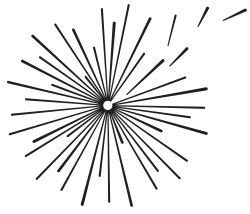


Verona Pharma

Breath of Innovation

Verona Pharma plc

2023 Annual Report

Verona Pharma
Breath of Innovation

Dear Shareholders,

2023 was a pivotal year for Verona Pharma with the acceptance for review of our New Drug Application ("NDA") by the US Food and Drug Administration ("FDA") and continued advancement of our commercialization strategy in preparation for the US launch of ensifentrine, if approved. In August, the FDA accepted for review our NDA seeking approval of ensifentrine for the maintenance treatment of patients with chronic obstructive pulmonary disease ("COPD") and assigned a Prescription Drug User Fee Act ("PDUFA") target action date of June 26, 2024.

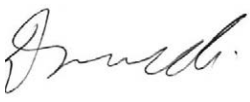
The NDA acceptance for review brings us closer to our goal of delivering ensifentrine to the millions of patients suffering from COPD. If successfully developed and approved, inhaled ensifentrine has the potential to be the first novel class of therapeutic in COPD in over 20 years. Supported by the results from our ENHANCE ("Ensifentrine as a Novel inHAled Nebulized COPD thErapy") trials, we believe ensifentrine's bronchodilator and non-steroidal anti-inflammatory activity has the potential to change the treatment paradigm for COPD.

While we remain focused on the US commercialization efforts for ensifentrine, we progressed development of two new programs: a fixed-dose combination formulation with ensifentrine and glycopyrrolate, a long-acting muscarinic antagonist ("LAMA"), for the maintenance treatment of patients with COPD via delivery in a nebulizer and a potential second indication for nebulized ensifentrine for the treatment of non-cystic fibrosis bronchiectasis ("NCFBE").

To support our commercialization activities and continued pipeline expansion, we enhanced our financial flexibility through a $400 million debt financing facility in December. We expect this facility, along with our existing cash, to support Verona Pharma's growth including the commercialization of ensifentrine, if approved, through at least 2026.

Alongside our progress in 2023, our development partner Nuance Pharma continued to enroll patients into a pivotal Phase 3 trial evaluating ensifentrine for the maintenance treatment of COPD in China. Nuance Pharma is developing and, if approved, will commercialize ensifentrine in Greater China and we look forward to providing future updates.

We expect 2024 to be a transformational year for Verona Pharma. We are finalizing our US launch preparations and look forward to commercializing ensifentrine in the second half of 2024, if approved. We also look forward to continued progress on our development programs as we work to build-out our pipeline.



David Zaccardelli
President and Chief Executive Officer
March 20, 2024

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: 001-38067

Verona Pharma plc

(Exact name of Registrant as specified in its Charter)

United Kingdom	**98-1489389**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
3 More London Riverside London SE1 2RE United Kingdom	**Not Applicable**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: +44 203 283 4200

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

Title of each class	Trading Symbol	Name of each exchange on which registered
Ordinary shares, nominal value £0.05 per share*	VRNA	The Nasdaq Stock Market LLC (Nasdaq Global Market)

* The ordinary shares are represented by American Depositary Shares (each representing 8 ordinary shares), which are exempt from the operation of Section 12(a) of the Securities Exchange Act of 1934, as amended, pursuant to Rule 12a-8 thereunder.

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 15(d) of the 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	☐	Small 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 ☒

The aggregate market value of the registrant's voting and non-voting common equity held by non-affiliates was approximately $1.5 billion as of June 30, 2023, the last business day of the registrant's most recently completed second fiscal quarter. Solely for purposes of this disclosure, shares held by executive officers, directors and certain shareholders of the registrant as of such date have been excluded because such persons or entities may be deemed to be affiliates of the registrant.

As of February 23, 2024, the registrant had 646,524,958 ordinary shares, nominal value £0.05 per share, outstanding, which if all held in ADS form, would be represented by 80,815,620 American Depositary Shares, each representing eight (8) ordinary shares.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement that the registrant intends to file with the Securities and Exchange Commission pursuant to Regulation 14A in connection with the registrant's 2024 Annual Meeting of Shareholders are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

GENERAL INFORMATION

All references in this Annual Report on Form 10-K (the "Annual Report"), to "Verona," the "company," the "group", "we," "us" and "our" refer to Verona Pharma plc and its consolidated subsidiaries. In this Annual Report, the U.S. Securities and Exchange Commission is referred to as the "SEC", the Securities Act of 1933, as amended, is referred to as the "Securities Act" and the Securities Exchange Act of 1934, as amended, is referred to as the "Exchange Act."

TRADEMARKS, TRADENAMES AND SERVICE MARKS

This Annual Report may include trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this Annual Report appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report contains statements that constitute forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words. All statements other than statements of historical facts contained in this Annual Report, including without limitation statements regarding our future results of operations and financial position, business strategy and plans and objectives of management for future operations, the development of ensifentrine or any other product candidates, including statements regarding the expected initiation, timing, progress and availability of data from our clinical trials and potential regulatory approvals and the expected regulations applicable to ensifentrine, research and development costs, timing and likelihood of success, potential collaborations, the duration of our patent portfolio, our estimates regarding expenses, future revenues, capital requirements, debt service obligations and our need for additional financing, the funding we expect to become available under the 2023 Term Loan and from cash receipts from U.K. tax credits, and the sufficiency of our cash and cash equivalents to fund operations, are forward-looking statements.

The forward-looking statements in this Annual Report are only predictions and are based largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this Annual Report and are subject to a number of known and unknown risks, uncertainties and assumptions, including the important factors described under the sections in this Annual Report entitled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and in our other filings with the SEC.

Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. We intend the forward-looking statements contained in this Annual Report to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act and Section 21E of the Exchange Act.

This Annual Report contains market data and industry forecasts that were obtained from industry publications. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. We have not independently verified any third-party information. While we believe the market position, market opportunity and market size information included in this Annual Report is generally reliable, such information is inherently imprecise.

SUMMARY RISK FACTORS

Our business is subject to numerous risks and uncertainties, including those described in Part I, Item 1A. "Risk Factors" in this Annual Report. You should carefully consider these risks and uncertainties when investing in our ADSs. The principal risks and uncertainties affecting our business include the following:

- We have a limited operating history and have never generated any product revenue;
- We may need additional funding to complete development of and commercialize ensifentrine and any future product candidates, if approved, or develop and commercialize other formulations or target indications of ensifentrine, if approved;
- The advances under the $400.0 million 2023 Term Loan are contingent upon achievement of certain clinical and regulatory milestones and other specified conditions. If we fail to meet those conditions, we will need to find alternative sources of funding;
- Changes in our tax rates, unavailability of certain tax credits or reliefs or exposure to additional tax liabilities or assessments could affect our profitability, and audits by tax authorities could result in additional tax payments for prior periods;
- We depend solely on the success of ensifentrine, our only product candidate under development;
- We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates;
- Ensifentrine may have serious adverse, undesirable or unacceptable side effects which may delay or prevent marketing approval;
- If we are unable to enroll patients in our clinical trials for other indications, or enrollment is slower than anticipated, our research and development efforts could be adversely affected;
- We may become exposed to costly and damaging liability claims, either when testing ensifentrine in the clinic or at the commercial stage, and our product liability insurance may not cover all damages from such claims;
- Regulatory approval processes are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for ensifentrine, our business will be substantially harmed;
- Enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize ensifentrine and may affect the prices we may set;
- Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties;
- We operate in a highly competitive and rapidly changing industry, which may result in others discovering, developing or commercializing competing products before or more successfully than we do;
- We rely, and expect to continue to rely, on third parties, including independent clinical investigators and clinical research organizations, to conduct our pre-clinical studies and clinical trials;
- The collaboration and license agreement with Nuance Pharma is important to our business. If Nuance Pharma is unable to develop and commercialize products containing ensifentrine in Greater China, if we or Nuance Pharma fail to adequately perform under the Nuance Agreement, or if we or Nuance Pharma terminate the Nuance Agreement, our business would be adversely affected;
- If we fail to enter into new strategic relationships for ensifentrine, our business, research and development and commercialization prospects could be adversely affected;
- We rely, and expect to continue to rely, on third party manufacturers and suppliers for production of the active pharmaceutical ingredient ensifentrine and formulated drug products derived therefrom. Our dependence on these third parties may impair the advancement of our research and development programs and the development of ensifentrine;
- We rely, and expect to continue to rely, on third parties for the sales, marketing, reimbursement and distribution of our drug products, and a failure by these third parties to adequately perform would adversely affect our business;

- Our and our manufacturers', suppliers' and other critical third parties' cybersecurity risk management program and processes may not be effective in protecting our systems, networks and Confidential Information;
- We rely on patents and other intellectual property rights to protect ensifentrine, the enforcement, defense and maintenance of which may be challenging and costly;
- We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent which might adversely affect our ability to develop, manufacture and market ensifentrine;
- We may be involved in lawsuits to protect or enforce patents covering ensifentrine, which could be expensive, time consuming and unsuccessful, and issued patents could be found invalid or unenforceable if challenged in court;
- Our future growth and ability to compete depends on our ability to retain our key personnel and recruit additional qualified personnel;
- We expect to expand our development, regulatory and sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations;
- The price of our American Depositary Shares may be volatile and may fluctuate due to factors beyond our control; and
- We will continue to incur increased costs as a result of operating as a public company in the United States, and our senior management are required to devote substantial time to new compliance initiatives and corporate governance practices.

Table of Contents

Item 1. Business

OVERVIEW

We are a clinical-stage biopharmaceutical company focused on developing and commercializing innovative therapeutics for the chronic treatment of respiratory diseases with significant unmet medical needs. Our product candidate, ensifentrine, is an investigational, first-in-class, inhaled, selective, dual inhibitor of the enzymes phosphodiesterase 3 and 4 ("PDE3" and "PDE4"), combining bronchodilator and non-steroidal anti-inflammatory activities in one molecule.

Initially, we are developing inhaled ensifentrine for the maintenance treatment of chronic obstructive pulmonary disease ("COPD"), a common, chronic, progressive, and life-threatening respiratory disease without a cure. If approved, ensifentrine is expected to be the first inhaled therapeutic with a novel mode of action for the maintenance treatment of COPD in over 20 years.

In August 2023, the U.S. Food and Drug Administration ("FDA") accepted for review our New Drug Application ("NDA") seeking approval of ensifentrine for the maintenance treatment of COPD and assigned a Prescription Drug User Fee Act ("PDUFA") target action date of June 26, 2024. The FDA stated it is not currently planning to hold an advisory committee meeting to discuss the application.

Based on the results from our successful Phase 3 ENHANCE ("Ensifentrine as a Novel inHAled Nebulized COPD thErapy") program, we believe ensifentrine, if approved, has the potential to change the treatment paradigm for COPD. Ensifentrine met the primary endpoint in both the ENHANCE-1 and ENHANCE-2 trials demonstrating statistically significant and clinically meaningful improvements in measures of lung function. In key secondary endpoints, ensifentrine demonstrated early and sustained improvements in symptoms and quality of life. In addition, other endpoint data demonstrated that ensifentrine substantially reduced the rate and risk of COPD exacerbations in ENHANCE-1 and ENHANCE-2. Ensifentrine was well tolerated in both trials.

During 2023, we presented additional analyses of data from the ENHANCE trials at international scientific conferences and the data were published in peer reviewed publications:

- In May 2023, we presented 12 abstracts and a symposium on expanded pre-specified and post hoc analyses of the ENHANCE trials including subgroup and pooled data covering exacerbations, use of rescue medication and healthcare utilization, at the American Thoracic Society International Conference ("ATS") 2023. An overview of the ENHANCE trial results was presented as part of the Clinical Trial Symposium reserved for highlighting new innovative medicines. In summary, ensifentrine demonstrated highly consistent results across all the clinically relevant subgroups and pooled analyses assessed including improvements in lung function and reductions in exacerbation rate and risk. Other key analyses demonstrated improvements with ensifentrine in symptoms and quality of life measures, including SGRQ* subdomains, as well as reductions in the use of rescue medication and healthcare utilization. Furthermore, ensifentrine was shown to be well tolerated in an expanded safety analysis.

*St. George's Respiratory Questionnaire is a validated patient reported outcome tool

- The abstracts were published on the ATS website and in the American Journal of Respiratory and Critical Care Medicine ("AJRCCM");
- In June 2023, the ENHANCE results were published in AJRCCM;
- In September 2023, we presented an analysis of the ENHANCE-1 24-week exacerbation data at ERS International Congress 2023, which demonstrated treatment with ensifentrine substantially decreased the rate and risk of moderate and severe COPD exacerbations. The abstract was published in the European Respiratory Journal; and
- In October 2023, we gave 4 presentations on pooled and subgroup post-hoc analyses from ENHANCE-1 and ENHANCE-2 covering data related to exacerbations, lung function, symptoms and quality of life endpoints and use of daily rescue medication, at CHEST Annual Meeting 2023. The data demonstrated treatment with ensifentrine substantially reduced the rate and risk of COPD exacerbations regardless of recent exacerbation history and was well tolerated. In addition, subgroup analyses showed treatment with ensifentrine resulted in improvements in lung function, symptoms, and quality of life measures, reductions in the rate and risk of exacerbations regardless of background therapy as well as reductions in daily rescue medication use. The data were published in the CHEST Annual Meeting online supplement. Also, at CHEST, we launched a disease awareness campaign highlighting how many COPD patients struggle to talk about their condition.

While we remain focused on the U.S. commercialization of ensifentrine, we are developing a fixed-dose combination formulation with ensifentrine and glycopyrrolate, a long-acting muscarinic antagonist ("LAMA"), for the maintenance treatment of patients with COPD via delivery in a nebulizer. Following development activities to confirm a feasible

formulation, in the second half of 2024, we plan to submit an Investigational New Drug application ("IND") to the FDA and, subject to clearance, initiate a Phase 2 clinical trial assessing the safety and efficacy of the fixed-dose combination formulation in COPD patients.

Also in the second half of 2024, we plan to commence a Phase 2 clinical trial to assess the efficacy and safety of nebulized ensifentrine in patients with non-cystic fibrosis bronchiectasis ("NCFBE"), subject to clearance by the FDA

In Phase 2 clinical trials, ensifentrine has demonstrated positive results in patients with COPD, asthma and cystic fibrosis ("CF"). Two additional formulations of ensifentrine have been evaluated in Phase 2 trials for the treatment of COPD: dry powder inhaler ("DPI") and pressurized metered-dose inhaler ("pMDI"). Ensifentrine has shown positive Phase 2 data in COPD trials when delivered by each of these formulations.

We believe the development of ensifentrine in cystic fibrosis and asthma as well as the additional formulations of ensifentrine provides pipeline expansion and lifecycle opportunities as well as potential for collaborations outside the US.

If approved, we intend to commercialize inhaled ensifentrine for the maintenance treatment of COPD in the United States ("U.S."). Although we believe ensifentrine will not be regulated as a drug device combination, patients use a readily available standard jet nebulizer to take ensifentrine. Outside the US, we intend to license ensifentrine to companies with expertise and experience in developing and commercializing products in those regions. To that end, we have entered into a strategic collaboration with Nuance Pharma Limited, a Shanghai-based specialty pharmaceutical company ("Nuance Pharma"), to develop and commercialize ensifentrine in Greater China. In 2023, Nuance enrolled the first subject in its pivotal Phase 3 trial evaluating ensifentrine for the maintenance treatment of COPD in China.

Overview of COPD and current treatments

COPD is a common, progressive, life-threatening respiratory disease without a cure. It causes loss of lung function, leading to debilitating breathlessness, hospitalizations, and death. COPD has a major impact on everyday life. Patients struggle with basic activities such as getting out of bed, showering, eating, and walking. Worldwide, COPD affects approximately 392 million people and is the third leading cause of death, according to the Global Initiative for Chronic Obstructive Lung Disease.

The goal of COPD pharmacological therapy is to improve patients' quality of life by reducing symptoms, decreasing the quantity and severity of exacerbations (often an escalation of symptoms) and to improve patients' ability to function.

For approximately 40 years, the treatment of COPD has been dominated by three classes of inhaled therapies approved for use by the FDA and the European Commission based on the European Medicines Agency's ("EMA") opinion: anti-muscarinics, beta-agonists and inhaled corticosteroids ("ICSs"). COPD patients are frequently treated with bronchodilators, including LAMAs and long-acting beta-agonists ("LABAs"), to relieve airway constriction and make it easier to breathe. In addition, patients at risk for exacerbations may be prescribed ICSs to prevent them.

Certain COPD patients are treated with the oral PDE4 inhibitor, roflumilast (Daliresp®), which has demonstrated a reduction in exacerbation risk in patients with severe chronic bronchitis. However, oral PDE4 therapy results in systemic exposure, which has been associated with unfavorable gastrointestinal side-effects such as nausea, emesis, diarrhea, abdominal pain, loss of appetite and weight loss.

Approximately 8.6 million COPD patients in the U.S. receive LAMA, LABA, or ICS treatments alone or in combination regardless of COPD severity. Despite these medications and the earlier use of dual (LAMA / LABA) and triple (LAMA / LABA / ICS) therapies, many patients continue to suffer debilitating symptoms. According to a December 2022 study by Phreesia, 49% of patients continue to have symptoms more than 24 days a month. This burden leaves a significant opportunity for new inhaled therapies that offer additional benefit added to the three main classes of treatment. New treatment options are urgently needed to help improve lung function and symptoms, reduce exacerbations and improve overall quality of life in these patients.

Ensifentrine

Ensifentrine is an investigational, first-in-class, inhaled, small molecule and selective, dual PDE3 and PDE4 inhibitor. This dual inhibition enables it to act as a bronchodilator and a non-steroidal anti-inflammatory agent in a single compound. Importantly, ensifentrine's therapeutic profile differentiates it from existing classes of bronchodilator and anti-inflammatory treatments. We are not aware of any other single compound in clinical development in the U.S. or Europe or approved by the FDA nor the European Commission for the treatment of respiratory diseases that acts both as a bronchodilator and anti-inflammatory agent. If successfully developed and approved, inhaled ensifentrine has the potential to be the first novel class of therapeutic in COPD in over 20 years and to become the only bronchodilator option that could be added to existing classes of inhaled therapies including LAMA, LABA and ICS.

Safety profile

Ensifentrine has been well tolerated in clinical trials involving approximately 3,000 subjects to date. Additionally, ensifentrine did not prolong the QT interval or impact other cardiac conduction parameters in a thorough QT study in healthy volunteers. It is delivered directly to the lungs by inhalation to maximize pulmonary exposure to ensifentrine while minimizing systemic exposure. This feature minimizes any systemic side-effects such as the gastrointestinal disturbance associated with oral PDE4 inhibitors. In addition, in non-clinical trials ensifentrine has demonstrated high selectivity for PDE3 and PDE4 over other enzymes and receptors, which is believed to minimize off-target effects.

