities from Equity, or ASC 480, is to classify the shares of common stock and the April 2023 Warrants issued in the April 2023 Offering as equity. We have also determined that the April 2023 Warrants were not in their entirety a derivative under the scope of ASC 815, Derivatives and Hedging, or ASC 815, due to the scope exception under ASC 815-10-15-74, nor are there any material embedded derivatives that require separate accounting. We allocated the net proceeds from the April 2023 Offering based on the relative fair value of the common stock and the April 2023 Warrants.

January 2023 Warrant Exercise Inducement Offer Letters

On January 20, 2023, we entered into warrant exercise inducement offer letters with certain holders of certain of our: (i) warrants issued in December 2019 to purchase 1,573 shares of common stock with an exercise price of $604.50 per share; (ii) warrants issued in May 2020 to purchase 5,598 shares of common stock with an exercise price of $398.75 per share, and (iii) warrants issued in March 2021 to purchase 89,001 shares of common stock with an exercise price of $180.00 per share (collectively, the January 2023 Existing Warrants).

Pursuant to the terms of the inducement letters, we agreed to amend the January 2023 Existing Warrants by lowering the exercise price of the January 2023 Existing Warrants to $10.00 per share. Additionally, the exercising holders agreed to exercise for cash all of their January 2023 Existing Warrants to purchase an aggregate of 96,172 shares of common stock in exchange for our agreement to issue to such exercising holders new warrants, or the January 2023 New Warrants, to purchase up to an aggregate of 192,344 shares of common stock. We received aggregate gross and net proceeds of approximately $1.0 million and $0.7 million, respectively, from the exercise of the January 2023 Existing Warrants by the exercising holders.

Each January 2023 New Warrant is exercisable into shares of common stock at a price per share of $10.76, will initially be exercisable six months following its date of issuance, or the January 2023 Initial Exercise Date, and will expire on the fifth anniversary of the January 2023 Initial Exercise Date.

February 2023 Warrant Exercise Inducement Offer Letter

On February 21, 2023, we entered into a warrant exercise inducement offer letter with Panacea Venture Healthcare Fund I, L.P., a holder of certain of our: (i) warrants issued in July 2018 to purchase 1,250 shares of common stock with an exercise price of $600.00 per share; (ii) warrants issued in December 2018 to purchase 9,960 shares of common stock with an exercise price of $607.50 per share; (iii) warrants issued in December 2019 to purchase 5,519 shares of common stock with an exercise price of $604.50 per share; and (iv) warrants issued in May 2020 to purchase 5,517 shares of common stock with an exercise price of $398.75 per share (collectively, the February 2023 Existing Warrants).

Pursuant to the terms of the inducement letter, we agreed to amend the February 2023 Existing Warrants by lowering the exercise price of the February 2023 Existing Warrants to $7.06 per share. Additionally, Panacea agreed to exercise for cash all of their February 2023 Existing Warrants to purchase an aggregate of 22,246 shares of common stock in exchange for our agreement to issue to Panacea new warrants, or the February 2023 New Warrants, to purchase up to an aggregate of 44,492 shares of common stock. We received aggregate gross and net proceeds of approximately $0.2 million and $0.1 million, respectively, from the exercise of the February 2023 Existing Warrants by Panacea.

Each February 2023 New Warrant is exercisable into shares of common stock at a price per share of $10.76, will initially be exercisable six months following its date of issuance, or the February 2023 Initial Exercise Date, and will expire on the fifth anniversary of the February 2023 Initial Exercise Date.

Accounting for the January 2023 and February 2023 Warrant Exercise Inducement Offer Letters

The amendment of the January 2023 Existing Warrants and the February 2023 Existing Warrants by lowering the exercise prices and issuing the January 2023 New Warrants and the February 2023 New Warrants is considered a modification of the January 2023 Existing Warrants and the February 2023 Existing Warrants under the guidance of ASU 2021-04. The modification is consistent with the "Equity Issuance" classification under that guidance as the reason for the modification was to induce the holders to cash exercise their warrants, resulting in the imminent exercise of the January 2023 Existing Warrants and the February 2023 Existing Warrants, which raised equity capital and generated net proceeds for us of approximately $0.7 million and $0.1 million, respectively. The total fair value of the consideration of the modification includes the incremental fair value of the January 2023 Existing Warrants and the February 2023 Existing Warrants (determined by comparing the fair values immediately prior to and immediately after the modification) and the initial fair value of the January 2023 New Warrants and the February 2023 New Warrants. The fair values were calculated using the Black-Scholes model and we determined that the total fair value of the consideration related to the modification of the January 2023 Existing Warrants and the February 2023 Existing Warrants, including the initial fair value of the January 2023 New Warrants and the February 2023 New Warrants, was $1.2 million and $0.3 million, respectively.

Series A Preferred Stock

We are authorized to issue 5,000,000 shares of preferred stock, with a par value of $0.001 per share.

On November 17, 2022, our Board of Directors declared a dividend of one one-thousandth (1/1,000th) of a share of Series A Preferred Stock, par value $0.001 per share, or Series A Preferred Stock, for each outstanding share of our common stock to stockholders of record at 5:00 p.m. Eastern Time on November 28, 2022. The Certificate of Designation of Series A Preferred Stock was filed with the Delaware Secretary of State and became effective on November 18, 2022 and authorized the issuance of 40,000 shares of Series A Preferred Stock. The dividend was based on the number of outstanding shares of common stock as of November 28, 2022 and resulted in 38,610.119 shares of Series A Preferred Stock that were declared as a stock dividend on December 2, 2022. Each share of Series A Preferred Stock entitles the holder thereof to 1,000,000 votes per share. The shares of Series A Preferred Stock vote together with the outstanding shares of common stock as a single class exclusively with respect to (1) any proposal to adopt an amendment to our Amended and Restated Certificate of Incorporation, as amended, to reclassify the outstanding shares of common stock into a smaller number of shares of common stock at a ratio specified in or determined in accordance with the terms of such amendment, or the Reverse Stock Split, and (2) any proposal to adjourn any meeting of stockholders called for the purpose of voting on the Reverse Stock Split. The Series A Preferred Stock was not entitled to vote on any other matter, except to the extent required under the General Corporation Law of the State of Delaware.

All shares of Series A Preferred Stock that are not present in person or by proxy at any meeting of stockholders held to vote on the Reverse Stock Split and the adjournment proposal as of immediately prior to the opening of the polls at such meeting, or the Initial Redemption Time, will automatically be redeemed in whole, but not in part, by us at the Initial Redemption Time. All shares that were not redeemed pursuant to the Initial Redemption Time will be redeemed if ordered by the Board of Directors or automatically upon the approval by our stockholders of the Reverse Stock Split at any meeting of the stockholders held for the purpose of voting on such proposal. Each share of Series A Preferred Stock is entitled to receive $0.01 in cash for each 10 whole shares of Series A Preferred Stock immediately prior to the redemption.

Upon issuance of the Series A Preferred Stock, we were not solely in control of the redemption of the shares of Series A Preferred Stock since the holders had the option of deciding whether to attend or return a proxy card for the Special Meeting, which determined whether a given holder's shares of Series A Preferred Stock were redeemed at the Initial Redemption Time. Since the redemption of the Series A Preferred Stock was not solely in the control of us, the shares of Series A Preferred Stock are classified within mezzanine equity. The shares of Series A Preferred Stock were recorded at redemption value, which approximates fair value.

On February 7, 2023, we held a Special Meeting of Stockholders, or the Special Meeting, where our stockholders voted on and approved an amendment to our Amended and Restated Certificate of Incorporation, as amended, to effect the Reverse Stock Split and adjourn the Special Meeting, at which point all shares of Series A Preferred Stock were redeemed, and were no longer issued and outstanding as of such date.