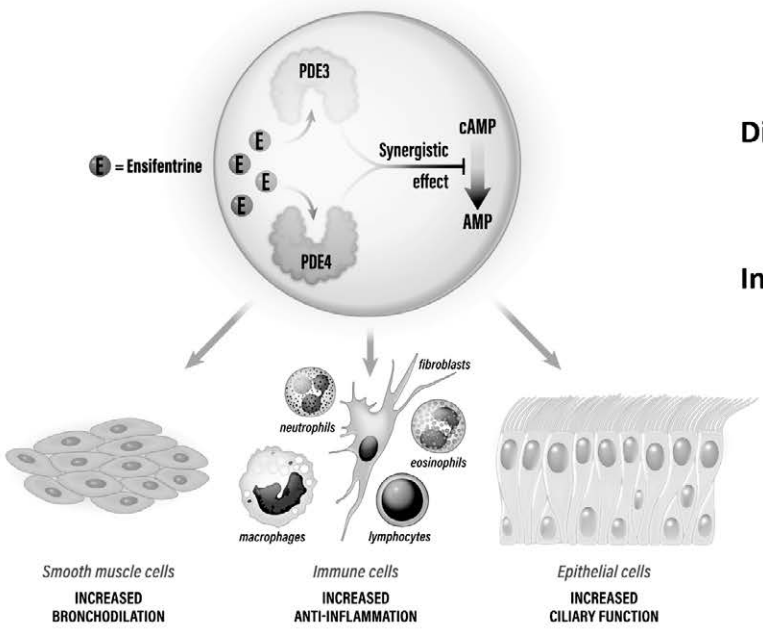
Differentiated profile

By selectively inhibiting PDE3 and PDE4, ensifentrine impacts three key mechanisms in respiratory disease: bronchodilation, inflammation and mucociliary clearance. Ensifentrine is designed to increase the levels of cellular cAMP and cGMP in smooth muscle cells and inflammatory cells, resulting in bronchodilator and anti-inflammatory effects. Ensifentrine has also been shown to stimulate the cystic fibrosis transmembrane conductance regulator ("CFTR"), which is an ion channel in the epithelial cells lining the airways. Mutations in the CFTR protein result in poorly or non-functioning ion channels, which cause CF. CFTR dysfunction is also potentially important in COPD. CFTR stimulation leads to improved electrolyte balance in the lung and thinning of the mucus, which facilitates mucociliary clearance and leads to improved lung function and potentially a reduction in lung infections.

Dual inhibition of PDE3 and PDE4 has shown enhanced or synergistic effects compared with inhibition of either PDE alone on contraction of airway smooth muscle and suppression of inflammatory mediator release in several preclinical studies. We believe these enhanced effects may increase the utility of ensifentrine in the treatment of respiratory diseases including COPD, NCFBE, asthma and CF.

Ensifentrine: Novel mechanism of action

Resulting in downstream bronchodilatory, anti-inflammatory, and ciliary effects



Direct mechanisms:

- Modulation of intracellular cAMP in cells that express PDE3, PDE4, or both

Indirect mechanisms:

- Reduction in macrophage activation that impacts cellular adhesion, chemotaxis, and survival of neutrophils and eosinophils
- CFTR activation and increased ciliary beat frequency in vitro

We believe ensifentrine has the potential to address the large unmet need in treating COPD with its improvements in lung function, COPD symptoms and quality of life.

Development of ensifentrine

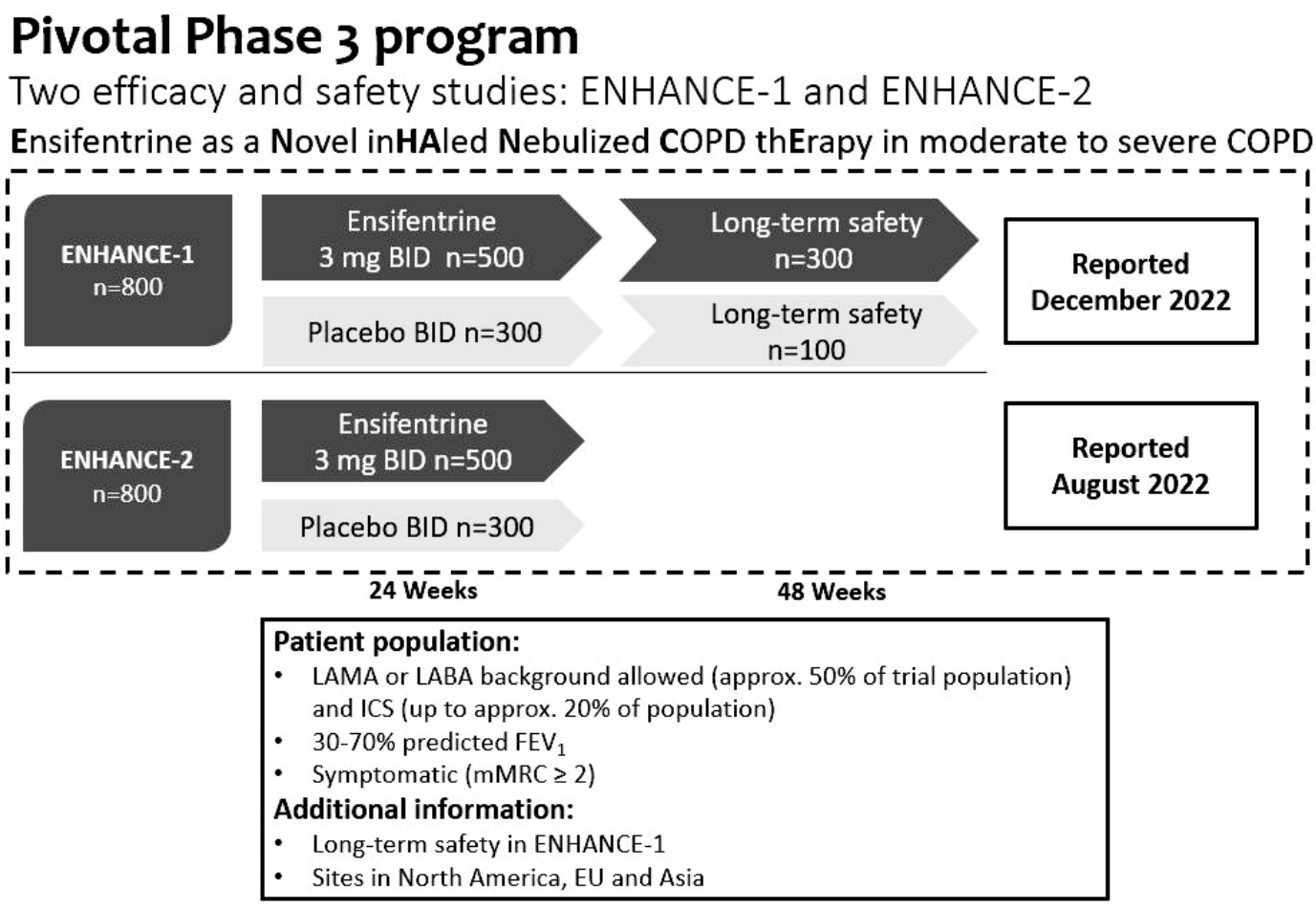
Clinical development of ensifentrine in COPD

Phase 3 ENHANCE program

Ensifentrine has successfully met the primary endpoints in two randomized, double-blind, placebo-controlled Phase 3 trials, ENHANCE-1 and ENHANCE-2, demonstrating statistically significant and clinically meaningful improvements in measures of lung function in moderate to severe COPD patients. Improvements in symptoms and quality of life measures were shown in both trials, which reached statistical significance in ENHANCE-1. Ensifentrine substantially reduced the rate and risk of moderate to severe COPD exacerbations in both trials. Ensifentrine was well tolerated in both trials.

The ENHANCE trials were designed to evaluate ensifentrine as monotherapy and added onto a single bronchodilator with approximately 50% of subjects receiving either a LAMA or a LABA. Additionally, approximately 20% of subjects received ICSs with their concomitant LAMA or LABA.

Each trial enrolled approximately 800 subjects, for a total of approximately 1,600 subjects, at sites primarily in the U.S. and Europe. The two trials provided replicate evidence of efficacy and safety data over 24 weeks and ENHANCE-1 also evaluated longer-term safety in approximately 400 subjects over 48 weeks.



Subject demographics and disease characteristics were well balanced between treatment groups in both trials.

- In ENHANCE-1 approximately 69% of subjects received background COPD therapy, either LAMA or a LABA. Additionally, approximately 20% of all subjects received ICS with concomitant LAMA or LABA.
- In ENHANCE-2 approximately 55% of subjects received background COPD therapy, either a LAMA or a LABA. Additionally, approximately 15% of all subjects received ICS with concomitant LAMA or LABA.

ENHANCE Program baseline characteristics

Demographics and baseline characteristics well balanced between groups

Parameter	ENHANCE-1		ENHANCE-2	
	Ensifentrine n=479	*Placebo n=284*	*Ensifentrine n=499*	*Placebo n=291*
Age, mean (SD)	65.1 (7.1)	64.9 (7.7)	65.0 (7.4)	65.3 (7.3)
Gender, % Male, n (%)	275 (57.4)	167 (58.8)	245 (49.1)	138 (47.4)
Moderate / Severe COPD, n (%) Mild / Very Severe COPD, n (%)	295 (61.6) / 180 (37.6) 1 (0.2) / 3 (0.6)	164 (57.7) / 119 (41.9) 0 / 0	266 (53.3) / 231 (46.3) 1 (0.2) / 1 (0.2)	143 (49.1) / 148 (50.9) 0 / 0
% Predicted FEV_1 mean, (SD)	52.9 (10.3)	51.7 (10.6)	50.8 (10.7)	50.4 (10.7)
% with Chronic Bronchitis, n (%)	387 (80.8)	216 (76.1)	322 (64.5)	190 (65.3)
% Current Smokers, n (%)	269 (56.2)	164 (57.7)	276 (55.3)	160 (54.9)
Background Meds: Yes, n (%) LAMA LAMA / ICS LABA LABA / ICS	331 (69.1) 151 (31.5) 4 (0.8) 89 (18.6) 87 (18.2)	192 (67.6) 76 (26.8) 5 (1.8) 45 (15.8) 66 (23.2)	275 (55.1) 168 (33.7) 1 (0.2) 34 (6.8) 72 (14.4)	160 (55.0) 90 (30.9) 0 23 (7.9) 47 (16.2)
E-RS Baseline, mean (SD)	14.1 (6.8)	13.3 (6.1)	13.3 (6.7)	13.3 (6.2)
SGRQ Baseline, mean (SD)	48.1 (18.3)	46.9 (17.1)	50.6 (17.4)	51.2 (16.4)

We reported positive top-line results from ENHANCE-2 and ENHANCE-1, in August and December 2022, respectively. Ensifentrine successfully met the primary endpoints in both trials, demonstrating statistically significant and clinically meaningful improvements in measures of lung function in moderate to severe COPD patients. Improvements in symptoms and quality of life measures were shown in both trials, which reached statistical significance in ENHANCE-1. Ensifentrine substantially reduced the rate and risk of moderate to severe COPD exacerbations and was well tolerated in both trials.

Highlights

Primary endpoint met (FEV_1 AUC 0-12 hr)

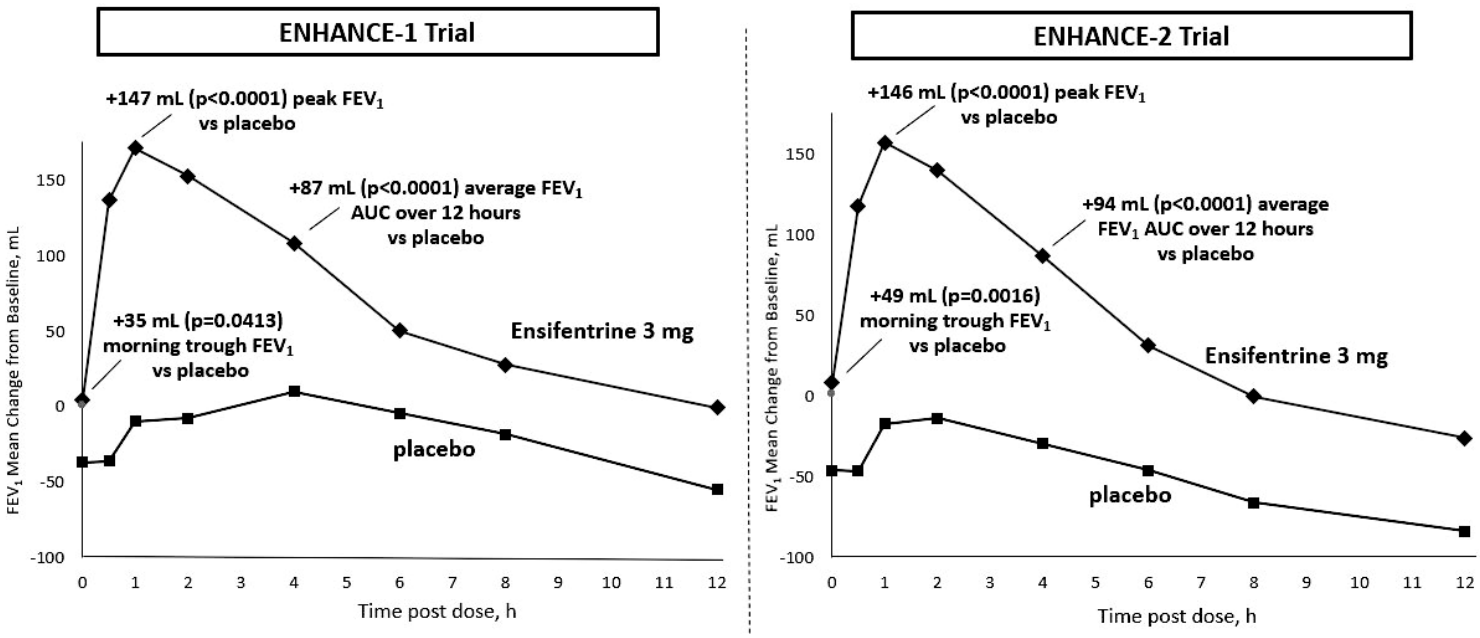
- Placebo corrected, change from baseline in average FEV_1 area under the curve 0-12 hours post dose at week 12 was 87 mL ($p<0.0001$) for ensifentrine in ENHANCE-1 and 94 mL ($p<0.0001$) for ensifentrine in ENHANCE-2.
- Demonstrated consistent improvements with ensifentrine in all subgroups including gender, age, smoking status, COPD severity, background medication, ICS use, chronic bronchitis, FEV_1 reversibility and geographic region.

Secondary endpoints evaluating lung function met:

- Placebo corrected, increase in peak FEV_1 of 147 mL ($p<0.0001$) 0-4 hours post dose at week 12 in ENHANCE-1 and 146 mL ($p<0.0001$) in ENHANCE-2.
- Placebo corrected, increase in morning trough FEV_1 of 35 mL ($p=0.0413$) at week 12 in ENHANCE-1 and 49 mL ($p=0.0016$) in ENHANCE-2, supporting twice daily dosing regimen.

Primary endpoint met in both ENHANCE trials

Statistically significant peak & morning trough FEV_1 measures



Exacerbation rate and risk reduced

- Subjects receiving ensifentrine demonstrated a 36% reduction in the rate of moderate to severe COPD exacerbations over 24 weeks (p=0.0503) compared to those receiving placebo in ENHANCE-1 and a 43% reduction (p=0.0090) in ENHANCE-2.

Exacerbation rate reduced in both ENHANCE trials

Consistent and clinically meaningful results

ENHANCE-1 Trial

Treatment	*Annualized Event Rate LS mean, (95% CI)*	*Rate Ratio (95% CI)*	*Exacerbation Rate Reduction*	*p-value*
Ensifentrine 3 mg (n = 477)	0.26 (0.17, 0.40)	0.64 (0.40, 1.00)	**36%**	0.0503
Placebo (n = 283)	0.41 (0.27, 0.63)	--	--	

ENHANCE-2 Trial

Treatment	*Annualized Event Rate LS mean, (95% CI)*	*Rate Ratio (95% CI)*	*Exacerbation Rate Reduction*	*p-value*
Ensifentrine 3 mg (n = 498)	0.24 (0.18, 0.32)	0.57 (0.38, 0.87)	**43%**	0.0090
Placebo (n = 291)	0.42 (0.30, 0.57)	--	--	

Exacerbation was defined as a ***worsening of symptoms*** requiring:

- Minimum of 3 days of treatment with oral/systemic steroids and/or antibiotics ***OR*** hospitalization

- In pooled exacerbation data from ENHANCE-1 and ENHANCE-2, ensifentrine demonstrated a 40% reduction in the rate of moderate to severe COPD exacerbations over 24 weeks (p=0.0012) compared to those receiving placebo.

Pooled data: significant 40% reduction in exacerbation rate

Protocol specified pooled analysis including ENHANCE-1 and ENHANCE-2

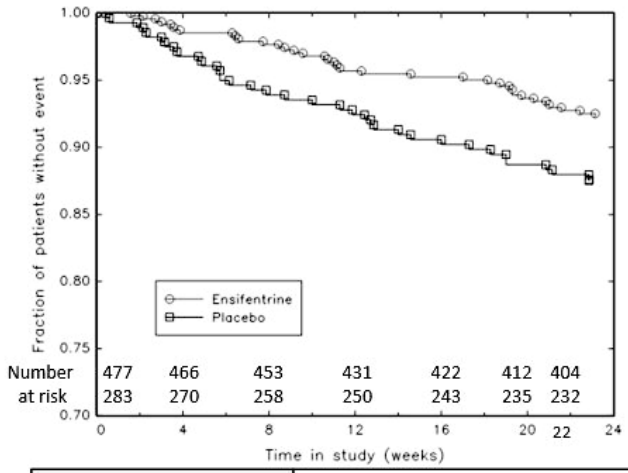
Treatment	*Annualized Event Rate LS mean, (95% CI)*	*Rate Ratio (95% CI)*	*Exacerbation Rate Reduction*	*P-value*
Ensifentrine 3 mg (n = 975)	0.27 (0.19, 0.39)	0.60 (0.44, 0.82)	**40%**	0. 0012
Placebo (n = 584)	0.45 (0.31, 0.65)	--	--	

- Treatment with ensifentrine significantly decreased the risk of a moderate/severe exacerbation as measured by time to first exacerbation when compared with placebo by 38% (p=0.0382) in ENHANCE-1 and by 42% (p=0.0089) in ENHANCE-2.

Time to first exacerbation significantly delayed across trials

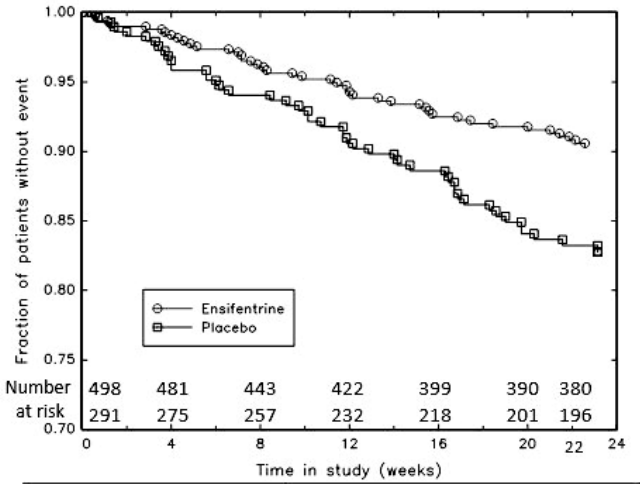
Consistent and clinically meaningful reduction in risk of a COPD exacerbation

ENHANCE-1 Trial



	Ensifentrine vs. Placebo (n = 760)
Hazard Ratio (95%, CI)	0.62 (0.39, 0.97)
Risk Reduction	**38%**
P-value	0.0382

ENHANCE-2 Trial

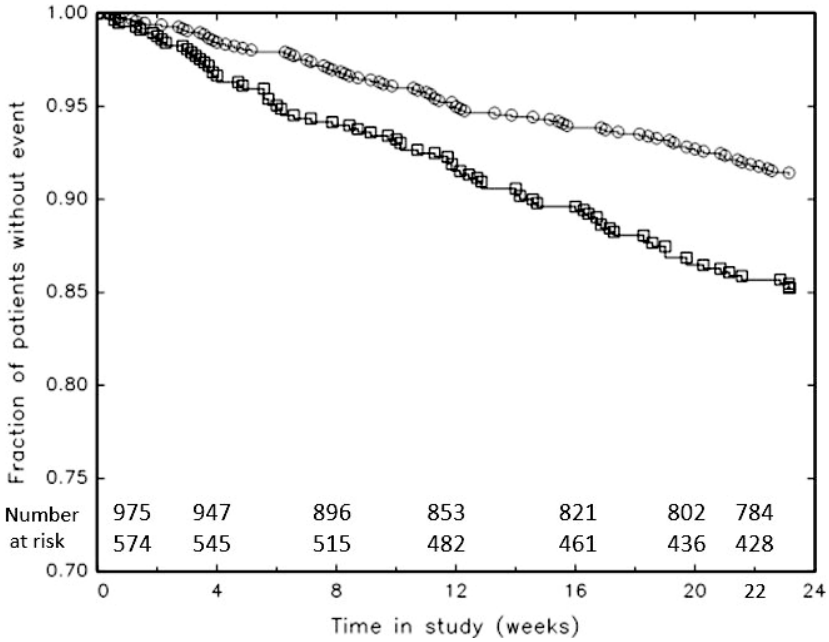


	Ensifentrine vs. Placebo (n = 789)
Hazard Ratio (95%, CI)	0.58 (0.38, 0.87)
Risk Reduction	**42%**
P-value	0.0089

- In pooled exacerbation data from ENHANCE-1 and ENHANCE-2, ensifentrine significantly decreased the risk of a moderate/severe exacerbation as measured by time to first exacerbation when compared with placebo by 41% (p=0.0009).

Pooled data:
significant 41% risk reduction in time to first exacerbation

Protocol specified pooled analysis including ENHANCE-1 and ENHANCE-2



	Ensifentrine vs. Placebo (n = 1,549)
Hazard Ratio (95%, CI)	0.59 (0.44, 0.81)
Risk Reduction	**41%**
P-value	0.0009

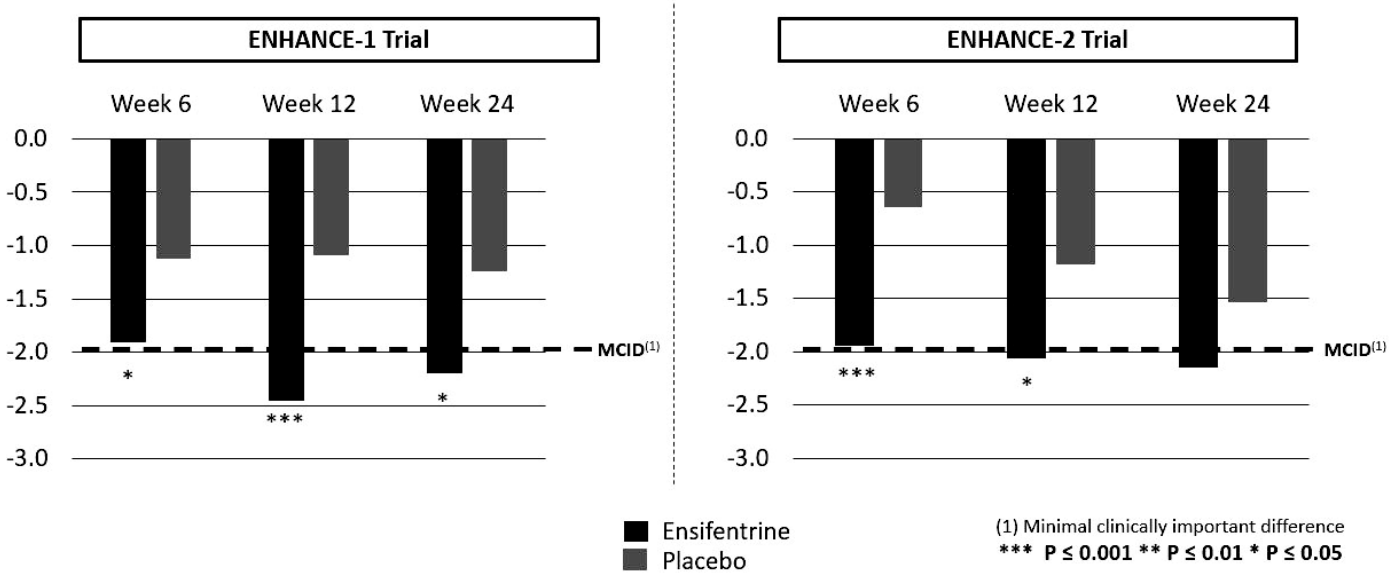
Ensifentrine
Placebo

COPD symptoms and Quality of Life ("QOL")

- In ENHANCE-1, daily symptoms as measured by E-RS* Total Score in the ensifentrine group improved from baseline to greater than the minimal clinically important difference ("MCID") of -2 units with a statistically significant improvement compared to placebo at week 24. Improvements in symptoms were early and sustained with statistical significance versus placebo at weeks 6, 12 and 24. Similar improvements were demonstrated in ENHANCE-2 but statistical significance was not achieved due to improvements observed in the placebo group over time.

Ensifentrine improved symptoms across trials

Early and sustained improvement in E-RS total score

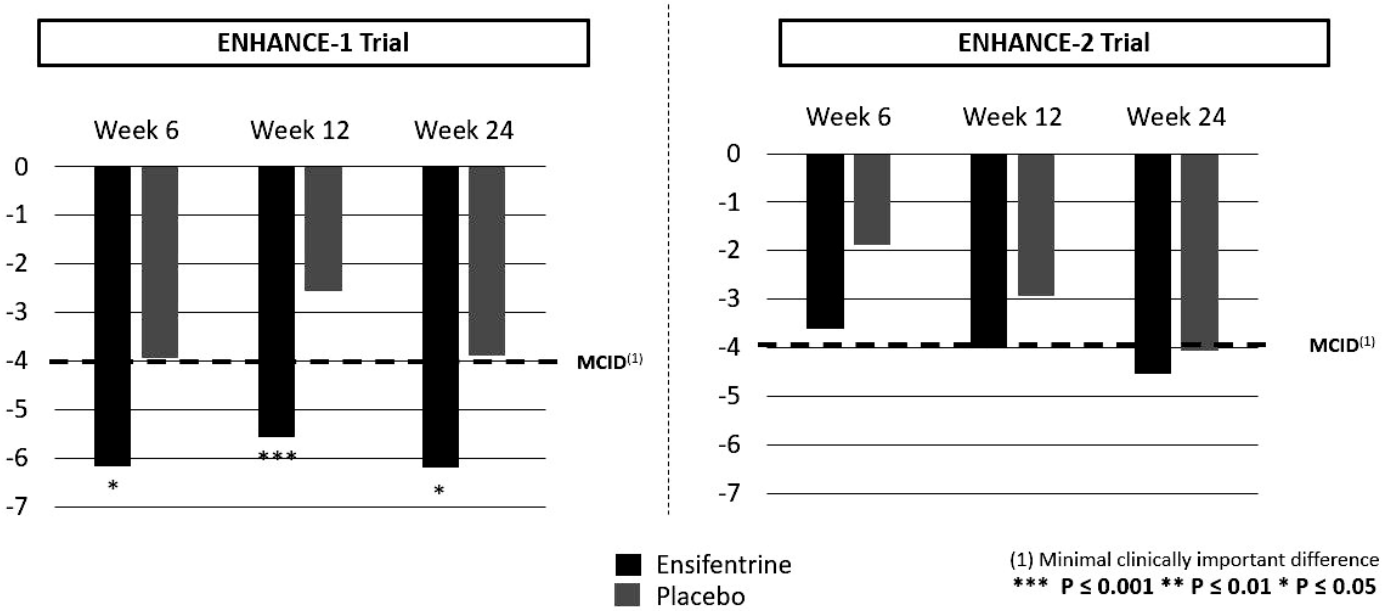


- In ENHANCE-1, QOL as measured by SGRQ* Total Score in the ensifentrine group improved from baseline to greater than the MCID of -4 units with a statistically significant improvement compared to placebo at week 24. Improvements in QOL were early and sustained with statistical significance versus placebo at weeks 6, 12 and 24. In ENHANCE-2, QOL as measured by SGRQ* Total Score in the ensifentrine group also improved from baseline to greater than the MCID of -4 units at weeks 12 and 24, numerically exceeding placebo at each measurement, but statistical significance was not achieved due to improvements observed in the placebo group over time.

*E-RS, Evaluating Respiratory Symptoms, and SGRQ, St. George's Respiratory Questionnaire, are validated patient reported outcome tools

Ensifentrine improved quality of life across trials

Early and sustained improvement in SGRQ total score



Favorable safety profile

- Ensifentrine was well tolerated with very few adverse events occurring in more than 1% of subjects and greater than placebo over 24 and 48 weeks.

Adverse events reported at low rates over 24 and 48 weeks

Few events greater than 1% and greater than placebo

ENHANCE-1 Trial

	Event	Ensifentrine 3 mg (n = 477)	Placebo (n = 283)
Subjects with at least one TEAE, n (%)		**221 (46.3)**	**114 (40.3)**
Any TEAE >1% and greater than placebo	Hypertension, n (%)	14 (2.9)	4 (1.4)
	Back pain, n (%)	12 (2.5)	1 (0.4)
	URT*, n (%)	10 (2.1)	5 (1.8)
	Pneumonia, n (%)	7 (1.5)	1 (0.4)
	Toothache, n (%)	6 (1.3)	2 (0.7)
	Atrial fibrillation, n (%)	6 (1.3)	2 (0.7)

ENHANCE-2 Trial

	Event	Ensifentrine 3 mg (n = 498)	Placebo (n = 291)
Subjects with at least one TEAE, n (%)		**176 (35.3)**	**103 (35.4)**
Any TEAE ≥1% and greater than placebo	Worsening of COPD, n (%)	11 (2.2)	5 (1.7)
	Nasopharyngitis, n (%)	9 (1.8)	3 (1.0)
	Diarrhea, n (%)	8 (1.6)	2 (0.7)
	Sinusitis, n (%)	6 (1.2)	0 (0)
	Hypertension, n (%)	5 (1.0)	1 (0.3)

* Upper respiratory tract infection

We believe ensifentrine, if approved, has the potential to change the treatment paradigm for COPD. The totality of data from clinical trials, in particular the top-line results from the ENHANCE program, including improvements in measures of lung function, symptoms, quality of life measures, and exacerbation reductions, coupled with the consistent safety results, support our belief.

ENHANCE Program summary

ENHANCE-1 and ENHANCE-2 demonstrated consistent results in COPD patients

Top-line Measurement	ENHANCE-1	ENHANCE-2
Average FEV_1 AUC (0-12 hours)	+87 mL (p<0.0001) vs placebo	+94 mL (p<0.0001) vs placebo
Peak FEV_1	+147 mL (p<0.0001) vs placebo	+146 mL (p<0.0001) vs placebo
Morning Trough FEV_1	+35 mL (p=0.0413) vs placebo	+49 mL (p=0.0016) vs placebo
Evening Trough FEV_1	+58 mL (p=0.0008) vs placebo	+54 mL (p=0.0016) vs placebo
Symptoms (E-RS Total Score)	-1.0 units (p=0.0111) vs placebo	-0.6 units (NS) vs placebo
Quality of Life (SGRQ Total Score)	-2.3 units (p=0.0253) vs placebo	-0.5 units (NS) vs placebo
Exacerbation rate	36% (p=0.0503) reduction in rate	43% (p=0.0090) reduction in rate
Time to first COPD exacerbation	38% (p=0.0382) reduction in risk	42% (p=0.0089) reduction in risk
Pooled exacerbation rate	40% (p=0.0012) reduction in rate	
Pooled time to first COPD exacerbation	41% (p=0.0009) reduction in risk	
Incidence of adverse events	Low incidence of adverse events at 24 and 48 weeks No safety signals associated with ensifentrine	

NS = not significant

Formulations

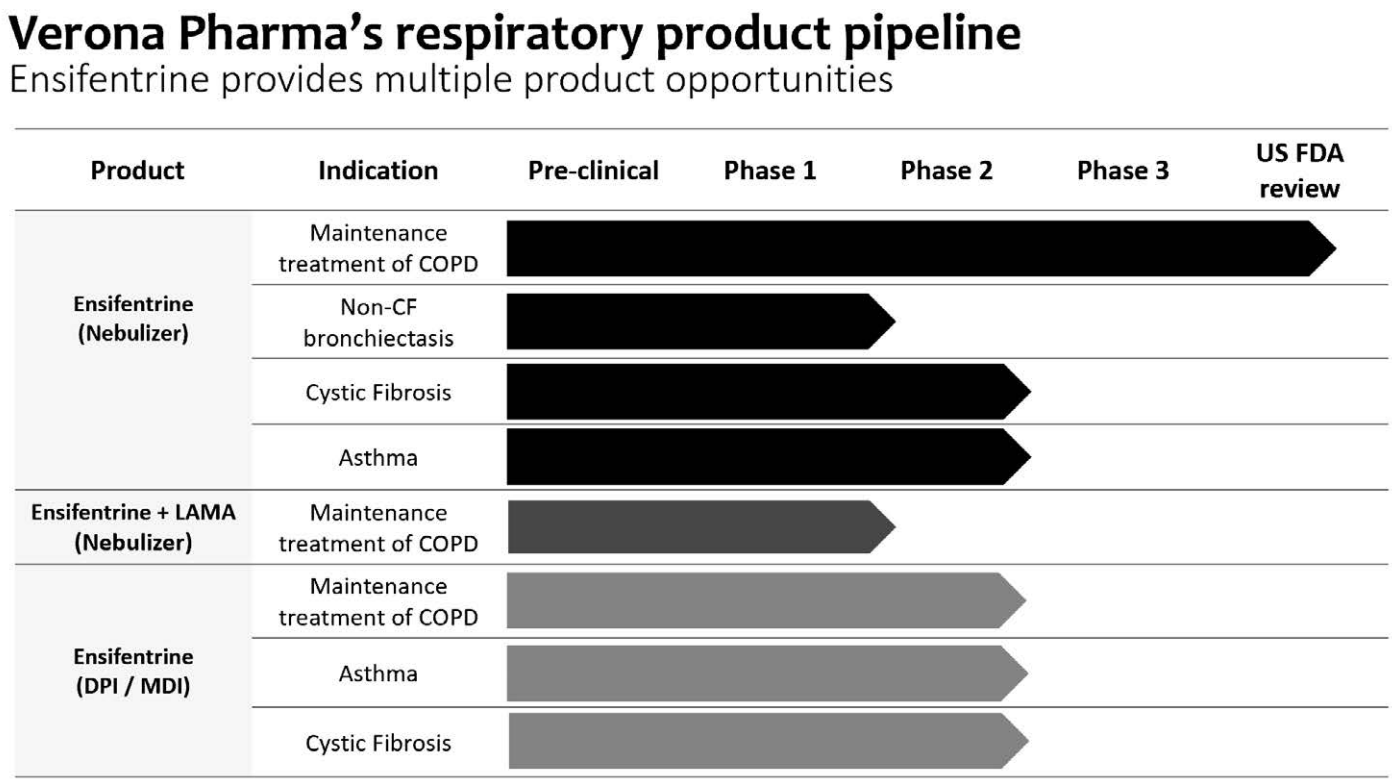
We have developed formulations of ensifentrine for the three most widely used inhalation devices: nebulizer, DPI and pMDI. The nebulized formulation of ensifentrine is designed to be suitable for use in a standard jet nebulizer, not a proprietary device. Delivery of COPD medications by nebulizer is important because such medications can be used by adults of almost any age and dexterity and regardless of peak inspiratory flow, offering advantages to patients who struggle to operate handheld inhaler devices or have low peak inspiratory flow. DPI and pMDI handheld inhaler formats are relatively portable and convenient and are also important delivery mechanisms.

While we continue to focus on development of the nebulized formulation of ensifentrine, we believe the development of pMDI and DPI formulations of ensifentrine provides additional lifecycle opportunities including new potential indications, formulation combinations and collaborations. In February 2021, we reported positive results from the second, multiple dose part of a Phase 2 trial with pMDI ensifentrine in patients with moderate to severe COPD. Ensifentrine delivered by pMDI met all of the primary and secondary lung function endpoints. The improvement in lung function was dose-ordered and statistically significant at peak and over the 12-hour dosing interval compared with placebo, and supports twice-daily dosing of ensifentrine via pMDI for the treatment of COPD. Data from the single dose part of the study were reported in March 2020.

We have successfully demonstrated proof of concept in Phase 2 COPD trials with all three formulations. In addition, the data from Phase 2 trials were consistent across the three formulations. All three dosage forms have demonstrated statistically significant and clinically meaningful improvements in lung function and duration of action, supporting twice-daily dosing and a safety profile similar to placebo.

Pipeline

The following table summarizes our development programs.



Planned Clinical Development Activities

Ensifentrine / LAMA fixed-dose combination

Fixed-dose combination therapies such as LABA / LAMA, LABA / ICS and LABA / LAMA / ICS are commonly used in the treatment of COPD and, based on our market research, an unmet need exists for a nebulized fixed-dose combination therapy. We believe the combination of ensifentrine with a LAMA could provide COPD patients with the first nebulized fixed-dosed combination with the potential to provide bronchodilation through a dual mechanism and also non-steroidal anti-inflammatory effects via PDE inhibition. We are developing a fixed-dose combination formulation with ensifentrine and glycopyrrolate, a LAMA, for the maintenance treatment of patients with COPD via delivery in a nebulizer. We have filed patent applications in multiple jurisdictions including the US.

If a feasible formulation is developed, in the second half of 2024, we plan to submit an IND application to the FDA and, if allowed to proceed, initiate a Phase 2 clinical trial assessing the safety and efficacy of the fixed-dose combination formulation in COPD patients.

Non-cystic fibrosis bronchiectasis

NCFBE is a chronic lung disease characterized by persistent cough, excess sputum production and frequent respiratory infections with more severe patients suffering exacerbations. The condition affects up to 500,000 adults in the U.S. and no therapies are specifically approved to treat it. Physicians currently use bronchodilators, antibiotics, steroids, mucus thinners and surgery.

Based on the clinical results of ensifentrine observed in patients with COPD, including improvements in lung function and symptoms of cough and sputum, we believe that ensifentrine could potentially be an effective treatment for NCFBE. We plan to commence a Phase 2 clinical trial to assess the efficacy and safety of nebulized ensifentrine in patients with NCFBE in the second half of 2024, if allowed to proceed by the FDA.

Potential additional indications for ensifentrine

Cystic fibrosis and asthma

In addition to COPD and NCFBE, we believe ensifentrine has potential applications in other respiratory diseases including CF and asthma providing pipeline expansion opportunities and the potential for collaborations outside the US.

CF is a progressive, fatal genetic disease without a cure and a median age of death of 46 years. The condition is characterized by thick, sticky mucus that damages many of the body's organs. It causes repeat and persistent lung infections that result in frequent exacerbations and hospitalizations. Other symptoms include malnutrition, constipation and diarrhea, and some adults develop diabetes, arthritis and liver problems.

CF is the most common fatal inherited disease in the U.S. and Europe. Approximately 40,000 people in the U.S. and an estimated 105,000 people worldwide have been diagnosed with CF across more than 90 countries and approximately 1,000 new cases are diagnosed each year, according to the Cystic Fibrosis Foundation. The U.S. and European regulatory authorities consider CF to be a rare, or orphan, disease and provide incentives to encourage development of effective new treatments. CF patients endure multiple daily medications, frequent exacerbations and hospitalizations. Ultimately, selected patients have lung transplants.