At-The-Market Program

On November 9, 2023, we entered into an At-The-Market Offering Agreement with Ladenburg, pursuant to which we may offer and sell, from time to time at our sole discretion, shares of our common stock through Ladenburg as agent and/or principal (subject to the limitations of General Instruction I.B.6 of Form S-3) through an at-the-market program, or the 2023 ATM Program. We are not obligated to make any sales under the 2023 ATM Program. When we issue sale notices to Ladenburg, we designate the maximum amount of shares to be sold by Ladenburg daily and the minimum price per share at which shares may be sold. Ladenburg may sell shares by any method permitted by law deemed to be an "at-the-market offering" as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended, or in privately negotiated transactions.

Sales under the 2023 ATM Program will be made pursuant to our "shelf" registration statement on Form S-3 (No. 333-261878) filed with the SEC on December 23, 2021, and declared effective on January 3, 2022 and a prospectus supplement related thereto. We are currently subject to the limitations contained in General Instruction I.B.6 of Form S-3. As a result, we are limited to selling no more than one-third of the aggregate market value of the equity held by non-affiliates, or the public float, during any 12-month period, and, as of April 16, 2024, we had sold substantially all that we are permitted to sell under the Form S-3 pursuant to General Instruction I.B.6. If our public float increases, we will have additional availability under such limitations, and if our public float increases to $75 million or more, we will no longer be subject to such limitations. There can be no assurance that our public float will increase or that we will no longer be subject to such limitations.

Either party may suspend the offering under the 2023 ATM Program by notice to the other party. The 2023 ATM Program will terminate upon the earlier of (i) the sale of all shares subject to the 2023 ATM Program or (ii) termination of the 2023 ATM Program in accordance with its terms. Either party may terminate the 2023 ATM Program at any time upon five business days' prior written notification to the other party in accordance with the related agreement.

We agreed to pay Ladenburg a commission of 3% of the gross sales price of any shares sold pursuant to the 2023 ATM Program. The rate of compensation will not apply when Ladenburg acts as principal, in which case such rate shall be separately negotiated. We also agreed to reimburse Ladenburg for the fees and disbursements of its counsel in an amount not to exceed $60,000, in addition to certain ongoing disbursements of its legal counsel up to $3,000 per calendar quarter.

During the fourth quarter of 2023, we sold 848,367 shares of our common stock under the 2023 ATM Program resulting in aggregate gross and net proceeds to us of approximately $0.8 million. During the first quarter of 2024, we sold 2,576,153 shares of our common stock under the 2023 ATM Program resulting in aggregate gross and net proceeds to us of approximately $1.4 million.

On September 17, 2020, we entered into an At-The-Market Offering Agreement with Ladenburg, or the 2020 ATM Program, pursuant to which we were able to offer and sell, from time to time at our sole discretion, up to a maximum of $10.0 million of shares of our common stock through Ladenburg as agent and/or principal under the 2020 ATM Program. For the year ended December 31, 2022, we sold 206,824 shares of our common stock under the 2020 ATM Program resulting in aggregate gross proceeds to us of approximately $4.4 million and net proceeds of approximately $4.3 million.

The shares of common stock issued and sold under the 2020 ATM Program were registered under our Registration Statement on Form S-3 (File No. 333-248874), which was declared effective by the SEC on September 29, 2020 and expired on September 29, 2023. The 2020 ATM Program was terminated by us and Ladenburg on November 9, 2023.

Common Shares Reserved for Future Issuance

Common shares reserved for potential future issuance upon exercise of warrants

The chart below summarizes shares of our common stock reserved for future issuance upon the exercise of warrants:

	December 31,			Expiration
(in thousands, except price per share data)	2023	2022	Exercise Price	Date
Investors - April 2023 financing	4,239	-	$ 2.93	04/24/28
Investors - February 2023 warrant repricing	44	-	$ 10.76	07/21/28
Investors - January 2023 warrant repricing	192	-	$ 10.76	06/20/28
Investors - March 2021 financing	96	185	$ 180.00	03/25/26
Service Agreement - 2021 warrants	3	3	$ 412.50	02/09/24
Investors - May 2020 financing	52	63	$ 399.00	05/22/25
Investors - December 2019 financing	22	29	$ 604.50	12/06/24
Investors - AEROSURF	20	20	$ -	02/14/24
Investors - December 2018 financing - long-term	-	26	$ 607.50	12/04/23
Battelle - 2018 payables restructuring agreement [(1)]	-	1	$ 975.00	12/07/23
Panacea Venture Management Company Ltd.	-	1	$ 600.00	07/02/23
LPH II Investments Limited	1	1	$ 828.00	04/04/25
Investors - February 2017 financing	2	2	$ 4,110.00	02/15/24
Battelle - 2014 collaboration agreement	1	1	$ 210,000.00	10/10/24
Total	4,672	332		

(1) See the section titled, "Note 13 – Collaboration, Licensing and Research Funding Agreements," for further details on the Battelle collaboration agreement.

Common shares reserved for potential future issuance upon granting of additional equity incentive awards

The 2020 Equity Incentive Plan, or the 2020 Plan, initially provided for up to a maximum of approximately 31,000 shares of common stock to be available for issuance pursuant to stock-based awards granted under the 2020 Plan. On August 15, 2023, at the Annual Meeting of Stockholders, our stockholders approved an amendment and restatement of the 2020 Plan to increase the authorized shares under the existing 2020 Plan by 645,000 shares and to remove the 2020 Plan's evergreen provision. See the section titled, "Note 12 – Stock Options and Stock-based Employee Compensation."

As of December 31, 2023, we had approximately 0.3 million shares available for potential future issuance under the 2020 Plan.

Note 12 – Stock Options and Stock-based Employee Compensation

Long-term Incentive Plans

On November 23, 2020, our Board of Directors adopted our 2020 Plan, which was subsequently approved on December 24, 2020 by written consent of our majority stockholders and became effective on January 20, 2021, or the Effective Date. On the Effective Date, the 2020 Plan replaced our 2011 long-term incentive plan, or the 2011 Plan, and the 2020 Plan became our primary plan for providing equity-based compensation to our eligible employees, consultants, and non-employee directors. Awards under the 2020 Plan may include stock options, stock appreciation rights, or SARs, restricted stock awards, or RSAs, restricted stock units, or RSUs, other performance and stock-based awards, and dividend equivalents.

On August 15, 2023, at the Annual Meeting of Stockholders, our stockholders approved an amendment and restatement of the 2020 Plan to increase the authorized shares under the existing 2020 Plan by 645,000 shares and to remove the 2020 Plan's evergreen provision.

As of December 31, 2023, there were approximately 0.7 million shares of our common stock authorized under the 2020 Plan, of which approximately 0.3 million shares remained available for issuance as of December 31, 2023.

An administrative committee, currently the Compensation Committee of the Board of Directors, or Committee delegates, may determine the types, the number of shares covered by, and the terms and conditions of, such awards. Eligible participants may include any of our employees, directors, advisors or consultants.

Stock options and RSUs outstanding and available for future issuance are as follows:

(in thousands)	December 31, 2023	2022
Stock Options and RSUs Outstanding		
2020 Plan	393	50
2011 Plan	29	30
Non-Plan	2	9
Total Outstanding	424	89
Available for Future Grants under the 2020 Plan	339	12

No SARs, RSAs, other performance and stock-based awards, or dividend equivalents have been granted under the 2020 Plan. Although individual grants may vary, option awards generally have a 10-year term, are exercisable upon vesting, and vest with respect to one-twelfth of the total number of shares subject to the options on a quarterly basis (every three months) or vest with respect to one-third of the total number of shares subject to the options on an annual basis (every twelve months). Non-Plan stock options outstanding are in connection with the hiring of certain executive officers and other employees for whom inducement grants were awarded in accordance with Nasdaq Listing Rule 5635(c)(4). The inducement grants vest in a series of three successive, equal installments beginning with the first anniversary of the grant date and have a 10-year term. Although individual awards may vary, RSUs generally vest with respect to one-third of the total number of shares subject to the RSUs on an annual basis (every twelve months).