In a Phase 2a clinical trial, a single dose of nebulized ensifentrine demonstrated an improvement in lung function in patients with CF. In addition, in preclinical studies, ensifentrine activated the cystic fibrosis transmembrane conductance regulator ("CFTR"), which is beneficial in reducing mucous viscosity and improving mucociliary clearance. We believe these data support the continued development of ensifentrine as a potential therapy for CF.

Asthma is a common chronic inflammatory lung condition that causes sporadic breathing difficulties. The disease causes narrowing and swelling of the airways leading to symptoms including difficulty breathing, wheezing, coughing and tightness in the chest. Exposure to triggers such as allergens or irritants can lead to asthma attacks.

Asthma attacks vary in severity and frequency. More than 260 million people worldwide suffer from asthma and it is the most common chronic disease among children, according to estimates from the World Health Organization. Approximately 60% of adult asthmatics in the U.S. have uncontrolled asthma despite regularly taking medication. Although there is no cure, symptoms may be prevented by avoiding triggers and through established maintenance therapies including bronchodilators, ICS, anti-IgE agents and leukotriene inhibitors.

Ensifentrine has shown potential in a Phase 2a clinical trial in asthma. The data from this trial, published in October 2019 in the journal *Pulmonary Pharmacology & Therapeutic*s, demonstrated that ensifentrine produced dose-dependent improvements in lung function that were comparable to current rescue medication, high dose nebulized albuterol. Importantly, ensifentrine was well tolerated and patients experienced fewer systemic effects than those receiving albuterol.

Our team

Our expert team has decades of experience in developing and commercializing respiratory therapeutics including the following COPD therapeutics: Advair®; Anoro Ellipta®; Breo®; Flovent®; Flutiform®; Incruse Ellipta®; Serevent®; Symbicort®; Tudorza Pressair® and Ventolin®.

MANUFACTURING

We do not have manufacturing facilities and rely on, and expect to continue to rely on, third-party contract manufacturing organizations ("CMOs") for the supply of current good manufacturing practices ("cGMP") compliant clinical trial materials of ensifentrine, and any future product candidates, as well as for commercial quantities of ensifentrine and any future product candidates, if approved.

While we may contract with other CMOs in the future, we currently have one CMO for the manufacture of ensifentrine drug substance and one CMO for each formulation of ensifentrine.

All of our current CMOs have commercial scale manufacturing capabilities. We believe that the ensifentrine drug substance and drug product manufacturing processes can be transferred to other CMOs to produce clinical and commercial supplies in the ordinary course of business.

COMMERCIALIZATION

During 2023, we continued to build our commercial capabilities and launch readiness in preparation for the potential approval of ensifentrine. Key pre-commercialization activities included the addition of experienced executives, launch of a disease awareness campaign, continued refinement and implementation of our patient support and distribution strategy as well as beginning development of our ensifentrine launch materials all supported by extensive market research.

We significantly expanded our headcount to 79 employees adding key leadership positions across medical affairs, compliance, manufacturing, finance and IT and deepened our commercial teams in marketing, market access and commercial operations. These appointments included Senior Vice President, Medical Affairs, Vice President, Compliance and Vice President, Pharmacovigilance.

In addition, we launched the disease awareness campaign, titled "Unspoken COPD". This campaign highlights how many patients still suffer from persistent symptoms that effect everyday life. The campaign encourages healthcare professionals ("HCPs") to enquire further to understand how their patients are coping with COPD.

Looking ahead, we will continue to progress our go-to-market strategy with the finalization of many key tactics including pricing, distribution and patient support services, HCP and patient engagement plans and the continued rollout of our disease awareness campaign.

United States

In the United States, we are preparing to commercialize nebulized ensifentrine ourselves, if approved. Current maintenance COPD treatments in the U.S. generate approximately $10 billion in sales. In the U.S., approximately 8.6 million patients receive chronic maintenance treatment for COPD. These patients receive LAMAs, LABAs, and ICS products alone or in combination across all COPD severities. Despite the use of these therapies, approximately 50% of patients report having symptoms for more than 24 days a month. This burden is significant and highlights the need for new and novel mechanisms of actions to treat COPD patients. These patients need therapies that can help improve their lung function and symptoms. In addition to the number of patients that remain symptomatic, COPD places a tremendous burden on the U.S. healthcare system with approximately $50 billion in direct and indirect costs.

Based on our market research, conducted with U.S. healthcare providers and payers, we believe ensifentrine would be widely adopted with use as an add on therapy across all symptomatic patients regardless of COPD severity and treatment. Most of ensifentrine's use would be as an add on therapy to current patients who are on LAMA, LABA / ICS, LAMA / LABA, or triple therapy. This is due to the urgent unmet need for new therapies to help improve lung function, symptoms and quality of life in these patients. Our market research also suggests the majority of ensifentrine usage would be initially commenced by pulmonologists. Due to this focused prescriber base, we anticipate a field sales force of approximately 100 representatives would be able to reach the potential ensifentrine opportunity.

International

COPD affects approximately 392 million people worldwide with many patients remaining undiagnosed. Our strategy outside of the U.S. including Asia, Europe and Latin America, is to establish partnerships with leading companies that can support the further development and commercialization of ensifentrine in those regions.

In June 2021, we executed on this strategy by entering into a strategic collaboration with Nuance Pharma, a Shanghai-based specialty pharmaceutical company, with a potential value of up to $219.0 million to develop and commercialize ensifentrine in Greater China. Under the terms of the agreement, we granted Nuance Pharma the exclusive rights to develop and commercialize ensifentrine in Greater China. In return, we received an aggregate $40.0 million upfront payment consisting of $25.0 million in cash and an equity interest valued at $15.0 million, as of June 9, 2021, in Nuance Biotech, the parent company of Nuance Pharma. We are eligible to receive further milestone payments of up to $179.0 million that are triggered upon achievement of certain clinical, regulatory and commercial milestones as well as tiered double-digit royalties on net sales in Greater China.

Nuance Pharma is responsible for all costs related to clinical development and commercialization in Greater China. A joint steering committee has been established to ensure ensifentrine's clinical development in the region aligns with our global development and commercialization strategy. In April 2023, Nuance Pharma announced it had enrolled the first subject in its pivotal Phase 3 trial evaluating ensifentrine for the maintenance treatment of COPD in mainland China. Nuance Pharma initiated a Phase 1 trial with ensifentrine in healthy volunteers in March 2023. These studies follow clearance from China's Center for Drug Evaluation for Nuance Pharma to begin Phase 1 and Phase 3 studies of ensifentrine for COPD in mainland China.

COMPETITION

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary drugs. We face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research

institutions. If successfully developed and commercialized, ensifentrine will compete with existing treatments and new treatments that may become available in the future.

Ensifentrine is a unique, first-in-class therapeutic candidate with both bronchodilator and non-steroidal anti-inflammatory properties in a single molecule. As far as we are aware, no other dual PDE3 and PDE4 inhibitor is on the market nor in clinical development in the U.S. or Europe. Based on our market research, we expect ensifentrine to be used across the patient spectrum regardless of severity. We expect it will mainly be used as an add on therapy in symptomatic patients across all existing classes of therapies (LAMA, LABA, ICS). Some healthcare providers have indicated that they would use ensifentrine as a monotherapy based on ensifentrine's clinical profile.

Consequently, we believe that, if approved, nebulized ensifentrine's unique profile will enable it to compete with all approved COPD therapies including nebulized and handheld inhaler formulations, DPI and pMDI. Furthermore, because ensifentrine's mechanism of action is complementary to available therapies, we believe it could be used in addition to these treatments.

Within the currently approved nebulizer products for the maintenance treatment of COPD, we consider ensifentrine's potential competitors in the U.S. market to be LABAs (Brovana® and Perforomist®) and LAMAs (Yupelri®).

In the DPI/pMDI maintenance treatment of COPD market, ensifentrine's current closest potential competitors are Symbicort®, a combination of a long-acting beta2-agonist bronchodilator and ICS marketed by AstraZeneca plc, Spiriva®, a long-acting anti-muscarinic bronchodilator marketed by Boehringer Ingelheim GmbH, Advair®, a combination of a long-acting beta2-agonist bronchodilator and ICS marketed by GlaxoSmithKline plc, Breo®, a combination of a long-acting beta2-agonist bronchodilator and ICS marketed by GlaxoSmithKline, and Anoro®, a combination of a long-acting beta2-agonist bronchodilator and long-acting anti-muscarinic bronchodilator marketed by GlaxoSmithKline. A triple-combination therapy of a LAMA, a LABA and ICS, developed by GlaxoSmithKline, Trelegy Ellipta®, has been approved in the U.S. and the European Union and AstraZeneca also has a triple-therapy combination product (LAMA / LABA / ICS), Breztri Aerosphere® that was approved in the U.S. in July 2020, in the European Union in December 2020 and in China in December 2019. In addition, Chiesi's triple-therapy combination product, Trimbow®, was approved in the European Union in 2017 and is in Phase 3 trials in the US.

Other potential therapies in clinical development for the prevention of COPD exacerbations include injectable biologics. Sanofi's anti-IL4, Dupixent®, has successfully completed a Phase 3 program and submitted a supplemental Biologics License Application for COPD in the US. AstraZeneca's anti-IL33, tozorakimab, GlaxoSmithKline's anti-IL5, Nucala®, and Chiesi's PDE4 inhibitor, tanimilast, are in Phase 3 trials. We are also aware of several anti-inflammatories and bronchodilators that are in Phase 2 clinical trials for the treatment of COPD.

INTELLECTUAL PROPERTY

We strive to protect and enhance the proprietary technologies, inventions and improvements that we believe are important to our business, including seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties. Our policy is to seek to protect our proprietary position by, among other methods, pursuing and obtaining patent protection in the U.S. and in jurisdictions outside of the U.S. related to our proprietary technology, inventions, improvements, platforms and our product candidates that are important to the development and implementation of our business.

As of December 31, 2023, our patent portfolio included eleven issued U.S. patents, seven pending U.S. patent applications (including four U.S. provisional patent applications), seventy-nine issued foreign patents and seventy-five pending foreign applications (including six international PCT applications). These patents and patent applications include claims directed to certain respirable formulations comprising ensifentrine, a crystalline form of ensifentrine, combinations of ensifentrine with certain respiratory drugs, certain salts of ensifentrine, ensifentrine for use in the treatment of cystic fibrosis and non-cystic fibrosis bronchiectasis and for use in the treatment of certain aspects of some other respiratory disorders, and a method of making ensifentrine, with expected expiry dates up to 2044.

We have registered "Verona Pharma" as a trademark in the United States and certain other key jurisdictions. We have also made applications to register potential trademarks in the United States for ensifentrine, if approved.

Individual patents extend for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued for regularly filed applications in the U.S. are granted a term of 20 years from the earliest effective non-provisional filing date. In addition, in certain instances, a patent term can be extended to recapture a portion of the U.S. Patent and Trademark Office, or the USPTO, delay in issuing the patent as well as a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective filing date. However, the actual protection afforded by a patent varies on a product-by-product basis, from country to country and depends upon many factors,

including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

Furthermore, we rely upon trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our collaborators, employees and consultants and invention assignment agreements with our employees. We also have confidentiality agreements or invention assignment agreements with our collaborators and selected consultants. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third party. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Our commercial success will also depend in part on not infringing upon the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, or our drugs or processes, obtain licenses or cease certain activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our future drugs may have an adverse impact on us. If third parties have prepared and filed patent applications prior to March 16, 2013 in the U.S. that also claim technology to which we have rights, we may have to participate in interference proceedings in the USPTO, to determine priority of invention. For more information, please see "Item 1A. Risk Factors - Risks Related to Intellectual Property and Information Technology."

License agreement with Ligand (formerly Vernalis)

In February 2005, Rhinopharma Limited ("Rhinopharma") entered into an assignment and license agreement with Ligand UK Development Limited (formerly Vernalis Development Limited) ("Ligand"), which since October 2018 has been a wholly owned subsidiary of Ligand Pharmaceuticals, Inc. In 2006, we acquired Rhinopharma and all its rights and liabilities under the assignment and license agreement. On March 24, 2022, we entered into an agreement with Ligand to amend the assignment and license agreement. We refer to the assignment and license agreement and the amendment agreement together as the Ligand Agreement. Pursuant to the Ligand Agreement, Ligand has assigned to us all its rights to certain patents and patent applications relating to ensifentrine and related compounds, or the Ligand Patents. We cannot further assign the Ligand Patents to a third party without Ligand's prior consent. Ligand also granted to us an exclusive, worldwide, royalty-bearing license under certain Ligand know-how to develop, manufacture and commercialize products, or the Licensed Products, based on PDE inhibitors developed using Ligand Patents, Ligand know-how and the physical stock of certain compounds, including ensifentrine, which we refer to as the Program IP, in the treatment of human or animal allergic or inflammatory disorders. Pursuant to the Ligand Agreement, we must maintain the Ligand Patents and use commercially reasonable and diligent efforts to develop and commercialize the Licensed Products.

In March 2022, we entered into an Amendment Agreement (the "Amendment") with Ligand whereby the Ligand Agreement was amended to clarify certain ambiguous terms in the Ligand Agreement. Pursuant to the Amendment we agreed to pay to Ligand (i) $2.0 million within five business days of the date of the Amendment and (ii) $15.0 million upon the first commercial sale of ensifentrine by us or a sub-licensee, which amount is payable in cash or, at the our discretion, by the issuance of Company equity of equivalent value, as determined based on the volume-weighted average price of the our American Depositary Shares on the Nasdaq Global Market over the ten (10) trading days including and prior to such milestone event.

We paid the $2.0 million to Ligand in March, 2022 and accounted for the $2.0 million payment at execution as selling, general and administrative expense in the consolidated statements of operations as the payment is related to a contract modification.

The Ligand Agreement expires on March 24, 2042, unless terminated earlier by either party in accordance with its terms. Either party may terminate the Ligand Agreement for bankruptcy or insolvency of the other party, or for an uncured material breach of the other party, conditional upon the party seeking to terminate obtaining a final judgment of the English High Court declaring that the other party is in material breach of its obligations under the Ligand Agreement. We may terminate the Ligand Agreement upon 90 days' prior written notice. Ligand may terminate the Ligand Agreement if we notify Ligand of our intention to abandon any Ligand Patents or allow any Ligand Patents to lapse. Upon termination of the Ligand Agreement, we must cease use of any Program IP and assign the Ligand Patents and any improvements thereto back to Ligand, provided however, that any of our sublicensees shall have the right to enter into a direct license agreement with Ligand for the portion of the Program IP that was sub-licensed by such sub-licensee.

GOVERNMENT REGULATION

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing and distribution of

drugs such as those we are developing. These agencies and other federal, state and local and foreign entities regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of our product candidates.

FDA drug approval process

In the U.S., the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA") and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to file an application for review or non-approval of a pending new drug applications ("NDA"), withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- Completion of non-clinical laboratory tests, animal studies, certain of which must be conducted and formulation studies in compliance with the FDA's good laboratory practice ("GLP") regulations;
- Submission to the FDA of an IND, which must become effective before human clinical trials may begin in the U.S.;
- Approval by an independent institutional review board ("IRB") or ethics committee at each clinical site before each trial may be initiated;
- Performance of adequate and well-controlled human clinical trials in accordance with good clinical practice ("GCP") requirements to establish the safety and efficacy of the proposed drug product for each indication;
- Submission to the FDA of an NDA after completion of all pivotal trials;
- Completion of an FDA advisory committee review, if required by the FDA;
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practice ("cGMP") requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity, and potential inspection of selected clinical investigation sites to assess compliance with GCP; and
- FDA review and approval of the NDA and U.S. Prescribing Information to permit commercial marketing of the product for particular indications for use in the U.S.

Non-clinical Studies

Non-clinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. An IND sponsor must submit the results of the non-clinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. An IND is a request for allowance from the FDA to ship in interstate commerce and administer an investigational drug product to humans. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

Clinical trials involve the administration of the investigational drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which among other things, include the requirement that all research subjects or a legal representative provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives or endpoints of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. While the IND is active, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or in vitro testing suggesting a significant risk to humans, and any clinically

important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which reviews the data and recommends whether or not a study may move forward at designated checkpoints. It may halt the clinical trial if it determines that there is an unacceptable safety risk or on other grounds, such as no demonstration of efficacy. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their www.clinicaltrials.gov website.

Human clinical trials are typically conducted in three phases, which may overlap or be combined:

- Phase 1: The drug candidate is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.
- Phase 2: The drug candidate is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3: The drug candidate is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

Post-approval trials, sometimes referred to as Phase 4 studies, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug. In addition, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the pre-clinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. In addition, the Pediatric Research Equity Act (PREA), requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and certain supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is deemed safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information

rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing.

Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity. Under the Prescription Drug User Fee Act guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision after it the application is submitted.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of a resubmitted NDA and may require additional clinical or pre-clinical testing in order for FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the NDA with a Risk Evaluation and Mitigation Strategy ("REMS") to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. The FDA may also require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

Expedited Development and Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates. For example, the fast track program is intended to expedite or facilitate the process for reviewing products that are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast track designation applies to the combination of the product candidate and the specific indication for which it is being studied. The sponsor of a fast track product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA is submitted, the application may be eligible for priority review. An NDA for a fast track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

A product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for breakthrough therapy designation to expedite its development and review. A product candidate can receive breakthrough therapy designation if preliminary clinical evidence indicates that the product candidate, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

Any marketing application for a drug submitted to the FDA for approval, including a product candidate with a fast track designation and/or breakthrough therapy designation, may be eligible for other types of FDA programs to expedite the FDA review and approval process, such as priority review. An NDA is eligible for priority review if the product candidate is designed to treat a serious or life-threatening disease or condition, and if approved, would provide a significant improvement in safety or effectiveness compared to available alternatives for such disease or condition. For new molecular entity NDAs, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date (as compared to ten months under standard review).

Additionally, depending on the design of the applicable clinical studies, product candidates studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled confirmatory clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit, and may require that such confirmatory studies be underway prior to granting accelerated approval. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required studies in a timely manner or if such studies fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Fast track designation, breakthrough therapy designation, priority review, and accelerated approval do not change the standards for approval but may expedite the development or approval process. Even if a product candidate qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Orphan drug designation and exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 individuals in the United States and when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same disease or condition for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. 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.

A designated orphan drug many not receive orphan drug exclusivity if it is approved for a use that is broader than the disease or condition for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if a second applicant demonstrates that its product is clinically superior to the approved product with orphan exclusivity or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products under which NDA applicants must pay a substantial "program fee" for each prescription drug product approved in an NDA.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the

FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- Restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- Fines, warning letters or holds on post-approval clinical trials;
- Refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- Product seizure or detention, or refusal to permit the import or export of products; or
- Injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties.

Drug Product Marketing Exclusivity

Market exclusivity provisions authorized under the FDCA can delay the submission or the approval of certain marketing applications. For example, the FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application ("ANDA") or an NDA submitted under Section 505(b)(2) (a "505(b)(2) NDA"), submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, 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 certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

The FDCA alternatively provides three years of non-patent exclusivity for an 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 new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the active agent for the original indication or condition of use. 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 any preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of marketing exclusivity available in the United States. Pediatric exclusivity provides for an additional six months of marketing exclusivity attached to another period of existing exclusivity or an available patent term if a sponsor conducts clinical trials in children in response to a "written request" from the FDA. The issuance of a written request does not require the sponsor to undertake the described clinical trials, and the FDA's grant of pediatric exclusivity does not require the FDA to approve labeling containing information on pediatric use based on the studies conducted.

Foreign regulation

In order to market any medicinal product outside of the U.S., similar regulatory requirements, including adherence to GLP, Good Clinical Practices ("GCP") and Good Manufacturing Practice ("GMP"), to initiate clinical trials and, subsequently, to obtain marketing approval of a new pharmaceutical product are in place in each jurisdiction and vary country to country.

Each jurisdiction will apply these regulations in their assessment of clinical trial applications and marketing authorization applications. The foreign regulatory approval process includes all of the risks associated with FDA approval set forth above, as well as additional country-specific regulation. The foreign regulatory approval process includes all of the risks associated with FDA approval set forth above, as well as additional country-specific regulation. Whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another. In addition, a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others. Failure to comply with applicable foreign regulatory requirements, may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Non-clinical studies and clinical trials

Similarly to the United States, the various phases of non-clinical and clinical research in the European Union ("EU") are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new biological substances. Non-clinical studies (pharmaco-toxicological) must be conducted in compliance with the principles of GLP, as set forth in EU Directive 2004/10/EC (unless otherwise justified for certain particular medicinal products - e.g., radio-pharmaceutical precursors for radio-labelling purposes). In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use ("ICH") guidelines on GCP as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU member states, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation ("CTR") which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the need for member states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which contains a centralized EU portal and database.

While the EU Clinical Trials Directive required a separate clinical trial application ("CTA") to be submitted in each member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application for multi-center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the EU Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the EU Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR.

Medicines used in clinical trials must be manufactured in accordance with GMP. Other national and EU-wide regulatory requirements may also apply.

Marketing authorization

In the EU, medicinal products can only be placed on the market after obtaining a marketing authorization ("MA"). To obtain regulatory approval of a product candidate under EU regulatory systems, we must submit a MA application ("MAA"). The process for doing this depends, among other things, on the nature of the medicinal product. There are two types of MAs:

- "Centralized MAs" are issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use ("CHMP") of the EMA, and are valid throughout the EU. The centralized procedure is mandatory for certain types of medicinal products, such as (i) medicines derived from biotechnology processes, (ii) advanced therapy medicinal products ("ATMP") (such as gene therapy, somatic cell therapy and tissue engineered products), (iii) orphan designated medicinal products, and (iv) products that contain a new active substance indicated for the treatment of certain diseases such as HIV/AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune diseases and other immune dysfunctions, and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the EU, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.
- "National MAs" are issued by the competent authorities of the member states of the EU and only cover their respective territory, and are available for product candidates not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in a member state of the EU, this national MA can be recognized in another member state through the mutual recognition procedure. If the product has not received a national MA in any member state at the time of application, it can be approved simultaneously in various member states through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the reference member state.

Under the above described procedures, in order to grant the MA, the EMA or the competent authorities of the member states of the EU make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy. MAs have an initial duration of five years. After these five years, the authorization may be renewed on the basis of a reevaluation of the risk-benefit balance.

Under the centralized procedure the maximum timeframe for the evaluation of a MAA by the EMA is 210 days, excluding clock stops. In exceptional cases, the CHMP might perform an accelerated assessment of a MAA in no more than 150 days (not including clock stops). Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIority MEdicines ("PRIME") scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. In March 2016, the EMA launched an initiative, the PRIME scheme, a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Product developers that benefit from PRIME designation can expect to be eligible for accelerated assessment but this is not guaranteed. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA's committee level. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Data and marketing exclusivity

In the EU, new products authorized for marketing, (i.e., reference products), generally receive eight years of data exclusivity and an additional two years of market exclusivity upon MA. If granted, the data exclusivity period prevents generic or biosimilar applicants from relying on the pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial authorization of the reference product in the EU. The overall 10-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those 10 years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new active substance, and products may not qualify for data exclusivity.

Pediatric development

In the EEA, MAAs for new medicinal products have to include the results of studies conducted in the pediatric population, in compliance with a pediatric investigation plan ("PIP"), agreed with the EMA's Pediatric Committee ("PDCO"). The PIP sets

out the timing and measures proposed to generate data to support a pediatric indication of the drug for which MA is being sought. The 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. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data are 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. We have received a waiver for pediatric data in COPD.

Orphan Medicinal Products

The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the United States. A medicinal product may be designated as orphan if its sponsor can establish that: (1) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition that has been authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition.

Orphan designation must be requested before submitting an MAA. An EU orphan designation entitles a party to incentives such as reduction of fees or fee waivers, protocol assistance, and access to the centralized procedure. Upon grant of a MA, orphan medicinal products are entitled to ten years of market exclusivity for the approved therapeutic indication which means that the EU regulatory authorities cannot accept another MAA, or grant an MA, or accept an application to extend a MA for a similar product for the same indication for a period of ten years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed PIP. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The orphan exclusivity period may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity, or where the prevalence of the condition has increased above the threshold. Additionally, MA may be granted to a similar product for the same indication at any time if (1) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; (2) the applicant consents to a second orphan medicinal product application; or (3) the applicant cannot supply enough orphan medicinal product.

Post-Approval Requirements

Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the EU member states. The holder of a MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance ("QPPV") who is responsible for the establishment and maintenance of that system, and oversees the safety profiles of medicinal products and any emerging safety concerns. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports ("PSURs").

All new MAA must include a risk management plan ("RMP") describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies.

The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each member state and can differ from one country to another.

The aforementioned EU rules are generally applicable in the European Economic Area ("EEA") which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland.

Failure by us or by any of our third-party partners, including suppliers, manufacturers and distributors to comply with EU and EU member state laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of medicinal products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or

criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the marketing authorization, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

Brexit and the Regulatory Framework in the United Kingdom

Since the end of the Brexit transition period on January 1, 2021, Great Britain (England, Scotland and Wales) has not been directly subject to EU laws, however under the terms of the Ireland/Northern Ireland Protocol, EU laws generally apply to Northern Ireland. The EU laws that have been transposed into U.K. law through secondary legislation remain applicable in Great Britain ("GB"), however new legislation such as the EU CTR is not applicable in GB.

Under the Medicines and Medical Devices Act 2021, the Secretary of State or an 'appropriate authority' has delegated powers to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices.

Since January 1, 2021, the Medicines and Healthcare products Regulatory Agency ("MHRA") has been the U.K.'s standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales, and Scotland, together, GB; broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA.

The U.K. regulatory framework in relation to clinical trials is derived from existing EU legislation (as implemented into U.K. law, through secondary legislation). On January 17, 2022, the MHRA launched an eight-week consultation on reframing the U.K. legislation for clinical trials, which aimed to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The MHRA responded to the consultation on March 21, 2023 and confirmed that it would bring forward changes to the legislation. The final legal texts introduced by the U.K. Government will ultimately determine the extent to which the U.K. clinical trials framework aligns with or diverges from the CTR.

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, including a 150-day assessment and a rolling review procedure. All existing EU MAs for centrally authorized products were automatically converted or grandfathered into U.K. MAs, effective in GB (only), free of charge on January 1, 2021, unless the MA holder has opted out. In order to use the centralized procedure to obtain a MA that will be valid throughout the EEA, companies must be established in the EEA. Therefore since Brexit, without first establishing an EEA entity, companies established in the U.K. can no longer use the EU centralized procedure and instead an EEA entity must hold any centralized MAs . In order to obtain a U.K. MA to commercialize products in the U.K., an applicant must be established in the U.K. and must follow one of the U.K. national authorization procedures or one of the remaining post-Brexit international cooperation procedures to obtain an MA to commercialize products in the U.K.. A new international recognition framework has been in place from January 1, 2024, whereby the MHRA will have regard to decisions on the approval of MAs made by the EMA and certain other regulators when determining an application for a new GB MA.

There is no pre-MA orphan designation. Instead, the MHRA will review applications for orphan designation in parallel to the corresponding MA application. The criteria are essentially the same, but have been tailored for the market, i.e., the prevalence of the condition in GB, rather than the EU, must not be more than five in 10,000. Should an orphan designation be granted, the period of market exclusivity will be set from the date of first approval of the product in GB.

Other Healthcare Laws

In addition to FDA restrictions on marketing of pharmaceutical and biological products, other U.S. federal and state healthcare regulatory laws restrict business practices in the pharmaceutical industry, which include, but are not limited to, state and federal anti-kickback, false claims and physician payment and drug pricing transparency laws. Similar laws exist in foreign jurisdictions.

The U.S. federal Anti-Kickback Statute prohibits, among other things, any person or entity from knowingly and willfully offering, paying, soliciting, receiving or providing any remuneration, directly or indirectly, overtly or covertly, to induce or in return for purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, or order of any good, facility, item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, formulary managers and beneficiaries on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do

not meet the requirements of a statutory or regulatory exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the U.S. federal Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated.

In addition, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

The federal false claims laws, including the civil False Claims Act, prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false, fictitious or fraudulent claim for payment to, or approval by, the federal government, knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. Actions under the civil False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the civil False Claims Act can result in very significant monetary penalties and treble damages. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved, or off-label, uses. Moreover, a claim including items or services resulting from a violation of the U.S. federal Anti-Kickback Statue constitutes a false or fraudulent claim for the purposes of the federal civil False Claims Act. In addition, the civil monetary penalties statute imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. Many states also have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

The 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, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians and certain other healthcare providers. The Physician Payments Sunshine Act imposes, among other things, annual reporting requirements for covered manufacturers for certain payments and "transfers of value" provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiology assistants and certified nurse-midwives) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit timely, accurately and completely the required information for all payments, transfers of value and ownership or investment interests may result in significant civil monetary penalties and additional penalties for "knowing failures." Covered manufacturers must submit reports by the 90th day of each subsequent calendar year. In addition, certain states require implementation of compliance programs and compliance with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, impose restrictions on marketing practices and/or tracking and reporting of gifts, compensation and other remuneration or items of value provided to physicians and other healthcare professionals and entities.

Violations of any such laws or any other governmental regulations that apply may result in significant criminal, civil and administrative penalties, including damages, fines, the possibility of exclusion from federal healthcare programs (including Medicare and Medicaid), disgorgement and corporate integrity agreements, which impose, among other things, rigorous operational and monitoring requirements on companies to resolve allegations of non-compliance with these laws. Similar sanctions and penalties, as well as imprisonment, also can be imposed upon executive officers and employees of such companies. Given the significant size of actual and potential settlements, it is expected that the government authorities will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws. Moreover, analogous state and foreign laws and regulations may be broader in scope than the provisions described above and may apply regardless of payor. These laws and regulations may differ from one another in significant ways, thus further complicating compliance efforts. For instance, in the EU, many EU member states have adopted specific

anti-gift statutes that further limit commercial practices for medicinal products, in particular vis-à-vis healthcare professionals and organizations. Additionally, there has been a recent trend of increased regulation of payments and transfers of value provided to healthcare professionals or entities and many EU member states have adopted national "Sunshine Acts" which impose reporting and transparency requirements (often on an annual basis), similar to the requirements in the United States, on pharmaceutical companies. Certain countries also mandate implementation of commercial compliance programs, or require disclosure of marketing expenditures and pricing information. Violation of any of such laws or any other governmental regulations that apply may result in penalties, including, without limitation, significant administrative, civil and criminal penalties, damages, fines, disgorgement, additional reporting obligations and oversight if a manufacturer becomes subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, the curtailment or restructuring of operations, exclusion from participation in governmental healthcare programs and imprisonment.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any pharmaceutical or biological products for which we obtain regulatory approval. In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Sales of any products for which we receive regulatory approval for commercial sale will therefore depend, in part, on the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government authorities, managed care plans, private health insurers and other organizations.

In the United States, the process for determining whether a third-party payor will provide coverage for a pharmaceutical or biological product typically is separate from the process for setting the price of such product or for establishing the reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication. A decision by a third-party payor not to cover our product candidates could reduce physician utilization of our products once approved and have a material adverse effect on our sales, results of operations and financial condition. Moreover, a third-party payor's decision to provide coverage for a pharmaceutical or biological product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Additionally, coverage and reimbursement for products can differ significantly from payor to payor. One third-party payor's decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the medical product or service, or will provide coverage at an adequate reimbursement rate. As a result, the coverage determination process will require us to provide scientific and clinical support for the use of our products to each payor separately and will be a time-consuming process.

In international markets, reimbursement and healthcare payment systems vary significantly by country. In the EU, governments influence the price of products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Member states are free to restrict the range of pharmaceutical products for which their national health insurance systems provide reimbursement, and to control the prices and reimbursement levels of pharmaceutical products for human use. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. Member states may approve a specific price or level of reimbursement for the pharmaceutical product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the pharmaceutical product on the market, including volume-based arrangements, caps and reference pricing mechanisms. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. The downward pressure on health care costs in general, particularly prescription products, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross border imports from low-priced markets exert a commercial pressure on pricing within a country.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of pharmaceutical or biological products have been a focus in this effort. Third-party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost-effectiveness of pharmaceutical or biological products, medical devices and medical services, in addition to questioning safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after FDA approval or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, was enacted, which, among other things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; introduced 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; extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care plans; imposed mandatory discounts for certain Medicare Part D beneficiaries as a condition for manufacturers' outpatient drugs coverage under Medicare Part D.

Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order initiating a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare.

Additionally, on August 2, 2011, the Budget Control Act of 2011 created measures for spending reductions was enacted, which, among other things, included aggregate reductions of Medicare payments to providers, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2032, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional action is taken by Congress. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further 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. In addition, in March 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminated the statutory Medicaid drug rebate cap, beginning January 1, 2024. The rebate was previously capped at 100% of a drug's average manufacturer price.

More recently, there has been heightened governmental scrutiny recently over the manner in which manufacturers set prices for their marketed products, which have resulted in several recent Congressional inquiries and proposed and enacted legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. On August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023), and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations. HHS has issued and will continue to issue guidance implementing the IRA, although the Medicare drug price negotiation program is currently subject to legal challenges. While the impact of the IRA on the pharmaceutical industry cannot yet be fully determined, it is likely to be significant.

We expect that additional state, federal 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 reduced demand for our products, once approved, or additional price increases. In particular, we anticipate that Medicare Part B will play an important role in the reimbursement of ensifentrine. Changes in how products are reimbursed through Medicare Part B may affect the overall coverage for ensifentrine, if approved. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors.

Similar political, economic and regulatory developments are occurring in the EU and may affect the ability of pharmaceutical companies to profitably commercialize their products.

On December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment ("HTA"), amending Directive 2011/24/EU, was adopted. While the Regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once applicable, it will have a phased implementation depending on the concerned products. The Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and provide the basis for cooperation at the EU level for joint clinical assessments in these areas. It will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary

cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

Data Privacy and Security Laws

Numerous state, federal and foreign laws, regulations and standards govern the collection, use, access to, confidentiality and security of health-related and other personal information, and could apply now or in the future to our operations or the operations of our partners. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health-related and other personal information. In addition, certain foreign laws govern the privacy and security of personal data, including health-related data. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Additional regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservation and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern the use, handling and disposal of various biologic, chemical and radioactive substances used in, and wastes generated by, operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. Equivalent laws have been adopted in certain other countries that impose similar obligations.

U.S. Foreign Corrupt Practices Act

The U.S. Foreign Corrupt Practices Act ("FCPA"), prohibits U.S. corporations and individuals from engaging in certain activities to obtain or retain business abroad or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize the payment of anything of value to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. The scope of the FCPA includes interactions with certain healthcare professionals in many countries. Equivalent laws have been adopted in other foreign countries that impose similar obligations.

EMPLOYEES

As of December 31, 2023, we had 79 full-time employees. None of our employees is party to a collective bargaining agreement or represented by a trade union or labor union. We consider our relationship with our employees to be good.

ADDITIONAL INFORMATION

We were incorporated in February 2005 as Isis Resources plc under the laws of England and Wales. In September 2006, we acquired Rhinopharma Limited, a private company incorporated in Canada, and changed our name to Verona Pharma plc. Our principal office is located at 3 More London Riverside, London, SE1 2RE, United Kingdom.

We make available our public filings, including annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and any amendments to those reports, with the SEC free of charge through our website at www.veronapharma.com in the “Investors” section as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the SEC. The information contained in, or accessible through, our website does not constitute a part of this Annual Report. The SEC also maintains a website at www.sec.gov that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including Verona Pharma plc.

Item 1A. Risk Factors

Investing in our ADSs involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Annual Report, including our Consolidated Financial Statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations". The occurrence of any of the events or developments described below could adversely affect our business, financial condition, results of operations and growth prospects. In such an event, the market price of our ADSs could decline, and you may lose all or part of your investment.

Risks Related to Our Business and Industry

We have a limited operating history and have never generated any product revenue.

We are a clinical-stage biopharmaceutical company with a limited operating history, and have incurred significant operating losses since our inception. We had net losses of $54.4 million and $68.7 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, we had an accumulated deficit of $388.4 million. Our losses have resulted principally from expenses incurred in research and development of ensifentrine, our only product candidate, and from general and administrative costs that we have incurred while building our business infrastructure. We may continue to incur significant operating losses for the foreseeable future as we expand our research and development efforts, advance our clinical development of ensifentrine in other formulations or for other indications, and seek to obtain regulatory approval for and commercialize ensifentrine in various formulations or for various indications. We anticipate that our expenses will increase substantially as we:

- initiate and conduct clinical trials of ensifentrine for the treatment of non-cystic fibrosis bronchiectasis ("NCFBE"), cystic fibrosis ("CF"), asthma or other indications;
- initiate and conduct other future clinical trials of ensifentrine in other formulations, including in combination with other active ingredients including fixed-dose combinations, for the treatment of COPD or other indications;
- initiate and conduct clinical pharmacology studies with any formulation;
- seek to discover and develop or in-license additional respiratory product candidates;
- conduct pre-clinical studies to support ensifentrine and potentially other future product candidates;
- develop the manufacturing processes and produce clinical and commercial supplies of the ensifentrine active pharmaceutical ingredient and formulated drug products derived from it;
- seek regulatory approvals of ensifentrine;
- grow commercial infrastructure to support the potential commercialization of ensifentrine, including sales, marketing, operations, reimbursement and distribution infrastructure and scale-up manufacturing capabilities to commercialize ensifentrine, if approved;
- maintain, expand and protect our intellectual property portfolio;
- secure, maintain or obtain freedom to operate for our in-licensed technologies and products;
- add clinical, scientific, operational, financial and management information systems and personnel, including personnel to support our product development and potential future commercialization efforts; and
- expand our operations in the United States, the United Kingdom ("UK") and possibly elsewhere.

Our expenses may also increase substantially if we experience any delays or encounter any issues with any of the above, including, but not limited to, failed pre-clinical studies or clinical trials, complex results, safety issues or regulatory challenges.

We have devoted substantially all of our financial resources and efforts to the research and development, pre-clinical studies and clinical trials, and commercialization of nebulized ensifentrine for the maintenance treatment of COPD in the US. We are continuing development of ensifentrine in other formulations and for other indications, and for commercialization in other territories.

To become and remain profitable, we must succeed in developing, and eventually commercializing, products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing clinical trials of ensifentrine in other formulations and other indications, discovering and developing additional product candidates, obtaining regulatory approval for ensifentrine and any future product candidates that

successfully complete clinical trials, establishing manufacturing, commercial and marketing capabilities and ultimately distributing and selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of some of these activities. We may never succeed in these activities and, even if we do, we may never generate revenue that is significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. If we are required by the FDA, the European Medicines Agency ("EMA"), or other regulatory authorities to perform studies in addition to those we currently anticipate, or if there are any delays in completing our clinical trials or the development of ensifentrine or any other product candidates, our expenses could increase and revenue could be further delayed.

Even if we do generate product royalties or product sales, we may never achieve or sustain profitability on a quarterly or annual basis. Our failure to sustain profitability would depress the market price of our ADSs and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. A decline in the market price of our ADSs also could cause our ADS holders to lose all or a part of their investment.