A summary of activity under our long-term incentive plans is presented below:

(in thousands, except for weighted-average data)

Stock Options	Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (In Years)
Outstanding at January 1, 2023	78	$ 381.00	
Granted	213	1.21	
Forfeited or expired	(14)	259.02	
Outstanding at December 31, 2023	277	$ 92.41	8.8
Vested and exercisable at December 31, 2023	56	$ 432.45	5.9
Vested and expected to vest at December 31, 2023	254	$ 94.53	8.8

(in thousands, except for weighted-average data)

Restricted Stock Units	Shares	Weighted- Average Grant Date Fair Value
Outstanding at January 1, 2023	11	$ 49.50
Awarded	142	1.21
Vested	(3)	48.55
Cancelled	(3)	49.57
Outstanding at December 31, 2023	147	$ 2.94

Based upon application of the Black-Scholes option-pricing formula described below, the weighted-average grant-date fair value of options granted during the years ended December 31, 2023 and 2022 was $1.03 and $42.00, respectively. The weighted-average grant-date fair value of RSUs granted during the years ended December 31, 2023 and 2022 was $1.21 and $49.50, respectively. The total intrinsic value of options outstanding, vested, and exercisable as of December 31, 2023 are each $0.

Stock-Based Compensation

We recognized stock-based compensation expense in accordance with ASC Topic 718 of $1.3 million and $3.1 million, respectively, for the years ended December 31, 2023 and 2022.

Stock-based compensation expense was classified as follows:

(in thousands)	Year Ended December 31, 2023	2022
Research and development	$ 383	$ 807
General and administrative	895	2,279
Total	$ 1,278	$ 3,086

The fair value of each option award is estimated on the grant date using the Black-Scholes option-pricing formula that uses assumptions noted in the following table. Expected volatilities are based upon the historical volatility of our common stock and other factors. We also use historical data and other factors to estimate option exercises, employee terminations and forfeiture rates. The risk-free interest rates are based upon the U.S. Treasury yield curve in effect at the time of the grant.

	Year Ended December 31, 2023	2022
Weighted average expected volatility	112%	106%
Weighted average expected term	6.0	6.9
Weighted average risk-free interest rate	4.33%	1.70%
Expected dividends	-	-

The total fair value of the underlying shares of the options vested during 2023 and 2022 is $2.8 million and $3.8 million, respectively. As of December 31, 2023, there was $0.6 million of total unrecognized compensation cost related to non-vested share-based compensation arrangements granted under the 2020 Plan and the 2011 Plan. That cost is expected to be recognized over a weighted-average vesting period of 2.1 years.

Note 13 – Collaboration, Licensing and Research Funding Agreements

Collaboration Agreement

Battelle Memorial Institute

In October 2014, we entered into a Collaboration Agreement with Battelle, or, as amended, the Battelle Collaboration Agreement, for the development of our ADS for use in a potential Phase 3 program. We had previously worked with Battelle, which has expertise in developing and integrating aerosol devices using innovative and advanced technologies, in connection with development of our Phase 2 ADS used in the AEROSURF Phase 2b clinical trial. Under the Battelle Collaboration Agreement, we and Battelle shared the costs of development for a three-stage development plan that included planning, executing the project plan and testing and completing verification and documentation of a new Phase 3 ADS, putting us in a position to manufacture a new Phase 3 ADS for use in the remaining AEROSURF development activities, including a potential Phase 3 clinical program, and, if approved, initial commercial activities. We retained final decision-making authority over all matters related to the design, registration, manufacture, packaging, marketing, distribution and sale of the Phase 3 ADS. We and Battelle shared the costs of the project plan equally. Battelle agreed to bear the cost of any cost overruns associated with the project plan and we agreed to bear the cost of any increase in cost resulting from changes in the scope of the product requirements. We also agreed that, if Battelle successfully completed the project plan in a timely manner, we would pay Battelle royalties equal to a low single-digit percentage of the worldwide net sales and license royalties on sales of AEROSURF for the treatment of RDS in premature infants, up to an initial aggregate limit of $25.0 million, which under a payment restructuring agreement (discussed below), was increased to $35.0 million. The Battelle Collaboration Agreement will end at the time we fulfill our payment obligations to Battelle, unless sooner terminated by a party as provided therein.

Pursuant to the A&R License Agreement described below, Licensee has agreed to assume certain of our obligations under the Battelle Collaboration Agreement.

Licensing and Research Funding Agreements

Lee's Pharmaceutical (HK) Ltd.

Term Sheet and Project Financing Agreement

On March 18, 2020, we entered into the Term Sheet with Lee's (HK), pursuant to which Lee's (HK) provided financing for the development of AEROSURF. In August 2020, we entered into a Project Financing Agreement with Lee's (HK), or the PF Agreement, formalizing the terms of the Term Sheet, and under which we received payments totaling $2.8 million through October 2020. On November 12, 2020, Lee's (HK) provided notice of termination of additional funding under the PF Agreement, and we and Lee's (HK) revised our plans for the continued development of AEROSURF. Lee's (HK) agreed to continue the development of AEROSURF in Asia at its own cost. Lee's (HK) agreed to fund an additional $1.0 million to us in 2021 for certain transition and analytical services to be provided by us with respect to the development of AEROSURF, which will be considered "Project Expenses" under the terms of the PF Agreement. In 2021, we received payments totaling $1.0 million from Lee's (HK) and no further amounts were due under the PF Agreement.

Since the 2018 acquisition of CVie Investments Limited and CVie Therapeutics, istaroxime has become our primary focus for investment and execution due to what we believe represents a greater potential value opportunity for us and our stockholders. Since completing our Phase 2 study of lucinactant (KL4 surfactant) for patients with severe COVID-19 associated ARDS and lung injury in January 2022, in order to preserve resources for the highest priority programs, we have begun to reduce costs not already being performed by our licensee, Lee's (HK) and Zhaoke, under the terms of our Original License Agreement. These costs include certain reductions in headcount dedicated to KL4 surfactant and the decommissioning of both our analytical and technical support laboratory, which previously conducted release testing of APIs and supportive research for our lyophilized and aerosolized KL4 surfactant, and our medical device development laboratory, which was previously used to conduct development activities and testing for our ADS technologies. To support the future development of our KL4 surfactant platform in markets outside of Asia, including the U.S., we are pursuing one or more licensing transactions.

To repay the funds provided under the terms of the PF Agreement, until such time as we have repaid 125% of the amounts funded by Lee's (HK) for the development of AEROSURF, we will pay to Lee's (HK) 50% of all revenue amounts and payments received by us for any sale, divestiture, license or other development and/or commercialization of the KL4/AEROSURF patent portfolio, excluding (i) payments for bona fide research and development services; (ii) reimbursement of patent expenses and (iii) all amounts paid to us under the Original License Agreement, minus certain deductions and certain reductions for any payments made by us with respect to third party intellectual property not previously funded by Lee's (HK).

As of December 31, 2023 and 2022, the liability balance related to the payments under the PF Agreement was $3.8 million and is recorded in other liabilities.

We have determined that the Term Sheet and the PF Agreement are within the scope of ASC 730-20, *Research and Development Arrangements*, or ASC 730-20. We concluded that there has not been a substantive and genuine transfer of risk related to the Term Sheet or the PF Agreement as there is a presumption that we are obligated to repay Lee's (HK) based on the significant related party relationship that existed at the time the parties entered into the Term Sheet and the PF Agreement, including Lee's (HK)'s ownership of outstanding shares of our common stock.