We will need additional funding to complete development and commercialization of any future product candidates, or development and commercialization of other formulations or target indications of ensifentrine, if approved. If we are unable to raise capital when needed, or if a failure of any financial institution where we maintain our cash and cash equivalents prevents or delays us from accessing uninsured funds, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our expenses to increase in connection with our ongoing and planned activities, particularly as we conduct clinical trials and prepare for commercialization of ensifentrine, and develop and prepare for the commercialization of ensifentrine in other formulations or for other indications. In addition, if we obtain regulatory approval for ensifentrine or any other product candidates, we expect to incur significant commercialization expenses related to activities including product positioning studies, product manufacturing, medical affairs, marketing, sales and distribution. Furthermore, we expect to incur ongoing costs associated with operating as a public company in the United States and maintaining a listing on the Nasdaq Global Market, or Nasdaq. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

If we obtain regulatory approval for ensifentrine for the treatment of COPD in the US, we estimate that our existing cash resources and additional funding expected to become available under the 2023 Term Loan will enable us to fund planned operating expenses and capital expenditure requirements through at least the end of 2026 including the commercial launch of ensifentrine. Future advances under the 2023 Term Loan are contingent upon achievement of certain regulatory and commercial milestones and other specified conditions. We have based this estimate on assumptions that may prove to be incorrect, and we could use our available capital resources sooner than we currently expect. In addition, our operating plan may change as a result of many factors unknown to us. These factors, among others, may necessitate that we seek additional capital sooner than currently planned. 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. We maintain the majority of our cash and cash equivalents in accounts with major U.S. and multi-national financial institutions, and our deposits at these institutions exceed insured limits. Market conditions can impact the viability of these institutions. In the event of failure of any of the financial institutions where we maintain our cash and cash equivalents, there can be no assurance that we would be able to access uninsured funds in a timely manner or at all. Any inability to access or delay in accessing these funds could adversely affect our business and financial position.

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

- the costs, timing and outcome of the regulatory submission and review of ensifentrine, including any post-marketing studies that could be required by regulatory authorities, if regulatory approval is received;
- the cost, progress and results of any other studies required to support the commercial positioning of ensifentrine for the treatment of COPD, if regulatory approval is received;
- the cost, progress and results of any clinical trials for the treatment of NCFBE, CF, asthma or other indications, or for other formulations of ensifentrine including fixed-dose combination products;
- the cost of manufacturing clinical and, if approved, commercial supplies of the ensifentrine active ingredient and derived formulated drug products;

- the scope, progress, results and costs of pre-clinical development, laboratory testing and clinical trials for ensifentrine in other indications and of the development of DPI and pMDI formulations of ensifentrine, or fixed-dose combination formulations of ensifentrine for the maintenance treatment of COPD and potentially NCFBE, CF, asthma and other respiratory diseases;
- the costs, timing and outcome of potential future commercialization activities, including manufacturing, marketing, sales and distribution, for ensifentrine;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims, including any claims by third parties that we are infringing upon their intellectual property rights;
- the timing and amount of revenue, if any, received from commercial sales of ensifentrine;
- the sales price and availability of adequate third-party coverage and reimbursement for ensifentrine;
- the effect of competing technological and market developments; and
- the extent to which we acquire or invest in businesses, products and technologies, including entering into licensing or collaboration arrangements for ensifentrine, although we currently have no commitments or agreements to complete any such transactions.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize ensifentrine. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect our business, the holdings or the rights of our shareholders, or the value of our ordinary shares or ADSs.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue our research and development programs relating to ensifentrine or any commercialization efforts, be unable to expand our operations, or be unable to otherwise capitalize on our business opportunities, as desired, which could harm our business and potentially cause us to discontinue operations.

We depend solely on the success of ensifentrine, our only product candidate under development. We cannot give any assurance that ensifentrine will receive regulatory approval for any indication, which is necessary before it can be commercialized. If we, and any collaborators with whom we have entered or may enter into agreements for the development and commercialization of ensifentrine, are unable to commercialize ensifentrine, or experience significant delays in doing so, our ability to generate revenue and our financial condition will be adversely affected.

We do not currently generate any revenues from sales of any products, and we may never be able to develop or commercialize a marketable product. We have invested substantially all of our efforts and financial resources in the development of ensifentrine, and we do not have any other product candidate currently under development. Our ability to generate royalty and product revenues, will depend heavily on the successful commercialization of ensifentrine, if approved, which may never occur. Ensifentrine will require regulatory approval, procurement of manufacturing supply, commercialization, substantial additional investment and significant marketing efforts before we generate any revenues from product sales. We are not permitted to market or promote ensifentrine or any product candidates in the United States, Europe or other countries before we receive regulatory approval from the FDA, the European Commission or comparable foreign regulatory authorities, and we may never receive such regulatory approval for ensifentrine or any future product candidate. In August 2023, the FDA accepted for review our NDA seeking approval of ensifentrine for the maintenance treatment of COPD and assigned a Prescription Drug User Fee Act ("PDUFA") target action date of June 26, 2024, but we cannot guarantee that it will be approved, or that it will be approved with the labeling claims necessary or desirable for the successful commercialization of ensifentrine. In addition, we have not submitted a marketing authorization application ("MAA") to the EMA or comparable applications to other regulatory authorities. The success of ensifentrine will depend on many factors, including the following:

- we may not be able to demonstrate that ensifentrine is safe and effective as a treatment for our targeted indications to the satisfaction of the applicable regulatory authorities;
- the applicable regulatory authorities may require additional pre-clinical or clinical trials, which would increase our costs and prolong our development;

- the results of clinical trials of ensifentrine may not meet the level of statistical or clinical significance required by the applicable regulatory authorities for marketing approval;
- the applicable regulatory authorities may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the contract research organizations ("CROs") that we retain to conduct clinical trials may take actions outside of our control that materially adversely impact our clinical trials;
- the applicable regulatory authorities may not find the data from pre-clinical studies and clinical trials sufficient to demonstrate that the clinical and other benefits of ensifentrine outweigh its safety risks or may disagree with our interpretation of data;
- our ability to demonstrate a non-clinical safety profile that is acceptable to the applicable regulatory authorities;
- unexpected operational or clinical issues may prevent completion or interpretation of clinical study results;
- unexpected manufacturing issues, product performance issues or stability issues may delay or otherwise adversely affect the progress of our clinical development program;
- if FDA or other regulatory authorities determine that inspections of the manufacturing facilities or clinical sites for our product candidates are required in connection with a marketing application, and such regulatory authorities are unable to conduct such inspections, whether due to geopolitical conflict, including war and terrorism, such as the ongoing conflicts in Europe and the Middle East, or travel restrictions, such as those imposed during the COVID-19 pandemic;
- the applicable regulatory authorities may not accept data generated at our clinical trial sites due to Good Clinical Practice ("GCP") compliance issues, misconduct, or other reasons;
- if our NDA is reviewed by an advisory committee, the FDA may have difficulties scheduling an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our application or may recommend that the FDA require, as a condition of approval, additional pre-clinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;
- the applicable regulatory authorities may require development of a risk evaluation and mitigation strategy ("REMS") or similar risk management measures as a condition of approval;
- the applicable regulatory authorities may identify deficiencies in the manufacturing processes or facilities of our third-party manufacturers;
- the applicable regulatory authorities may change their approval policies or adopt new regulations;
- if we license ensifentrine to others, the efforts of those parties in completing clinical trials of, receiving regulatory approval for, and commercializing ensifentrine;
- through our clinical trials, we may discover factors that limit the commercial viability of ensifentrine or make the commercialization of ensifentrine unfeasible;
- if we retain rights under a collaboration agreement for ensifentrine, our efforts in completing pre-clinical studies and clinical trials of, receiving marketing approvals for, establishing commercial manufacturing capabilities for, and commercializing ensifentrine; and
- if approved, acceptance of ensifentrine by patients, the medical community and third-party payors, effectively competing with other therapies, a continued acceptable safety profile following approval and qualifying for, maintaining, enforcing and defending our intellectual property rights and claims.

An unfavorable outcome in any of these factors could result in our experiencing significant delays or an inability to successfully commercialize ensifentrine.

We cannot be certain that ensifentrine or any future product candidates will be successful in clinical trials or receive regulatory approval. Further, ensifentrine or any future product candidates may not receive regulatory approval even if they are successful in clinical trials. If we do not receive regulatory approvals for ensifentrine or any future product candidates, we may not be able to continue our operations. Even if we successfully obtain regulatory approvals to manufacture and market ensifentrine or any future product candidates, our revenues will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval and have commercial rights. If the markets for patient subsets that we are targeting are not as significant as we estimate, we may not generate significant revenues from sales of such products, if approved.

We have submitted an NDA for regulatory approval to commercialize ensifentrine in the United States. We may in the future seek regulatory approval to commercialize ensifentrine in the European Union ("EU") and additional countries. While the scope of regulatory approval is similar in many countries, to obtain separate regulatory approval in multiple countries requires us to comply with the numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of ensifentrine, and we cannot predict success in these jurisdictions.

Our limited operating history may make it difficult for investors to evaluate the success of our business to date and to assess our future viability.

Since our inception in 2005, we have devoted substantially all of our resources to developing ensifentrine, building our intellectual property portfolio, developing our supply chain, planning our business, raising capital and providing general and administrative support for these operations. We have completed multiple Phase 1 and 2 clinical trials in different formulations of ensifentrine and for different indications, and two registrational Phase 3 clinical trials for nebulized ensifentrine for the maintenance treatment of COPD. We have not yet successfully obtained regulatory approvals, manufactured a commercial-scale product or arranged for a third party to do so on our behalf or conducted sales and marketing activities necessary for successful product commercialization. Additionally, we are not profitable and have incurred losses in each year since our inception, and we expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Consequently, any predictions investors make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

The terms of our credit facility place restrictions on our operating and financial flexibility, and our existing and any future indebtedness could adversely affect our ability to operate our business.

In December 2023, Verona Pharma, Inc. entered into a term loan facility (the "Loan Agreement"), with Oxford Finance LLC ("Oxford"), as collateral agent and certain funds managed by Oxford and Hercules Capital, Inc. (together the "Lenders"), pursuant to which a term loan facility in an aggregate amount of up to $400.0 million, which we refer to as the 2023 Term Loan, is available to us in five tranches. We received the first tranche of $50.0 million (the "Term A Loan") at closing of the Loan Agreement. Each advance under the 2023 Term Loan accrues interest at a floating per annum rate (the "Basic Rate") equal to (a) the greater of (i) the 1-Month CME Term SOFR (as defined in the Loan Agreement) reference rate on the last business day of the month that immediately precedes the month in which the interest will accrue and (ii) 5.34%, plus (b) 5.85%; provided, however, that (i) in no event shall the Basic Rate (x) for the Term A Loan be less than 11.19% and (y) for each other advance be less than the Basic Rate on the business day immediately prior to the funding date of such advance, (ii) the Basic Rate for the Term A Loan for the period from closing through and including December 31, 2023 shall be 11.19% and (iii) the Basic Rate for each advance shall not increase by more than 2.00% above the applicable Basic Rate as of the funding date of each such advance.

Our outstanding indebtedness, including any additional indebtedness incurred beyond our borrowings under the 2023 Term Loan, combined with our other financial obligations and contractual commitments could have significant adverse consequences, including:

- requiring us to dedicate a portion of our cash resources to the payment of interest and principal, reducing money available to fund working capital, capital expenditures, product candidate development and other general corporate purposes;
- increasing our vulnerability to adverse changes in general economic, industry and market conditions;
- subjecting us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing;
- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; and
- placing us at a competitive disadvantage compared to our competitors that have less debt or better debt servicing options.

We intend to satisfy our current and future debt service obligations with our then existing cash and cash equivalents. However, we may not have sufficient funds, and may be unable to arrange for additional financing, to pay the amounts due under the Loan Agreement or any other debt instruments. Failure to satisfy our current and future debt obligations, including covenants to take or avoid specific actions, under the Loan Agreement could result in an event of default and, as a result, the Lenders could accelerate all of the amounts due. In the event of an acceleration of amounts due under the Loan Agreement as a result of an event of default, we may not have sufficient funds or may

be unable to arrange for additional financing to repay our indebtedness while still pursuing our current business strategy. In addition, our lenders could seek to enforce their security interests in any collateral securing such indebtedness

Further, if we are liquidated, the Lenders' right to repayment would be senior to the rights of holders of our American Depositary Shares ("ADS") or of our shareholders to receive any proceeds from the liquidation. Any declaration by the Lenders of an event of default could significantly harm our business and prospects and could cause the price of our ADSs to decline. In addition, the covenants under the Loan Agreement, the pledge of our assets as collateral and the negative pledge with respect to our intellectual property could limit our ability to obtain additional debt financing. If we raise any additional debt financing, the terms of such additional debt could further restrict our operating and financial flexibility.

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

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of securities offerings, debt financings, license and collaboration agreements and research grants. If we raise capital through securities offerings, the ownership interest of our ADS holders and shareholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect these holders' rights as holders of our ADSs. Debt financing, if available, could result in fixed payment obligations, and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, to acquire, sell or license intellectual property rights, to make capital expenditures, to declare dividends, or other operating restrictions. If we raise additional funds through collaboration or licensing agreements, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. In addition, we could also be required to seek funds through arrangements with collaborators or others at an earlier stage than otherwise would be desirable. If we raise funds through research grants, we may be subject to certain requirements, which may limit our ability to use the funds or require us to share information from our research and development. Raising additional capital through any of these or other means could adversely affect our business and the holdings or rights of our ADS holders and shareholders, and may cause the market price of our ADSs to decline.

Our business may become subject to economic, political, regulatory and other risks associated with international operations.

As a company based in the United Kingdom and listed on Nasdaq, our business is subject to risks associated with conducting business internationally. Many of our suppliers and collaborative and clinical trial relationships are located outside the United Kingdom and the United States. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- differing regulatory requirements for drug approvals in non-U.S. countries;
- differing jurisdictions could present different issues for securing, maintaining or obtaining freedom to operate in such jurisdictions;
- potentially reduced protection for intellectual property rights;
- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. regulations and customs, tariffs and trade barriers;
- changes in non-U.S. currency exchange rates of the euro and currency controls;
- changes in a specific country's or region's political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or non-U.S. governments;
- differing reimbursement regimes and price controls in certain non-U.S. markets;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the United States;

- difficulties associated with staffing and managing international operations, including differing labor relations;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, such as the ongoing conflicts in Europe and the Middle East, or natural disasters including earthquakes, typhoons, floods and fires, or public health emergencies, such as the COVID-19 pandemic.

Exchange rate fluctuations may materially affect our results of operations and financial condition.

Although we are based in the United Kingdom, our financial statements are denominated in U.S dollars and many of our business activities are carried out with partners outside the U.S. and United Kingdom and these transactions may be denominated in another currency. As a result, our business and the price of our ADSs may be affected by fluctuations in foreign exchange rates not only between the pound sterling and the U.S. dollar, but also the currencies of other countries, which may have a significant impact on our results of operations and cash flows from period to period. Currently, we do not have any exchange rate hedging arrangements in place.

Risks Related to Development, Clinical Testing and Regulatory Approval

Clinical drug development and regulatory approval involve a lengthy and expensive process, with uncertain outcomes. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and regulatory approval of our product candidates.

Clinical drug development is a lengthy and expensive process with uncertain timelines and uncertain outcomes. If clinical trials of ensifentrine are prolonged or delayed, or if ensifentrine in later stage clinical trials fails to show the safety and efficacy required by regulatory authorities, we or our collaborators may be unable to obtain required regulatory approvals and be unable to commercialize ensifentrine on a timely basis, or at all.

To obtain the requisite regulatory approvals to market and sell ensifentrine, we or any collaborator for ensifentrine must demonstrate through extensive pre-clinical studies and clinical trials that ensifentrine is safe and effective in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of pre-clinical studies and early-stage clinical trials of ensifentrine may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through pre-clinical studies and initial clinical trials. Regulators' interpretations of results may differ from our own, and expectations can change over time while a product is in clinical development.

A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. The FDA may require us to conduct additional pre-clinical studies or clinical trials that may not be successful, or may not be considered successful by regulators. With respect to ensifentrine, our only product candidate, we have completed multiple Phase 1 and 2 clinical trials for different formulations of ensifentrine and for different indications, and two registrational Phase 3 clinical trials for nebulized ensifentrine for the maintenance treatment of COPD. Based on the results from these studies, we submitted an NDA seeking approval of ensifentrine for the maintenance treatment of COPD, and in August 2023, the FDA accepted for review our NDA and assigned a PDUFA target action date of June 26, 2024. The FDA's filing communication and a November 2023 mid-cycle communication each gave preliminary notice of two review issues regarding the degree to which certain secondary data, such as trough, and exploratory data, such as exacerbation, included in the application could be used to support a favorable benefit-risk profile or efficacy finding, respectively. The FDA noted in both communications that these comments were preliminary in nature and did not reflect a final decision on the information reviewed.

If we wish to commercialize nebulized ensifentrine for the maintenance treatment of COPD in other territories, the regulatory authorities in such territories may require us to conduct additional pre-clinical studies or clinical trials, and if we wish to commercialize ensifentrine in other formulations or for other indications, we will be required to conduct further clinical studies.

We may experience delays in clinical trials and we do not know whether planned clinical trials will begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all. Our clinical trials can be delayed, suspended, or terminated, or the utility of data from these trials may be compromised, for a variety of reasons, including the following:

- inability to generate sufficient preclinical, toxicology or other in vivo or in vitro data to support the initiation or continuation of clinical trials;
- delays in or failure to obtain regulatory agreement on clinical trial design or implementation, including dose and frequency of administration;
- delays in or failure to obtain regulatory authorization to commence a trial;
- delays in or failure to reach agreement on acceptable terms with prospective 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;
- inability of a CRO to meet their contracted obligations regarding subject enrollment, data collection, data monitoring, laboratory sample management, programming and analysis or other activities;
- delays in or failure to obtain institutional review board ("IRB"), or ethics committee approval or positive opinion at each site;
- delays in or failure to recruit suitable patients to participate in a trial;
- failure to have patients complete a trial or return for post-treatment follow-up;
- clinical sites deviating from trial protocol or dropping out of a trial or committing gross misconduct or fraud;
- delays to the addition of new clinical trial sites;
- inability to achieve or maintain double blinding of ensifentrine;
- unexpected technical issues during manufacture of ensifentrine and the corresponding drug products;
- variability in drug product performance and/or stability;
- discoveries that may reduce the commercial viability of ensifentrine;
- inability to manufacture sufficient quantities of ensifentrine for use in clinical trials;
- the quality or stability of ensifentrine falling below acceptable standards for either safety or efficacy;
- third-party actions claiming infringement by ensifentrine in clinical trials and obtaining injunctions interfering with our progress;
- business interruptions resulting from geo-political actions, including war and terrorism, such as the ongoing conflicts in Europe and the Middle East, or natural disasters including earthquakes, typhoons, floods and fires;
- trade sanctions imposed by the United States or other governments impacting our ability to transfer money to certain countries, such as Russia, to pay clinical trials sites in those countries;
- safety or tolerability concerns causing us or our collaborators, as applicable, to suspend or terminate a trial if we or our collaborators find that the participants are being exposed to unacceptable health risks;
- changes in regulatory requirements, policies and guidelines;
- lower than anticipated retention rates of patients and volunteers in clinical trials;
- failure of our third-party research contractors to comply with regulatory requirements or to meet their contractual obligations to us in a timely manner, or at all; and
- difficulty in certain countries in identifying the sub-populations that we are trying to evaluate in a particular trial, which may delay enrollment.

We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Review Committee or Data Safety Monitoring Board for such trial or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, failure of our clinical trials to demonstrate adequate efficacy and safety, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or other regulatory authority. The FDA or other regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or other regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or other regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of ensifentrine.

If we experience delays in the completion of any clinical trial of ensifentrine for any indication, or of any other product candidate, or any clinical trial of ensifentrine or any other product candidate is terminated, the commercial prospects of such product candidates may be harmed, and our ability to generate product revenues, if any, will be delayed. Moreover, any delays in completing our clinical trials will increase our costs, slow down the development and approval process and jeopardize our ability to commence product sales and generate revenue, if any. Significant clinical trial delays could also allow our competitors to bring products to market before we do or shorten any periods during which we have the exclusive right to commercialize our product candidates and could impair our ability to commercialize our product candidates. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of ensifentrine or any other product candidate.

Clinical trials must be conducted in accordance with the laws and regulations of the FDA, EU rules and regulations and other applicable regulatory authorities' legal requirements, regulations or guidelines, and are subject to oversight by these governmental agencies and IRBs (or other ethics committees) at the medical institutions where the clinical trials are conducted. In addition, clinical trials must be conducted with supplies of ensifentrine produced under current good manufacturing practice ("cGMP") and similar foreign requirements and other regulations. Furthermore, we rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and while we have agreements governing their committed activities, we have limited influence over their actual performance. We depend on our collaborators and on medical institutions and CROs to conduct our clinical trials in compliance with GCP requirements. To the extent our collaborators or the CROs fail to enroll participants for our clinical trials, fail to conduct the study to GCP standards or are delayed for a significant time in the execution of trials, including achieving full enrollment, we may be affected by increased costs, program delays or both. In addition, clinical trials that are conducted in countries outside the EU and the United States may subject us to further delays and expenses as a result of increased shipment costs, additional regulatory requirements and the engagement of non-EU and non-U.S. CROs, as well as expose us to risks associated with clinical investigators who are unknown to the FDA or the EMA, and different standards of diagnosis, screening and medical care.

In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation ("CTR"), which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the EU Clinical Trials Directive required a separate clinical trial application ("CTA"), to be submitted in each member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application for multi-center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the EU Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the EU Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third-party service providers, such as CROs, may impact our developments plans.

It is currently unclear to what extent the U.K. will seek to align its regulations with the EU. The U.K. regulatory framework in relation to clinical trials is derived from existing EU legislation (as implemented into U.K. law, through secondary legislation).

On January 17, 2022, the U.K. Medicines and Healthcare products Regulatory Agency ("MHRA"), launched an eight-week consultation on reframing the U.K. legislation for clinical trials, which aimed to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The resulting legislative changes will be closely watched and will determine the extent to which the U.K. clinical trials framework aligns with or diverges from the (EU) CTR. Under the terms of the Protocol on Ireland/Northern Ireland, provisions of the (EU) CTR which relate to the manufacture and import of investigational medicinal products and auxiliary medicinal products apply in Northern Ireland. A decision by the U.K. Government not to closely align its regulations with the new approach that has been adopted in the EU may have an effect on the cost of conducting clinical trials in the U.K. compared with other countries.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted.

Ensifentrine may have serious adverse, undesirable or unacceptable side effects which may delay or prevent marketing approval. If such side effects are identified during the development of ensifentrine or following approval, if any, we may need to abandon our development of ensifentrine, the commercial profile of any approved label may be limited, or we may be subject to other significant negative consequences following marketing approval, if any.

Undesirable side effects that may be caused by ensifentrine 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 other comparable foreign authorities. During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries, and discomforts, to their study doctor. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions. It is possible that as we test our product candidates in larger, longer and more extensive clinical trials, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in previous trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. Many times, side effects are only detectable after investigational products are tested in large-scale clinical trials or, in some cases, after they are made available to patients on a commercial scale following approval. We have completed more than 20 Phase 1, 2 and 3 clinical trials of ensifentrine. In these trials, some patients have experienced mild to moderate adverse reactions, including urinary tract infection, back pain and hypertension.

Results of our future clinical trials could reveal a high and unacceptable severity and prevalence of adverse side effects. In such an event, our trials could be suspended or terminated and the FDA or other comparable foreign regulatory authorities could order us to cease further development of or deny approval of ensifentrine for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Additionally, if ensifentrine receives marketing approval and we or others later identify undesirable or unacceptable side effects caused by ensifentrine, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such products and require us to take ensifentrine off the market;
- regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies;
- regulatory authorities may require a medication guide outlining the risks of such side effects for distribution to patients, or that we implement a REMS plan or similar risk management measures to ensure that the benefits of ensifentrine outweigh its risks;
- we may be required to change the way ensifentrine is administered, conduct additional clinical trials or change the labeling of ensifentrine;
- we may be subject to limitations on how we may promote ensifentrine;
- sales of ensifentrine may decrease significantly;
- we may be subject to litigation or product liability claims; and
- our reputation may suffer.

Any of these events could prevent us or any collaborators from achieving or maintaining market acceptance of ensifentrine or could substantially increase commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenue from the sale of ensifentrine.

We may not be successful in our efforts to develop ensifentrine in different formulations, including fixed-dose combinations, and/or for multiple indications, including NCFBE, CF, asthma or other respiratory diseases.

Part of our strategy is to continue to develop ensifentrine in indications other than COPD, such as NCFBE, CF and asthma and other formulations including fixed-dose combinations, MDI and DPI. Although our research and development efforts to date have suggested that ensifentrine has the potential to treat NCFBE, CF and asthma, we may not be able to develop ensifentrine in these indications or any other disease, or development may not be successful. In addition, the potential use of ensifentrine in other diseases may not be suitable for clinical development, including as a result of difficulties enrolling patients in any clinical studies we plan to initiate or the potential for harmful side effects or other characteristics that might suggest marketing approval and market acceptance are unlikely. If we do not continue to successfully develop and begin to commercialize ensifentrine for multiple indications or formulations, we will face difficulty in obtaining product revenues in future periods, which could significantly harm our financial position.

We depend on enrollment of patients in our clinical trials for ensifentrine. If we are unable to enroll patients in our clinical trials, or enrollment is slower than anticipated, our research and development efforts could be adversely affected.

Successful and timely completion of clinical trials for ensifentrine will require that we enroll a sufficient number of patient candidates. Trials may be subject to delays as a result of patient enrollment taking longer than anticipated or patient withdrawal and other external factors. Patient enrollment depends on many factors, including the size and nature of the patient population, the severity of the disease under investigation, eligibility criteria for the trial, the proximity of patients to clinical sites, the design of the clinical protocol, the ability to obtain and maintain patient consents, the risk that enrolled patients will drop out of a trial, the availability of competing clinical trials, the availability of new drugs approved for the indication the clinical trial is investigating and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies. These factors may make it difficult for us to enroll enough patients to complete our clinical trials in a timely and cost-effective manner. Higher than expected numbers of patients could also discontinue participation in the clinical trials. Delays in the completion of any clinical trial of ensifentrine or other product candidates will increase our costs, slow down our development and approval of ensifentrine and delay or potentially jeopardize our ability to commence product sales and generate revenue. In addition, some of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of ensifentrine.

We may become exposed to costly and damaging liability claims, either when testing ensifentrine in the clinic or at the commercial stage, and our product liability insurance may not cover all damages from such claims.

We are exposed to potential product liability and professional indemnity risks that are inherent in the research, development, manufacturing, marketing and use of pharmaceutical products. Currently, we have no products that have been approved for commercial sale; however, the current and future use of ensifentrine by us and any collaborators in clinical trials, and the sale of ensifentrine, if approved, in the future, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical companies, our collaborators or others selling ensifentrine. Any claims against us, regardless of their merit, could be difficult and costly to defend and could adversely affect the market for ensifentrine or any prospects for commercialization of ensifentrine. In addition, regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for ensifentrine;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend related litigation;
- diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- regulatory investigation, product recalls or withdrawals, or labeling, marketing or promotional restrictions;

- loss of revenue; and
- the inability to commercialize or promote ensifentrine.

Although the clinical trial process is designed to identify and assess potential side effects, it is always possible that a drug, even after regulatory approval, may exhibit unforeseen side effects. If ensifentrine were to cause adverse side effects during clinical trials or after approval, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use ensifentrine.

Although we maintain product liability insurance for ensifentrine, it is possible that our liabilities could exceed our insurance coverage. We intend to expand our insurance coverage to include the sale of commercial products if we obtain marketing approval for ensifentrine. However, we may not be able to maintain insurance coverage at a reasonable cost or obtain insurance coverage that will be adequate to satisfy any liability that may arise. If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

The regulatory approval processes of the FDA, the EMA and comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for ensifentrine, our business will be substantially harmed.

The time required to obtain approval by the FDA, the European Commission and comparable foreign regulatory authorities is unpredictable, but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for ensifentrine and it is possible that ensifentrine or any product candidates we may develop in the future will never obtain regulatory approval.

Prior to obtaining approval to commercialize a product candidate in the United States or abroad, we or our collaborators must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or foreign regulatory agencies, that such product candidate is safe and effective for its intended uses. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our product candidate are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. The FDA or foreign regulatory agencies may also require us to conduct additional preclinical studies or clinical trials for ensifentrine either prior to or post-approval, or it may object to elements of our clinical development program.

Ensifentrine could fail to receive regulatory approval for many reasons, including the following:

- we may be unable to demonstrate to the satisfaction of the FDA, the EMA or comparable foreign regulatory authorities that ensifentrine is safe and effective, with the required level of statistical significance, for its proposed indication;
- we may be unable to demonstrate that ensifentrine's benefits outweigh its safety risks;
- the FDA, the EMA or comparable foreign regulatory authorities may disagree with our interpretation of data from pre-clinical studies or clinical trials or may find the data to be unacceptable;
- the FDA, the EMA or comparable foreign regulatory authorities may find that the dose or doses evaluated in Phase 3 clinical trials or the way in which double blinding was effected to be unacceptable;
- the data collected from clinical trials of ensifentrine may, for various reasons, be insufficient to support the submission or approval of an NDA in the United States, a MAA in the EU, or other comparable submission to obtain regulatory approval in other countries;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;
- FDA or comparable regulatory authorities may identify issues of GCP noncompliance or unacceptable practices at clinical sites or CROs participating in our clinical studies, rendering clinical data insufficient to support approval;

- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval;
- the FDA, the EMA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials; and
- the FDA, the EMA or comparable foreign regulatory authorities may disagree with our proposed product specifications and performance characteristics.

This lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market ensifentrine. The FDA, the EMA and other regulatory authorities have substantial discretion in the approval process, and determining when or whether regulatory approval will be obtained for ensifentrine. Even if we believe the data collected from clinical trials of ensifentrine are promising, such data may not be sufficient to support approval by the FDA, the European Commission or any other regulatory authority. For example, in August 2023, the FDA accepted for review our NDA seeking approval of ensifentrine for the maintenance treatment of COPD and assigned a PDUFA target action date of June 26, 2024. The NDA filing communication and a November 2023 mid-cycle review each gave preliminary notice of two review issues regarding the degree to which certain secondary data, such as trough, and exploratory data, such as exacerbation, included in the application could be used to support a favorable benefit-risk profile or efficacy finding, respectively. The FDA noted in both communications that these comments were preliminary in nature and did not reflect a final decision on the information reviewed.

In addition, even if we were to obtain approval for any jurisdiction, regulatory authorities may approve ensifentrine for fewer or more limited indications than we request, may not approve the price we intend to charge for ensifentrine, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve ensifentrine with a label that does not include the labeling claims necessary or desirable for the successful commercialization of ensifentrine. Any of the foregoing scenarios could materially harm the commercial prospects for ensifentrine.

In addition, FDA and foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products (potentially reducing the duration of regulatory data protection, revising the eligibility for expedited pathways, etc.) was published on April 26, 2023. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revision may however have a significant impact on the biopharmaceutical industry and our business in the long term.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA and comparable foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's or foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's or foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies, such as the EMA following its relocation to Amsterdam and resulting staff changes, may also slow the time necessary for new drugs, or modifications to cleared or approved drugs, to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, the FDA postponed most inspections of domestic and foreign manufacturing facilities at various points. Even though the FDA has since resumed standard inspection operations, any resurgence of the virus or emergence of new variants may lead to further inspection-related or administrative delays. If a prolonged government shutdown occurs, or if global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could

significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Even if ensifentrine obtains regulatory approval, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, ensifentrine, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with ensifentrine.

If the FDA or a comparable foreign regulatory authority approves ensifentrine, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and record keeping for ensifentrine will be subject to extensive and ongoing regulatory requirements. These requirements include payment of annual user fees, submissions of safety and other post-marketing information and reports, facility registration and drug listing, as well as continued compliance with cGMP and similar foreign requirements for the manufacture of ensifentrine and GCP requirements for any clinical trials that we conduct post-approval, all of which may result in significant expense and limit our ability to commercialize ensifentrine. In addition, any approval we may obtain for ensifentrine may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post-approval study or risk management requirements. For example, the FDA may require a REMS in order to approve our product candidates, which could entail requirements for a medication guide, physician training and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools.

We and our contract manufacturers will also be subject to periodic inspection by the FDA and other regulatory authorities to monitor compliance with these requirements and the terms of any product approval we may obtain. If we or a regulatory authority discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facilities where the product is manufactured, a regulatory authority may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. In addition, failure to comply with FDA and other comparable foreign regulatory requirements may subject our company to administrative or judicially imposed sanctions, including:

- delays in or the rejection of product approvals;
- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;
- restrictions on the products, manufacturers or manufacturing process;
- warning or untitled letters;
- civil and criminal penalties;
- injunctions;
- suspension or withdrawal of regulatory approvals;
- product seizures, detentions or import bans;
- voluntary or mandatory product recalls and publicity requirements;
- total or partial suspension of production; and
- imposition of restrictions on operations, including costly new manufacturing requirements.

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

In addition, the policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. 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 be subject to enforcement action and we may not achieve or sustain profitability.

The FDA and other foreign regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses which may result in significant liability if we are found to have violated such laws.

If ensifentrine is approved for any indication and we are found to have improperly promoted off-label uses for ensifentrine, 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, such as our product candidates, if approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies 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 U.S. federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The FDA has 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 ensifentrine, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

In Europe, off-label use is not per se regulated by the EU pharmaceutical legislation and a difference is made between the strict regulation of medicinal product and the use of medicinal products in medical practice. Off-label use is deferred to national regulation and may vary depending on the EU Member State(s).

Even if we obtain marketing approval of ensifentrine for any indication in a major pharmaceutical market such as the United States or EU, we may never obtain approval or commercialize ensifentrine in other major markets, which would limit our ability to realize its full market potential.

In order to market any products in a country or territory, we must establish and comply with numerous and varying regulatory requirements of such country or territory regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking regulatory approvals in all major markets could result in significant delays, difficulties and costs for us and may require additional pre-clinical studies or clinical trials which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of ensifentrine in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We currently do not have any product candidates approved for sale in any jurisdiction, whether in the EU, the United States or any other international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our target market will be reduced and our ability to realize the full market potential of ensifentrine will be compromised.

Our employees and independent contractors, including principal investigators, CROs, consultants, vendors and collaboration partners 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, vendors and collaboration partners may engage in fraudulent conduct or other illegal activities. Misconduct by these parties could include intentional, reckless or negligent conduct or unauthorized activities that violate: (i) the laws and regulations of the FDA, the EU and other similar regulatory bodies and the EU, including those laws that require the reporting of true, complete and accurate information to such authorities; (ii) manufacturing standards; (iii) federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations in the United States and abroad; or (iv) laws that require the reporting of true, complete and accurate financial information and data. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creating fraudulent data in our pre-clinical 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 comply with such laws or regulations. Additionally, 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 results of operations, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid and other U.S. federal healthcare programs or healthcare programs in other jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

Interim, "top-line," or 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 interim, top-line or preliminary data from our clinical trials, 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 top-line or preliminary 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. Top-line or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the top-line or preliminary data we previously published. As a result, top-line and preliminary data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. 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 interim data and final data could significantly harm our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If the interim, top-line or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

Risks Related to Healthcare Laws and Other Legal Compliance Matters

Enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize ensifentrine and may affect the prices we may set.

In the United States, the EU and other foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, was enacted, which substantially changes the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following:

- an annual, non-deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents, which is apportioned among these entities according to their market share in certain government healthcare programs;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 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;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- 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;
- extension of a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of a Center for Medicare and Medicaid Innovation at the Centers for Medicare and Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order initiating a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, the Budget Control Act of 2011 has, among other things, led to aggregate reductions of Medicare payments to providers, which, due to subsequent legislative amendments to the statute, will remain in effect through 2032, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional action is taken by Congress. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further 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. In addition, the American Rescue Plan Act of 2021 was signed into law, which eliminates the statutory Medicaid drug rebate cap, beginning January 1, 2024. The rebate was previously capped at 100% of a drug's average manufacturer price. These laws and any laws enacted in the future may result in additional reductions in Medicare and other health care funding, which could have a material adverse effect on our customers and accordingly, our financial operations.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Most recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D continue to penalize price increases that outpace inflation; and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services, or HHS, to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations, although the Medicare drug price negotiation program is currently subject to legal challenges. The impact of the IRA on the pharmaceutical industry cannot yet be fully determined but, is likely to be significant.

Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to submit a report within 90 days on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. In response to the executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the CMS Innovation Center which will be evaluated on their ability to lower the cost of drugs, promote accessibility and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future.

We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for ensifentrine or additional pricing pressures.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological 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. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for ensifentrine or put pressure on our product pricing.

In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize ensifentrine, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of health care in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of ensifentrine, restrict or regulate post-approval activities and affect our ability to commercialize ensifentrine, if approved. In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

On December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment ("HTA") amending Directive 2011/24/EU, was adopted. While the Regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once applicable, it will have a phased implementation depending on the concerned products.

The Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and provide the basis for cooperation at the EU level for joint clinical assessments in these areas. It will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and

continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we or our collaborators are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or our collaborators are not able to maintain regulatory compliance, ensifentrine may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute ensifentrine, if approved. Such laws include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the U.S. federal false claims and civil monetary penalties laws, including the civil False Claims Act, which, among other things, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services; similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- the U.S. federal legislation commonly referred to as Physician Payments Sunshine Act, enacted as part of the ACA, and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to the government information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiology assistants and certified nurse-midwives), and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;
- analogous state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or

otherwise restrict payments that may be made to healthcare providers and other potential referral sources; and state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and

- in the EU, interactions between pharmaceutical companies and health care professionals and health care organizations, are also governed by strict laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct both at EU level and in the individual EU member states. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of pharmaceutical products is prohibited in the EU. Relationships with healthcare professionals and associations are subject to stringent anti-gift statutes and anti-bribery laws, the scope of which differs across the EU. In addition, national "Sunshine Acts" may require pharmaceutical companies to report/publish transfers of value provided to health care professionals and associations on a regular (e.g. annual) basis. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Ensuring that our internal operations and business arrangements with third parties comply with applicable healthcare laws and regulations involves substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from U.S. government funded healthcare programs, such as Medicare and Medicaid, or similar programs in other countries or jurisdictions, a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition.

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal information, such as information that we may collect in connection with clinical trials. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulations, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our business, results of operation, and financial condition.

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. In the United States, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and regulations implemented thereunder, or collectively HIPAA, imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. Most healthcare providers, including research institutions from which we obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA. We do not believe that we are currently acting as a covered entity or business associate under HIPAA and thus are not directly subject to its requirements or penalties. However, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered healthcare provider or research institution that has not satisfied HIPAA's requirements for disclosure of individually identifiable health information.