We have determined that the appropriate accounting treatment under ASC 730-20 is to record the proceeds received from Lee's (HK) as cash and cash equivalents, as we have the ability to direct the usage of funds, and a long-term liability on our consolidated balance sheet when received. The liability will remain on the balance sheet until we repay such amounts as a result of any revenues and payments received by us for any sale, divestiture, license or other development and/or commercialization of the KL4/AEROSURF patent portfolio. We have also determined that the Term Sheet and the PF Agreement are not in their entirety a derivative under the scope of ASC 815, due to the scope exception under ASC 815-10-15-59, nor are there any embedded derivatives that require separate accounting.

A&R License Agreement

Previously, we were developing a KL4 surfactant platform, including AEROSURF (lucinactant for inhalation), to address a range of serious respiratory conditions in children and adults. In order to focus our resources on the development of our istaroxime pipeline, we suspended all internal AEROSURF clinical activities in November 2020, and, in January 2022 we began to reduce all other costs related to the KL4 surfactant platform that were not already being performed by our licensee, Lee's (HK) and Zhaoke, under the terms of the Original License Agreement.

On August 17, 2022, we entered into an Amended and Restated License, Development and Commercialization Agreement, or the A&R License Agreement, with Lee's (HK) and Zhaoke effective as of August 9, 2022. We refer to Zhaoke and Lee's (HK) together as the "Licensee." The A&R License Agreement amends, restates, and supersedes the Original License Agreement.

Under the A&R License Agreement, we granted to Licensee an exclusive license, with a right to sublicense, to develop, register, make, use, sell, offer for sale, import, distribute, and otherwise commercialize our KL4 surfactant products, including SURFAXIN®, the lyophilized dosage form of SURFAXIN, and aerosolized KL4 surfactant, in each case for the prevention, mitigation and/or treatment of any respiratory disease, disorder, or condition in humans worldwide, except for Andorra, Greece, and Italy (including the Republic of San Marino and Vatican City), Portugal, and Spain, or the Licensed Territory, which countries are currently exclusively licensed to Laboratorios Del Dr. Esteve, S.A., or Esteve. If and when the exclusive license granted to Esteve terminates as to any country, such country automatically becomes part of the Licensed Territory of Licensee.

Under the Original License Agreement, Lee's (HK) previously made an upfront payment to us of $1.0 million. Pursuant to the terms of the A&R License Agreement, we may also receive up to $78.9 million in potential clinical, regulatory and commercial milestone payments. We are also entitled to receive a low double-digit percentage of Licensee's non-royalty sublicense income. We are also eligible to receive tiered royalties based on a percentage of Net Sales (as defined in the A&R License Agreement) that ranges from low single digit to low teen percentages, depending on the product. Royalties are payable on a product-by-product and country-by-country basis until the latest of (i) the expiration of the last valid patent claim covering the product in the country of sale, (ii) the expiration or revocation of any applicable regulatory exclusivity in the country of sale, and (iii) ten years after the first commercial sale of the product in the country of sale. Thereafter, in consideration of licensed rights other than patent rights, royalties shall continue for the commercial life of each product but at substantially reduced rates. In addition, the royalty rates are subject to reduction by as much as 50% in a given country based on generic competition in such country.

The A&R License Agreement is considered to be a contract modification in accordance with ASC Topic 606. No additional performance obligations were identified in the contract modification, and no future material performance obligations are due.

All revenue related to the $1.0 million upfront payment under the Original License Agreement was appropriately recognized as of the second quarter of 2019. Regulatory and commercialization milestones under the A&R License Agreement were excluded from the transaction price, as all milestone amounts were fully constrained under the guidance. Consideration related to sales-based milestones and royalties under the A&R License Agreement will be recognized when the related sales occur, provided that the reported sales are reliably measurable and that we have no remaining performance obligations, as such sales were determined to relate predominantly to the license granted to Licensee and therefore have also been excluded from the transaction price. We will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

Under the A&R License Agreement, Licensee will be solely and exclusively responsible for all costs and activities related to the development, manufacturing, regulatory approval and commercialization of licensed products in the Licensed Territory including all royalties payable in respect of third-party intellectual property rights sublicensed by us to Licensee and all intellectual property prosecution, maintenance and defense activities and costs. Licensee may sublicense certain activities under the A&R License Agreement to an affiliate of Licensee but may not grant sublicenses to unaffiliated third parties without our prior consent and, if the proposed sublicense will cover the U.S., without first complying with rights of first offer and rights to match granted to us under the A&R License Agreement. A sublicensee and a subcontractor may not be a competitor identified by us. Sublicenses under the A&R License Agreement do not include the right to further sublicense.

The term of the A&R License Agreement will continue on a country-by-country basis for the commercial life of the products. Either party may terminate the A&R License Agreement in the event of bankruptcy or a material breach of the A&R License Agreement by the other party that remains uncured for a period of sixty (60) days (or within 30 days after delivery of a Default Notice (as defined in the A&R License Agreement) if such material breach is solely based on the breaching party's failure to pay amount due under the A&R License Agreement). At any time after the second anniversary of the A&R License Agreement, Licensee may terminate the A&R License Agreement in its entirety or on a product-by-product basis. In addition, either party may terminate the A&R License Agreement with respect to any individual product in a country if a regulatory authority in such country terminates, suspends or discontinues development of such product and such termination, suspension or discontinuance persists for a period in excess of eighteen (18) months. Upon termination of the A&R License Agreement in its entirety or with respect to a particular product or country, generally all related rights and licenses granted to Licensee will terminate, all rights under our technology will revert to us, and Licensee will cease all use of our technology, in each case in relation to the terminated product(s) and country(ies), as applicable.

License, Development and Commercialization Agreement with Lee's Pharmaceutical (HK) Ltd.

On January 12, 2024, we entered into a License, Development and Commercialization Agreement with Lee's (HK) effective as of January 7, 2024 under which we granted an exclusive license, with a right to sublicense, to develop, register, make, use, sell, offer for sale, import, distribute and otherwise commercialize products that incorporate istaroxime for intravenous administration, rostafuroxin for oral administration, and our proprietary dual-mechanism SERCA2a activators for intravenous or oral administration, in each case for the prevention, mitigation and/or treatment of any disease, disorder or condition in humans including acute decompensated heart failure, cardiogenic shock, and chronic use following discharge of an individual hospitalized for acute decompensated heart failure in the Greater China region (See the section titled, "Note 18 – Subsequent Events").

Philip Morris USA Inc. and Philip Morris Products S.A.

In 2008, we entered into the U.S. License Agreement with PMUSA and, as PMUSA had assigned its ex-U.S. rights to PMPSA effective on the same date and on substantially the same terms and conditions, we entered into a license agreement with PMPSA with respect to rights outside of the U.S., which we refer to, together with the U.S. License Agreement, as the PM License Agreements. Under the PM License Agreements, we hold exclusive worldwide licenses to the ADS technology for use with pulmonary surfactants (alone or in combination with any other pharmaceutical compound(s)) for all respiratory diseases and conditions (the foregoing uses in each territory, or the Exclusive Field), and an exclusive license in the U.S. for use with certain non-surfactant drugs to treat specified respiratory indications in humans in designated hospital settings. The PM License Agreements provide for payment of royalties at a rate equal to a low single-digit percent of sales of products sold in the Exclusive Field (as defined in the PM License Agreements) in the territories, including sales of aerosol devices that are not based on the ADS technology (unless we exercise our right to terminate the license with respect to a specific indication). While there is no legal obligation under the agreements to make minimum royalty payments, in the event we do not make quarterly minimum royalty payments, PMUSA and PMPSA can terminate the agreements. In making such payments, we are entitled to a reduction of future royalties in an amount equal to the excess of any minimum royalty paid over royalties actually earned in prior periods.

Pursuant to the A&R License Agreement described above, Licensee has agreed to assume certain of our obligations under the PM License Agreements.

On January 16, 2024, we entered into Amendment No. 1 to the U.S. License Agreement with PMUSA and also entered into Amendment No. 1 to the License Agreement with PMPSA in which the parties extinguished and released their respective rights, obligations and claims in respect of quarterly payments in effect immediately prior to January 17, 2024 (See the section titled, "Note 9 – Other Current Liabilities").

Johnson & Johnson and Ortho Pharmaceutical Corporation

We, Johnson & Johnson, or J&J, and its wholly owned subsidiary, Ortho Pharmaceutical Corporation, are parties to a license agreement granting to us an exclusive worldwide license to the J&J KL4 surfactant technology. Under the license agreement, we are obligated to pay fees of up to $2.5 million in the aggregate upon our achievement of certain milestones, primarily upon receipt of marketing regulatory approvals for certain designated products. We have paid $1.0 million to date for milestones that have been achieved. In addition, the license agreement requires that we make royalty payments at different rates, depending upon type of revenue and country, in amounts in the range of a high single-digit percent of net sales (as defined in the license agreement) of licensed products sold by us or sublicensees, or, if greater, a percentage of royalty income from sublicensees in the low double digits.

Pursuant to the A&R License Agreement described above, Licensee has agreed to assume certain of our obligations under our license agreement with J&J.

Laboratorios del Dr. Esteve, S.A.

We have a strategic alliance with Esteve for the development, marketing and sales of a broad portfolio of potential KL4 surfactant products in Andorra, Greece, and Italy (including the Republic of San Marino and Vatican City) Portugal, and Spain, or, collectively, the Territory. Antonio Esteve, Ph.D., a principal of Esteve, served as a member of our Board of Directors from May 2002 until January 2013. Under the alliance, Esteve will pay us a transfer price on sales of our KL4 surfactant products. We are responsible for the manufacture and supply of all of the covered products and Esteve will be responsible for all sales and marketing in the Territory. Esteve is obligated to make stipulated cash payments to us upon our achievement of certain milestones, primarily upon receipt of marketing regulatory approvals for the covered products. In addition, Esteve has agreed to contribute to Phase 3 clinical trials for the covered products by conducting and funding development performed in the Territory. As part of a 2004 restructuring, Esteve returned certain rights to us in certain territories, or the Former Esteve Territories, and we agreed to pay Esteve 10% of any cash up front and milestone fees (up to a maximum aggregate of $20.0 million) that we receive in connection with any strategic collaborations for the development and/or commercialization of certain of our KL4 surfactant products in the Former Esteve Territories.

Universita degli Studi di Milano-Bicocca

Effective April 13, 2015, CVie Therapeutics, entered into an Agreement for Scientific Collaboration with the Universita degli Studi di Milano-Bicocca, or Bicocca, in Milan, Italy, focused on defining the role of SERCA2a and phospholamban, or PLN, in modulating cardiac contraction, and discovering new small molecules to modulate SERCA2a activity or new drugs for treating chronic and acute human heart failure. The term of the collaboration agreement would have expired after three years but was extended for approximately an additional year, with the option for further renewal.

Under the collaboration agreement, intellectual property resulting from the collaboration, including patents and know-how, will be jointly owned by the parties. For the development of any new SERCA2a compounds and diagnostic products suitable for further clinical development, we have the option to purchase Bicocca's interest for up to 12 months after the filing of a patent application. If the option is not exercised, then the parties shall remain joint owners and each can use the intellectual property with consent of the other on terms to be defined. If we exercise an option, we have agreed to pay Bicocca (corresponding to stage of development): (i) € 0.1 million upon completion and the proof of concept of biological efficacy for new compounds modulating the SERCA2a activity caused by PLN mutations; and (ii) € 1.5 million upon obtaining marketing authorization in the U.S., EU, or China of new compounds with the corresponding companion diagnostic assay. We have also agreed to pay royalties for any purchased intellectual property arising out of the collaboration in the range of a low- to mid-single digit percent of net sales for any products sold in any country for a period of ten years from the date of the first commercial sale.

On March 19, 2021, we entered into an Agreement for Scientific Collaboration, or the New SERCA2a Agreement, with Bicocca, which extends our collaboration. The New SERCA2a Agreement amends and restates the recently expired terms of the prior collaboration agreement. Under the New SERCA2a Agreement, we will provide Bicocca with approximately € 0.2 million for research activities and to cover laboratory space and operation costs. Results obtained from the collaboration will be jointly owned by the parties. However, Bicocca will assign to us its interest in patent applications and patents covering any new SERCA2a compounds and diagnostic products suitable for further clinical development. We have agreed to pay Bicocca (corresponding to stage of development): (i) € 25,000 for execution of an assignment to us of Bicocca's interest in the patent at issue, (ii) € 75,000 for new SERCA2a compounds developed up to Phase 1 studies in humans upon the completion and availability of the proof of concept of biological efficacy of new compounds on modulating the SERCA2a activity in cell-free systems, or its functional counterpart in isolated cells and (iii) € 1.5 million upon obtaining marketing authorization in the U.S., EU, or China of new compounds with the corresponding companion diagnostic assay. We have also agreed to pay royalties on products generated from the collaboration in the range of a fraction of a single digit to a low single digit percent of net sales for any products sold in any country for a period of ten years from the date of the first commercial sale or until the expiry of patent(s) covering the products. In connection with our research activities, Bicocca agreed to provide us exclusive use of a research laboratory for the collaboration, and nonexclusive access to a physiology laboratory within the university. Bicocca served as our primary location in Milan, Italy.

Our agreement with Universita Degli Studi di Milano-Bicocca, the institution that has performed many preclinical studies with istaroxime and our preclinical families of compounds, expired on July 31, 2022. If additional preclinical work is required for any reason, we will need to re-engage with Bicocca or find another vendor to provide those services.

Note 14 – Related Party Transactions

Lee's Holdings

As of December 31, 2023 and 2022, Lee's Holdings' beneficial ownership of our issued and outstanding shares of common stock was 2% and 13%, respectively.

We entered into the following transactions with Lee's Holdings during 2023 and 2022:

- On August 17, 2022, we entered into the A&R License Agreement, with Lee's (HK) and Zhaoke, effective as of August 9, 2022. We may receive up to $78.9 million in potential clinical, regulatory, and commercial milestone payments under the A&R License Agreement. We are also entitled to receive a low double-digit percentage of Licensee's non-royalty sublicense income (See the section titled, "Note 13 – Collaboration, Licensing and Research Funding Agreements – Lee's Pharmaceutical (HK) Ltd.)");

- In March 2020, we entered into the Term Sheet with Lee's (HK), pursuant to which Lee's (HK) had agreed to provide financing for the development of AEROSURF. In August 2020, we entered into the PF Agreement with Lee's (HK), formalizing the terms of the Term Sheet, under which we received payments of $1.0 million in 2021. As of December 31, 2023 and 2022, the liability balance related to the payments under the PF Agreement was $3.8 million and is recorded in other liabilities. The liability will remain on the balance sheet until we repay such amounts as a result of any revenues and payments received by us for any sale, divestiture, license or other development and/or commercialization of the KL4/AEROSURF patent portfolio. No further amounts are due under the PF Agreement as of December 31, 2023 (See the section titled, "Note 13 – Collaboration, Licensing and Research Funding Agreements – Lee's Pharmaceutical (HK) Ltd.)"); and

- During 2022, we incurred $0.4 million in research and development expenses for services provided by an affiliate of Lee's Holdings, $0.3 million of which was in accrued expenses as of December 31, 2022.

Panacea Venture Management Company Ltd.

As of December 31, 2023 and 2022, Panacea Venture Management Company Ltd.'s, or Panacea's, beneficial ownership of our issued and outstanding shares of common stock was 1% and 9%, respectively.

James Huang is a founding and Managing Partner of Panacea. In connection with the CVie Acquisition in December 2018, Mr. Huang was appointed as a director and Chairman of our Board. In April 2023, Mr. Huang resigned from this position.

On February 21, 2023, we entered into a warrant exercise inducement offer letter with Panacea Venture Healthcare Fund I, L.P., a related party of Panacea and a holder of certain of the February 2023 Existing Warrants. Pursuant to the terms of the inducement letter, we agreed to amend the February 2023 Existing Warrants by lowering the exercise price of the February 2023 Existing Warrants to $7.06 per share. Additionally, Panacea agreed to exercise for cash all of their February 2023 Existing Warrants to purchase an aggregate of 22,246 shares of common stock in exchange for our agreement to issue to Panacea new warrants to purchase up to an aggregate of 44,492 shares of common stock. We received aggregate gross and net proceeds of approximately $0.2 million and $0.1 million, respectively, from the exercise of the February 2023 Existing Warrants by Panacea (See the section titled, "Note 11 – Mezzanine Equity and Stockholders' Equity").

Note 15 – Litigation

We are not aware of any pending or threatened legal actions that would, if determined adversely to us, have a material adverse effect on our business and operations.

We have from time to time been involved in disputes and proceedings arising in the ordinary course of business, including in connection with the conduct of our clinical trials. In addition, as a public company, we are also potentially susceptible to litigation, such as claims asserting violations of securities laws. Any such claims, with or without merit, if not resolved, could be time-consuming and result in costly litigation. There can be no assurance that an adverse result in any future proceeding would not have a potentially material adverse effect on our business, results of operations and financial condition.

Note 16 – Income Taxes

The components of the benefit for income taxes for the years ended December 31, 2023 and 2022 is as follows:

	December 31,	
(in thousands)	**2023**	**2022**
Deferred expense (benefit):		
Foreign	$ -	$ (1,367)
Total deferred expense (benefit)	-	(1,367)
Total income tax expense (benefit)	$ -	$ (1,367)

For the year ended December 31, 2022, we recorded a deferred income tax benefit of $1.4 million. The deferred income tax benefit recorded relates solely to the reduction of the deferred tax liabilities as a result of the loss on impairment of intangible assets related to rostafuroxin for the year ended December 31, 2022.

The reconciliation of the income tax benefit computed at the federal statutory rates to our recorded tax benefit for the years ended December 31, 2023 and 2022 is as follows:

(in thousands)	December 31, 2023	December 31, 2022
Income tax benefit, statutory rates	$ (4,261)	$ (8,521)
State taxes on income, net of federal benefit	(625)	903
Net operating loss expirations	5,875	3,485
Intangibles	613	2,561
Research and development tax credit	490	825
Foreign rate differential	37	196
Stock compensation	464	-
Employee related and other	(575)	467
Change in state tax rates	23,993	-
Other	-	(17)
Income tax expense / (benefit), statutory rates	26,011	(101)
Valuation allowance	(26,011)	(1,266)
Income tax benefit, net	$ -	$ (1,367)

The tax effects of temporary differences that give rise to deferred tax assets and deferred tax liabilities as of December 31, 2023 and 2022, are as follows:

(in thousands)	December 31, 2023	December 31, 2022
Long-term deferred assets:		
Net operating loss carryforwards (federal and state)	$ 158,926	$ 185,591
Research and development tax credit	17,081	17,671
Compensation expense on stock	3,940	4,166
Other accrued	1,386	1,293
Capitalized R&D expenses	3,606	2,369
Depreciation	355	191
Total long-term deferred tax assets	185,294	211,281
Long-term deferred liabilities:		
IPR&D	(5,058)	(5,061)
Total long-term deferred tax liabilities	(5,058)	(5,061)
Valuation allowance	(185,294)	(211,281)
Deferred tax liabilities, net	$ (5,058)	$ (5,061)

We are in a net deferred tax liability position as of December 31, 2023 and 2022. Because we have never realized a profit, management has fully reserved the net deferred tax asset since realization is not assured. It is our policy to classify interest and penalties recognized on uncertain tax positions as a component of income tax expense. There was neither interest nor penalties accrued as of December 31, 2023 and 2022, nor were any incurred in 2023 or 2022.

At December 31, 2023 and 2022, we had available carryforward net operating losses for federal tax purposes of $620.4 million and $637.4 million, respectively, research and development tax credit carryforward of $16.5 million and $17.0 million, respectively and orphan drug tax credit carryforwards of $0.6 million for both periods. Of the $620.4 million of federal net operating loss carryforwards, $101.1 million can be carried forward indefinitely. The remaining federal net operating loss, research and development tax credit carryforwards and orphan drug credit carryforward will continue to expire through 2042.

At December 31, 2023 and 2022, we had available carryforward losses of approximately $576.3 million and $593.3 million, respectively, for state tax purposes. Of the $576.3 million state tax carryforward losses, $575.3 million is associated with the state of Pennsylvania, with the remainder associated with the other five (5) states within which we have established tax nexus.

The Tax Cuts and Jobs Act resulted in significant changes to the treatment of research and development, or R&D, expenditures under Internal Revenue Code Section 174. For tax years beginning after December 31, 2021, taxpayers are required to capitalize and amortize all R&D expenditures that are paid or incurred in connection with their trade or business for tax purposes. Specifically, costs for U.S.-based R&D activities must be amortized over five years and costs for foreign R&D activities must be amortized over 15 years, both using a midyear convention. During the year ended December 31, 2023, we capitalized $5.4 million and $2.0 million of domestic and foreign R&D expenses, respectively.

Future realization of the tax benefits of existing temporary differences and net operating loss carryforwards ultimately depends on the existence of sufficient taxable income within the carryforward period. As of December 31, 2023 and 2022, we performed an evaluation to determine whether a valuation allowance was needed. We considered all available evidence, both positive and negative, which included the results of operations for the current and preceding years. We determined that it was not possible to reasonably quantify future taxable income and determined that it is more likely than not that all of the deferred tax assets will not be realized. Accordingly, we maintained a full valuation allowance as of December 31, 2023 and 2022.

Under Internal Revenue Code Section 382, if a corporation undergoes an "ownership change," the corporation's ability to use its pre-change NOL carryforwards and other pre-change tax attributes to offset its post-change income may be limited. We have not completed a study to assess whether an "ownership change" has occurred or whether there have been multiple ownership changes since we became a "loss corporation" as defined in Section 382. Future changes in our stock ownership, which may be outside of our control, may trigger an "ownership change." In addition, future equity offerings or acquisitions that have equity as a component of the purchase price could result in an "ownership change." If an "ownership change" has occurred or does occur in the future, utilization of the NOL carryforwards or other tax attributes may be limited, which could potentially result in increased future tax liability to us.

Utilization of net operating loss, or NOL, and R&D credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes may limit the amount of NOL and R&D credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. There also could be additional ownership changes in the future, which may result in additional limitations in the utilization of the carryforward NOLs and credits.

A full valuation allowance has been provided against our deferred tax assets and, if a future assessment requires an adjustment, an adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the consolidated balance sheets or statements of operations if an adjustment were required.

Note 17 – Leases

Our operating leases consist primarily of facility leases for our operations in Warrington, Pennsylvania and Taipei, Taiwan.

We maintain our corporate headquarters and operations in Warrington, Pennsylvania. The facility serves as the main operating facility for drug development, regulatory, research and development, and administration. We also maintain offices in Taipei, Taiwan where we perform certain manufacturing development and preclinical activities.

In January 2021, we entered into a lease amendment to extend the term of our Warrington, Pennsylvania lease for a period of five years commencing on March 1, 2022 and expiring on February 28, 2027.

Throughout the term of our leases, we are responsible for paying certain variable lease costs, in addition to the rent, as specified in the lease, including a proportionate share of applicable taxes, operating expenses and utilities.

The following table contains a summary of the lease costs recognized under ASC 842 and other information pertaining to our operating leases for the years ended December 31, 2023 and 2022:

(in thousands)	Year Ended December 31, 2023	2022
Operating lease cost	$ 536	$ 692
Variable lease cost	13	9
Sublease income	(44)	-
Total lease cost	$ 505	$ 701
Other Information		
Operating cash flows used for operating leases	$ 559	$ 730
Weighted average remaining lease term (in years)	3.2	4.1
Weighted average incremental borrowing rate	7.07%	7.08%

Future minimum lease payments under our non-cancelable operating leases as of December 31, 2023, are as follows:

(in thousands)	December 31, 2023
2024	$ 531
2025	570
2026	581
2027	97
Total lease payments	1,779
Less imputed interest	(182)
Total operating lease liabilities	$ 1,597

Note 18 – Subsequent Events

License Agreement with Lee's Pharmaceutical (HK) Ltd.

On January 12, 2024, we entered into a License, Development and Commercialization Agreement with Lee's (HK) effective as of January 7, 2024, or the Lee's (HK) License Agreement. Under the Lee's (HK) License Agreement, we granted an exclusive license, with a right to sublicense, to develop, register, make, use, sell, offer for sale, import, distribute and otherwise commercialize products that incorporate istaroxime for intravenous administration, rostafuroxin for oral administration, and our proprietary dual-mechanism SERCA2a activators for intravenous or oral administration (collectively, the Products and each, a Product), in each case for the prevention, mitigation and/or treatment of any disease, disorder or condition in humans including acute decompensated heart failure, cardiogenic shock, and chronic use following discharge of an individual hospitalized for acute decompensated heart failure, or Field, in the People's Republic of China, Hong Kong, Macau, Taiwan, Singapore, South Korea, Thailand, Vietnam, Brunei, Myanmar, Cambodia, East Timor, Indonesia, Laos, Malaysia, and the Philippines, or the New Licensed Territory.

Under the Lee's (HK) License Agreement, we may receive up to $3.1 million in potential upfront pre-development, development, clinical, and regulatory milestone payments and up to $135.25 million in sales milestone payments. We are also entitled to receive a low double-digit percentage of Lee's (HK) non-royalty sublicense income.

We are eligible to receive tiered royalties based on a percentage of Net Sales (as defined in the Lee's (HK) License Agreement) that ranges from low single-digit to low double-digit percentages, depending on the Product. Royalties are payable on a product-by-product and country-by-country basis until the latest of (i) the expiration of the last valid patent claim covering the Product in the country of sale, (ii) the expiration or revocation of any applicable regulatory exclusivity in the country of sale, and (iii) ten years after the first commercial sale of the Product in the country of sale. Thereafter, in consideration of licensed rights other than patent rights, royalties shall continue for the commercial life of each Product but at substantially reduced rates. In addition, the royalty rates are subject to reduction by as much as 50% in a given country based on generic competition in such country.

Under the Lee's (HK) License Agreement, Lee's (HK) will be solely and exclusively responsible for all costs and activities related to the development, manufacturing, regulatory approval and commercialization of Products in the New Licensed Territory, with the exception of certain costs in connection with filing fees payable to regulatory authorities in the New Licensed Territory relative to a Product for which we hold the applicable marketing authorization. Lee's (HK) may sublicense its rights to its affiliates and may grant sublicenses to third-party subcontractors to perform certain activities under the Lee's (HK) License Agreement on behalf of Lee's (HK) or its affiliates but may not otherwise grant sublicenses to unaffiliated third parties without our prior consent. A sublicensee and a subcontractor may not be a competitor identified by us. Sublicenses granted under the Lee's (HK) License Agreement may not include the right to further sublicense. The Lee's (HK) License Agreement establishes a joint steering committee and a joint development committee to oversee the regional development (with us retaining final decision rights over clinical protocols) and a joint commercialization committee.

During the term of the Lee's (HK) License Agreement, we receive an exclusive (even as to Lee's (HK)), sublicensable license under any Lee's (HK) and its affiliate's intellectual property that covers a Product (including its manufacture and use) and any improvements to the licensed technology developed solely by or on behalf of Lee's (HK) or jointly with us, to (i) develop Product in the Field to obtain or maintain regulatory approval outside of the New Licensed Territory, and (ii) use, sell, offer for sale, import, export, make, have made, distribute, warehouse, market, promote, apply for and submit applications for drug approval and reimbursement approval and otherwise commercialize Product in the Field outside of the New Licensed Territory. After the term of the Lee's (HK) License Agreement, or in the event that we wish to obtain an exclusive license under certain patent rights during or after the term, we have the option to negotiate an exclusive royalty-bearing license under any such intellectual property, provided that such royalties shall not exceed specified low single-digit caps.

Under the Lee's (HK) License Agreement, each party is responsible for prosecution and maintenance of its respective solely-owned patents, and the parties shall decide on a case-by-case basis the appropriate allocation of costs and control concerning matters regarding the prosecution, maintenance, defense and infringement of any jointly-owned patents. The Lee's (HK) License Agreement provides for cooperation between the parties with respect to enforcement of patent rights. As between the parties, we have the first right to enforce patent rights against third parties at our own expense. If we decline to enforce such rights, Lee's (HK) has the right to enforce such rights at its own expense. In the event that a third party claims that a Product used or sold by Lee's (HK) (or its affiliate or sublicensee) is infringing on a patent in the New Licensed Territory, Lee's (HK) is responsible for defending against such third party claim at its cost and expense, with the exception of certain counterclaims that we may bring.

The term of the Lee's (HK) License Agreement will continue on a country-by-country basis for the commercial life of the Products. Either party may terminate the Lee's (HK) License Agreement in the event of bankruptcy or a material breach of the Lee's (HK) License Agreement by the other party that remains uncured for a period of sixty days (or within 30 days after delivery of a Default Notice (as defined in the Lee's (HK) License Agreement) if such material breach is solely based on the breaching party's failure to pay amount due under the Lee's (HK) License Agreement). In addition, either party may terminate the Lee's (HK) License Agreement with respect to any individual Product in a country if a regulatory authority in such country terminates, suspends or discontinues development of such Product and such termination, suspension or discontinuance persists for a period in excess of 18 months. Upon termination of the Lee's (HK) License Agreement in its entirety or with respect to a particular Product or country, generally all related rights and licenses granted to Lee's (HK) will terminate, all rights under our technology will revert to us, and Lee's (HK) will cease all use of our technology, in each case in relation to the terminated Product(s) and country(ies), as applicable.

Exchange and Termination Agreement with Deerfield Management Company, L.P.

On January 24, 2024, we and affiliates of Deerfield entered into an Exchange and Termination Agreement, or the Exchange and Termination Agreement. Pursuant to the Milestone Agreement, among other things, Deerfield had the right to receive the Milestone Payments, which, if achieved, could potentially total up to $15.0 million.

Pursuant to the Exchange and Termination Agreement, Deerfield agreed to terminate its rights to receive the Milestone Payments and all related rights and obligations in respect of such Milestone Payments in exchange for (i) cash in the aggregate amount of $200,000, $100,000 of which was paid on January 24, 2024 and $100,000 of which will be paid no later than the earlier to occur of (a) January 24, 2025 and (b) us receiving a specified amount of gross proceeds from debt or equity financings occurring on or after January 24, 2024, and (ii) an aggregate of 608,272 shares of our common stock, par value $0.001 per share. The shares of the common stock were issued to Deerfield in a transaction exempt from registration pursuant Section 4(a)(2) of the Securities Act of 1933.

Contemporaneously with the execution of the Exchange and Termination Agreement, we and Deerfield entered into a Registration Rights Agreement pursuant to which we have agreed to, among other matters, register for resale with the SEC the shares of the common stock issued to Deerfield pursuant to the Exchange and Termination Agreement.

Asset Purchase Agreement with Varian Biopharmaceuticals

On April 2, 2024, we entered into the Asset Purchase Agreement with Varian. Pursuant to the Asset Purchase Agreement, we purchased all of the assets of Varian's business associated with the Licence Agreement, including the Licence Agreement, all rights in molecules and compounds subject to the Licence Agreement, know-how and inventory of drug substance, or the Transferred Assets. We also assumed all liabilities arising on or after April 2, 2024, relating to the research, development, manufacturing, registration, commercialization, use, handling, supply, storage, import, export or other disposition or exploitation of any and all products associated with the Transferred Assets.

In consideration of the purchase of the Transferred Assets, (i) on April 2, 2024, we issued a total of 5,500 shares of our Series B Convertible Preferred Stock, par value $0.001 per share, or the Series B Preferred Stock, to certain creditors of Varian and (ii) agreed to pay up to $2.3 million in milestone payments upon the achievement of certain regulatory and clinical development milestones with our option to pay such milestone payments either in cash or our common stock.

The Asset Purchase Agreement contains customary representations and warranties, covenants, closing conditions and indemnification provisions for a transaction of this nature, including, without limitation, confidentiality and non-compete undertakings by Varian.

Series B Preferred Stock

The terms of the Series B Preferred Stock are as set forth in the Series B Certificate of Designation of Series B Preferred Stock, as filed with the Delaware Secretary of State and effective on April 3, 2024. The Series B Certificate of Designation authorizes a total of 5,500 shares of Series B Preferred Stock, or the Series B Preferred Stock, with an initial conversion price of $0.3603, or the Preferred Conversion Price, which is subject to adjustment as provided in the Series B Certificate of Designation to no lower than $0.0721. The Series B Preferred Stock has a stated value of $1,000 per share, or the Stated Value, which equal to an aggregate Stated Value of $5,500,000 as of April 2, 2024. Each share of Series B Preferred Stock is initially convertible into 15,265 shares of our common stock, subject to adjustment as provided in the Series B Certificate of Designation. No fractional shares will be issued upon conversion; rather any fractional share will be rounded up to the nearest whole share.

From and after April 2, 2024, each holder of a share of Series B Preferred Stock is entitled to receive dividends, or Dividends, which are computed on the basis of a 360-day year and twelve 30-day months and will increase the Stated Value of the Series B Preferred Stock on each dividend date (as defined in the Series B Certificate of Designation).

Dividends on the Series B Preferred Stock will accrue at 10.0% per annum, or the Dividend Rate, and be payable by way of inclusion of the Dividends in the Conversion Amount (as defined in the Series B Certificate of Designation) on each Conversion Date (as defined in the Series B Certificate of Designation) in accordance with the Series B Certificate of Designation or upon any redemption in accordance with the Series B Certificate of Designation or upon any required payment upon any Bankruptcy Triggering Event (as defined in the Series B Certificate of Designation). From and after the occurrence and during the continuance of any Triggering Event (as defined in the Series B Certificate of Designation), the Dividend Rate will automatically be increased to 18.0% per annum.

The Preferred Conversion Price is subject to adjustment upon the occurrence of specified events and subject to price-based adjustment in the event of any stock split, stock dividend, stock combination, recapitalization or other similar transaction involving our common stock at a price below the then-applicable Preferred Conversion Price, as described in further detail in the Series B Certificate of Designation.

Securities Purchase Agreement and Convertible Notes

On April 2, 2024, we entered into the Purchase Agreement with the Buyers. Pursuant to the Purchase Agreement, we agreed to sell the Notes for $1.5 million of gross proceeds. The Notes have an initial conversion price of $0.3603, which is subject to adjustment upon the occurrence of specified events to no lower than $0.0721, subject to any stock split, stock dividend, stock combination, recapitalization or other similar transaction involving our common stock.

The Notes will be senior obligations of the Company. The Notes will accrue interest at a rate of 10.0% per annum, payable in arrears on the first calendar day of each calendar month, beginning on May 2, 2024, unless an event of default has occurred, upon which interest will accrue at 18.0% per annum. The Notes mature on January 2, 2025 unless earlier converted or redeemed (upon the satisfaction of certain conditions).

We may, subject to certain conditions, redeem all, but not less than all, of the amount then remaining under the Notes in cash at a premium of 20% of the greater of (i) the amount then outstanding under the Notes, and (ii) the equity value of our common stock underlying the Notes, which is calculated using the greatest closing sale price of our common stock on any trading day during the period commencing on the date of notice of such redemption and ending on the date we make the entire payment required pursuant to the Purchase Agreement. The Notes can also be redeemed by us under various other circumstances, such as a change of control, events of default, or at the option of the Buyer under limited circumstances, with any such redemption subject to the terms and conditions as set forth in the Notes.

The Notes contain certain conversion limitations, providing that no conversion may be made if, after giving effect to the conversion, the holder, together with any of its affiliates, would own in excess of 4.99% of our outstanding shares of common stock.

The Notes contain certain customary affirmative and negative covenants regarding the incurrence of indebtedness, the existence of liens, the repayment of indebtedness, the payment of cash in respect of dividends, distributions or redemptions and the transfer of assets, among other matters. The Notes also contain certain customary events of default, including, among other things, the failure to file and maintain an effective registration statement covering the certain registrable securities, subject to certain exceptions.

We agreed to seek stockholder approval for the issuance of all of the shares of common stock issuable upon conversion of the Notes and the Series B Preferred Stock in accordance with the rules and regulations of the Nasdaq Stock Market.

We additionally agreed that, subject to certain exceptions, without the consent of the holders holding at least a majority of our common stock underlying the Series B Preferred Stock and our common stock underlying the Notes for the period commencing on April 2, 2024 and ending on the date immediately following the 90th trading day after the Applicable Date (as defined in the Purchase Agreement), or the Restricted Period, neither we nor our subsidiaries shall directly or indirectly issue, offer, sell, grant any option or right to purchase, or otherwise dispose of (or announce any issuance, offer, sale, grant of any option or right to purchase or other disposition of) any equity security or any equity-linked or related security (including, without limitation, any equity security (as that term is defined under Rule 405 promulgated under the Securities Act of 1933, as amended), any Convertible Securities (as defined in the Purchase Agreement), any debt, any preferred stock or any purchase rights) (any such issuance, offer, sale, grant, disposition or announcement (whether occurring during the Restricted Period or at any time thereafter) is referred to as a Subsequent Placement).

Subject to the limitations described in the Purchase Agreement, for so long as the Notes are outstanding, we will be prohibited from effecting or entering into an agreement to effect any Subsequent Placement involving a Variable Rate Transaction (as defined in the Purchase Agreement). Additionally, the Purchase Agreement contains a participation right, which provides that, subject to certain exceptions, at any time on or prior to the fourth anniversary of April 2, 2024, neither we nor our subsidiaries shall, directly or indirectly, effect any Subsequent Placement unless we comply with the notice procedures as outlined in the Purchase Agreement with respect to each Buyer, providing the opportunity for such Buyer to participate in such Subsequent Placement on a pro rata basis as described in the Purchase Agreement.

Executive Officers

Craig E. Fraser
President, Chief Executive Officer and Chairman

Steven Simonson, M.D.
Senior Vice President, Chief Medical Officer

Eric Curtis
Senior Vice President, Chief Operating Officer

Board of Directors

Craig E. Fraser
President, Chief Executive Officer and Chairman

Jed Latkin
Chief Operating Officer and Head of Finance of ProPhase Labs, Inc.

Saundra Pelletier
President and Chief Executive Officer, and Interim Chair of Evofem Biosciences, Inc.

Robert Scott, M.D.
Former Chief Medical Officer and Head of Development for AbbVie

Mark Strobeck, Ph.D.
Director, President and CEO of Rockwell Medical, Inc.

Principal Executive Offices

2600 Kelly Road, Suite 100
Warrington, PA 18976
(215) 488-9300

Investor Relations

Eric Curtis
Senior Vice President, Chief Operating Officer
ecurtis@windtreetx.com

Transfer Agent

Continental Stock Transfer & Trust Company
1 State Street, 30th Floor
New York, New York 10004-1561

Independent Registered Public Accounting Firm

EisnerAmper LLP
One Logan Square
130 North 18th Street, Suite 3000
Philadelphia, PA 19103