Certain states have also adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. For example, California enacted the California Consumer Privacy Act, ("CCPA"), which went into effect on January 1, 2020. The CCPA, among other things, creates data privacy obligations for covered companies and provides privacy rights to California consumers, including rights to access and delete their information, to opt out of certain information sharing, and receive detailed information about how their personal information is used. The CCPA also creates a private right of action with statutory damages for certain data breaches, thereby potentially increasing risks associated with a data breach. Although the law includes limited exceptions for health-related information, it may regulate or impact our processing of personal information depending on the context. Further, the California Privacy Rights Act ("CPRA") generally went into effect on January 1, 2023 and significantly amends the CCPA. It imposes additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It also creates a new California data protection agency authorized to issue substantive regulations and will likely result in increased privacy and information security enforcement. Additional compliance investment and potential business process changes may be required. Similar laws have passed in other states and are continuing to be proposed at the state and federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

We are also subject to diverse laws and regulations relating to data privacy and security in the EU and the EEA, including the General Data Protection Regulation ("GDPR"). The GDPR went into effect in May 2018 and imposes strict requirements for processing the personal data of individuals within the EEA. The GDPR imposes strict obligations on the ability to process health-related and other personal data of individuals within the EEA, including in relation to use, collection, analysis, and transfer (including cross-border transfer) of such personal data. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. In addition to fines, a breach of the GDPR may result in regulatory investigations, reputational damage, orders to cease/change our data processing activities, enforcement notices, assessment notices (for a compulsory audit) and/ or civil claims (including class actions). Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States, and the efficacy and longevity of current transfer mechanisms between the EEA and the United States remains uncertain. Case law from the Court of Justice of the European Union ("CJEU") states that reliance on the standard contractual clauses—a standard form of contract approved by the European Commission as an adequate personal data transfer mechanism—alone may not necessarily be sufficient in all circumstances and that transfers must be assessed on a case-by-case basis. On July 10, 2023, the European Commission adopted its Adequacy Decision in relation to the new EU-US Data Privacy Framework ("DPF"), rendering the DPF effective as a GDPR transfer mechanism to U.S. entities self-certified under the DPF, rendering the DPF effective as a GDPR transfer mechanism to U.S. entities self-certified under the DPF. We expect the existing legal complexity and uncertainty regarding international personal data transfers to continue. In particular, we expect the DPF Adequacy Decision to be challenged and international transfers to the United States and to other jurisdictions more generally to continue to be subject to enhanced scrutiny by regulators. As a result, we may have to make certain operational changes and we will have to implement revised standard contractual clauses and other relevant documentation for existing data transfers within required time frames.

Relatedly, since the beginning of 2021, following the United Kingdom's withdrawal from the EEA and the European Union, and the expiry of the transition period, companies have had to comply with both the GDPR and the GDPR as incorporated into United Kingdom national law, the latter regime having the ability to separately fine up to the greater of £17.5 million or 4% of global turnover. On October 12, 2023, the U.K. Extension to the DPF came into effect (as approved by the U.K. Government), as a data transfer mechanism from the U.K. to U.S. entities self-certified under the DPF. As we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business.

Compliance with applicable 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. Failure by us or our collaborators and third-party providers to comply with applicable data protection laws and regulations could result in government enforcement actions (which could include

civil or criminal penalties), private litigation and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects about whom we or our potential collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose such information. 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.

The increasing focus on environmental sustainability and social initiatives could increase our costs, harm our reputation and adversely impact our financial results.

There has been increasing public focus by investors, environmental activists, the media and governmental and nongovernmental organizations on a variety of environmental, social and other sustainability matters. We may experience pressure to make commitments relating to sustainability matters that affect us, including the design and implementation of specific risk mitigation strategic initiatives relating to sustainability. If we are not effective in addressing environmental, social and other sustainability matters affecting our business, or setting and meeting relevant sustainability goals, our reputation and financial results may suffer. In addition, we may experience increased costs in order to execute upon our sustainability goals and measure achievement of those goals, which could have an adverse impact on our business and financial condition.

In addition, this emphasis on environmental, social and other sustainability matters has resulted and may result in the adoption of new laws and regulations, including new reporting requirements. If we fail to comply with new laws, regulations or reporting requirements, our reputation and business could be adversely impacted.

We are subject to environmental, health and safety laws and regulations, and we may become exposed to liability and substantial expenses in connection with environmental compliance or remediation activities.

Our sub-contracted operations, including our research, development, testing and manufacturing activities, are subject to numerous environmental, health and safety laws and regulations. These laws and regulations govern, among other things, the controlled use, handling, release and disposal of and the maintenance of a registry for, hazardous materials and biological materials, such as chemical solvents, human cells, carcinogenic compounds, mutagenic compounds and compounds that have a toxic effect on reproduction, laboratory procedures and exposure to blood-borne pathogens. If we fail to comply with such laws and regulations, we could incur significant costs associated with civil or criminal fines, penalties or other sanctions.

As with other companies engaged in activities similar to ours, we face a risk of environmental liability inherent in our current and historical activities, including liability relating to releases of or exposure to hazardous or biological materials. Environmental, health and safety laws and regulations are becoming more stringent. We may be required to incur substantial expenses in connection with future environmental compliance or remediation activities, in which case, our production and development efforts may be interrupted or delayed.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses.

Our operations are subject to anti-corruption laws, including the U.K. Bribery Act 2010, or Bribery Act, the U.S. Foreign Corrupt Practices Act, or FCPA, and other anti-corruption laws that apply in countries where we do business and may do business in the future. The Bribery Act, FCPA and these other laws generally prohibit us, our officers and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We may in the future operate in jurisdictions that pose a high risk of potential Bribery Act or FCPA violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the Bribery Act, FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which any of our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We also are subject to other laws and regulations governing any international operations, including regulations administered by the governments of the United Kingdom and the United States, and authorities in the EU, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, or, collectively, the Trade Control laws. In particular, we engaged a number of clinical trial sites in Russia in connection with our Phase 3 ENHANCE clinical program and, with the ongoing conflict between Russia and Ukraine, and resulting sanctions imposed by the United States and other governments, there is an increased risk that our ability to pay clinical sites or conduct clinical trials in Russia, may be impacted.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the Bribery Act, the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the Bribery Act, the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures and legal expenses. Any investigation of any potential violations of the Bribery Act, the FCPA, other anti-corruption laws or Trade Control laws by U.K., U.S. or other authorities, even if it is ultimately determined that we did not violate such laws, could be costly and time consuming, require significant personnel resources and harm our reputation.

We will seek to build and continuously improve our systems of internal controls and to remedy any weaknesses identified. There can be no assurance, however, that the policies and procedures will be followed at all times or effectively detect and prevent violations of the applicable laws by one or more of our employees, consultants, agents or collaborators and, as a result, we could be subject to fines, penalties or prosecution.

Risks Related to Commercialization

We operate in a highly competitive and rapidly changing industry, which may result in others discovering, developing or commercializing competing products before or more successfully than we do.

The biopharmaceutical and pharmaceutical industries are highly competitive and subject to significant and rapid technological change. Our success is highly dependent on our ability to discover, develop and obtain marketing approval for new products on a cost-effective basis and to market them successfully. If ensifentrine is approved for any indication, we will face intense competition from a variety of businesses, including large, fully integrated pharmaceutical companies, specialty pharmaceutical companies and biopharmaceutical companies, academic institutions, government agencies and other private and public research institutions in Europe, the U.S. and other jurisdictions. These organizations may have significantly greater resources than we do and conduct similar research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and marketing of products that may compete with ensifentrine.

Given the number of products already on the market to treat COPD, asthma, CF and NCFBE, we expect to face intense competition if ensifentrine is approved for these indications. Companies including Boehringer Ingelheim, GlaxoSmithKline, AstraZeneca, Novartis, Vertex, Viatris, Theravance, Gilead and Genentech currently have treatments on the market for COPD, CF and asthma, and we anticipate that new companies will enter these markets in the future. While no treatments for NCFBE currently have marketing approval in the U.S. or EU, there are products in late-stage clinical development that could be approved in the future. If we successfully develop and commercialize ensifentrine for any indication, it will compete with existing therapies and new therapies that may become available in the future. The highly competitive nature of, and rapid technological changes in, the biopharmaceutical and pharmaceutical industries could render ensifentrine obsolete, less competitive or uneconomical. Our competitors may, among other things:

- have significantly greater name recognition, financial, manufacturing, marketing, drug development, technical and human resources than we do, and future mergers and acquisitions in the biopharmaceutical and pharmaceutical industries may result in even more resources being concentrated in our competitors;
- develop and commercialize products that are safer, more effective, less expensive, more convenient or easier to administer, or have fewer or less severe side effects;
- obtain quicker regulatory approval;
- establish superior proprietary positions covering our products and technologies;
- implement more effective approaches to sales, marketing and distribution; or
- form more advantageous strategic alliances.

Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. In addition, any collaborators we may have may decide to market and sell products that compete with ensifentrine. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer or less severe side effects, are more convenient or are less expensive than ensifentrine. Our competitors may also obtain FDA or other regulatory approval for their product candidates more rapidly than we may obtain approval for ours, which could result in our competitors establishing or strengthening their market position before we are able to enter the market.

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

The availability and adequacy of coverage and 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 ensifentrine, assuming approval. Our ability to achieve acceptable levels of coverage and reimbursement by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize ensifentrine. Assuming we obtain coverage for ensifentrine by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Moreover, for drugs and biologics administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such products. We cannot be sure that coverage and reimbursement in the United States, the EU or elsewhere will be available for ensifentrine or any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

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 ensifentrine as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with ensifentrine, pricing of existing drugs may limit the amount we will be able to charge for ensifentrine. 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 ensifentrine. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize ensifentrine, and may not be able to obtain a satisfactory financial return on ensifentrine.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. 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 and biologics. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for ensifentrine.

Obtaining and maintaining reimbursement status is time consuming and costly. No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. 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 ensifentrine 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. Specifically, we believe that ensifentrine will be reimbursed either under Medicare Part B or Medicare Advantage programs, and changes within how products are reimbursed under these programs could occur and those changes may affect the overall coverage of ensifentrine in the future.

Outside the United States, 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 ensifentrine. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for ensifentrine. Accordingly, in markets outside the United States, the reimbursement for ensifentrine may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States 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 ensifentrine. We expect to experience pricing pressures in connection with the sale of ensifentrine 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.

In addition, even if a pharmaceutical product obtains a marketing authorization in the EU, there can be no assurance that reimbursement for such product will be secured on a timely basis or at all.

Ensifentrine may not gain market acceptance, in which case our ability to generate product revenues will be compromised.

Even if the FDA or any other regulatory authority approves the marketing of ensifentrine, whether developed on our own or with a collaborator, physicians, healthcare providers, patients or the medical community may not accept or use ensifentrine. If ensifentrine does not achieve an adequate level of acceptance, we may not generate significant product revenues or any profits from operations. The degree of market acceptance of ensifentrine will depend on a variety of factors, including:

- the timing of market introduction;
- the number and clinical profile of competing products;
- the clinical indications for which ensifentrine is approved;
- our ability to provide acceptable evidence of safety and efficacy;
- the prevalence and severity of any side effects;
- relative convenience, frequency, and ease of administration;
- cost effectiveness;
- marketing, sales, and distribution support;
- availability of adequate coverage, reimbursement and adequate payment from health maintenance organizations and other insurers, both public and private; and
- other potential advantages over alternative treatment methods.

If ensifentrine fails to gain market acceptance, this will adversely impact our ability to generate revenues. Even if ensifentrine achieves market acceptance, the market may prove not to be large enough to allow us to generate significant revenues.

We are currently developing our commercial capabilities and infrastructure, including sales, marketing, operations, distribution, and reimbursement infrastructure. If we are not successful in developing commercial capabilities and infrastructure, including sales, marketing, operations, distribution and reimbursement capabilities on our own or through collaborations, we may not be successful in commercializing ensifentrine.

We are developing sales, marketing, and operations, distribution and reimbursement capabilities and infrastructure and we have not previously marketed, sold or distributed pharmaceutical products. The establishment of commercial capabilities and infrastructure, including sales, marketing, operations, distribution, and reimbursement with technical expertise and supporting distribution capabilities to commercialize ensifentrine, is expensive and time consuming. Some or all of these costs are incurred in advance of any approval of ensifentrine. In addition, we may not be able to hire a sales force that is sufficient in size or has adequate expertise in the medical markets that we intend to target. Any failure or delay in the development of our internal sales, marketing and distribution capabilities on our own or through collaborations would adversely impact the commercialization of ensifentrine.

To the extent that we enter into collaboration agreements with respect to marketing, sales or distribution, our product revenue may be lower than if we directly marketed or sold ensifentrine, if approved. In addition, any revenue we receive will depend in whole or in part upon the efforts of these third-party collaborators, which may not be successful and are generally not within our control. If we are unable to enter into these arrangements on acceptable terms or at all, we may not be able to successfully commercialize ensifentrine. If we are not successful in commercializing ensifentrine, either on our own or through collaborations with one or more third parties, our future product revenue will suffer and we may incur significant additional losses.

Risks Related to Our Dependence on Third Parties

We rely, and expect to continue to rely, on third parties, including independent clinical investigators and CROs, to conduct our pre-clinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize ensifentrine and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon third parties, including independent clinical investigators and CROs, to conduct our pre-clinical studies and clinical trials and to monitor and manage data for our ongoing pre-clinical and clinical programs. We rely on these parties for execution of our pre-clinical studies and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our third-party contractors and CROs 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 products in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we fail to exercise adequate oversight over any of our CROs or if we or any of our CROs fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot provide assurance that upon a regulatory inspection of us or our CROs or other third parties performing services in connection with our clinical trials, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under applicable cGMP and similar foreign regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Further, these investigators and CROs are not our employees and we will not be able to control, other than by contract, the amount of resources, including time, which they devote to ensifentrine and clinical trials. If independent investigators or CROs fail to devote sufficient resources to the development of ensifentrine, or if their performance is substandard, it may delay or compromise the prospects for approval and commercialization of ensifentrine. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated.

Our existing and future CROs have or may have the right to terminate their agreements with us in the event of an uncured material breach. In addition, some of our CROs have an ability to terminate their respective agreements with us if it can be reasonably demonstrated that the safety of the subjects participating in our clinical trials warrants such termination, if we make a general assignment for the benefit of our creditors or if we are liquidated.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. Switching or adding CROs involves additional cost and requires management's time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays could occur, which could materially impact our ability to meet our desired clinical development timelines. In addition, if our CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for, or commercialize, ensifentrine. As a result, our results of operations and the commercial prospects for ensifentrine would be harmed, our costs could increase and our ability to generate revenues could be delayed.

The collaboration and license agreement with Nuance Pharma is important to our business. If Nuance Pharma is unable to develop and commercialize products containing ensifentrine in Greater China, if we or Nuance Pharma fail to adequately perform under the Nuance Agreement, or if we or Nuance Pharma terminate the Nuance Agreement, our business would be adversely affected.

We entered into a collaboration and license agreement with Nuance Pharma effective June 9, 2021 (the "Nuance Agreement") under which we granted Nuance Pharma the exclusive rights to develop and commercialize products containing ensifentrine (the "Nuance Licensed Products") in Greater China (China, Taiwan, Hong Kong and Macau).

The Nuance Agreement will continue on a jurisdiction-by-jurisdiction and product-by-product basis until the expiration of royalty payment obligations with respect to such product in such jurisdiction unless earlier terminated by the parties. Either party may terminate the Nuance Agreement for an uncured material breach or bankruptcy of the other party. Nuance Pharma may also terminate the Nuance Agreement at will upon 90 days' prior written notice.

Termination of the Nuance Agreement could cause significant setbacks in our ability to develop and commercialize the Nuance Licensed Products in Greater China. Any suitable alternative collaboration or license agreement would take considerable time to negotiate and could also be on less favorable terms to us. In addition, under the Nuance Agreement, Nuance Pharma agreed to assume all costs related to clinical development and commercialization of the Nuance Licensed Products in Greater China. If the Nuance Agreement were to be terminated, and whether or not we identify another suitable collaborator, we may need to seek additional financing to support the clinical development and commercialization of the Nuance Licensed Products in Greater China, which could have a material adverse effect on our business.

Under the Nuance Agreement, we are dependent upon Nuance Pharma to successfully develop and commercialize Nuance Licensed Products. Although we have formed a joint steering committee with Nuance Pharma to oversee and coordinate the overall conduct of the clinical development and commercialization of the Nuance Licensed Products in Greater China, we do not control all aspects of Nuance Pharma's development and commercialization or the resources it allocates to the development of the Nuance Licensed Products identified under the Nuance Agreement. Our interests and Nuance Pharma's interests may differ or conflict from time to time, or we may disagree with Nuance Pharma's level of effort or resource allocation. Nuance Pharma may internally prioritize programs under development within the collaboration differently than we would, or it may not allocate sufficient resources to effectively or optimally develop or commercialize the Nuance Licensed Products. If these events were to occur, our ability to receive revenue from the commercialization of the Nuance Licensed Products would be reduced, and our business would be adversely affected. In addition, under the Nuance Agreement, we have an obligation to supply Nuance Pharma with the ensifentrine drug product for their development and commercialization activities in Greater China and if our supply price is too high, the price at which Nuance Pharma sells the drug product in Greater China may not be competitive, which could have a material adverse effect on Nuance Pharma's ability to successfully commercialize Nuance Licensed Products and the returns that we generate under the Nuance Agreement. Furthermore, the safety and/or efficacy data from Nuance Pharma's clinical development activities could for various reasons differ from our data and could potentially impact our clinical development and commercialization activities, including our ability to obtain regulatory approval of ensifentrine in the United States and other countries.

If we fail to enter into new strategic relationships for ensifentrine, our business, research and development and commercialization prospects could be adversely affected.

Our development program for ensifentrine and the potential commercialization of ensifentrine will require substantial additional cash to fund expenses. Therefore, we may decide to enter into collaborations with pharmaceutical or biopharmaceutical companies for the development and potential commercialization of

ensifentrine. For example, we may seek a collaborator for development of our DPI or pMDI formulation of ensifentrine for the maintenance treatment of COPD and potentially asthma and other respiratory diseases.

We face significant competition in seeking appropriate collaborators. Collaborations are complex and time consuming to negotiate and document. We may also be restricted under existing and future collaboration agreements from entering into agreements on certain terms with other potential collaborators. We may not be able to negotiate collaborations on acceptable terms, or at all. If that were to occur, we may have to curtail the development of ensifentrine, reduce or delay its development program, delay its potential commercialization or reduce the scope of our sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we will not be able to bring ensifentrine to market and generate product revenue. If we do enter into a collaboration agreement, we could be subject to the following risks, among others, any of which could adversely affect our ability to develop and commercialize ensifentrine:

- we may not be able to control the amount and timing of resources that the collaborator devotes to the development of ensifentrine;
- the collaborator may experience financial difficulties;
- we may be required to relinquish important rights such as marketing, distribution and intellectual property rights;
- a collaborator could move forward with a competing product developed either independently or in collaboration with third parties, including our competitors;
- safety and/or efficacy data from a collaborator's clinical development activities may conflict with our data and could potentially impact our global clinical development and commercialization activities;
- a collaborator may unlawfully use or disclose confidential information and materials in breach of confidentiality obligations to us;
- business combinations or significant changes in a collaborator's business strategy may adversely affect our willingness to complete our obligations under any arrangement;
- we or a collaborator could fail to adequately perform our obligations under the agreement and/or the agreement could fall into dispute;
- we may be involved in lawsuits to protect or enforce patents covering ensifentrine, or relating to the terms of our collaborations, which could be expensive, time consuming and unsuccessful; or
- the collaboration may not provide sufficient funds to be profitable for us after we fulfill our payment liabilities under our agreement with Ligand Pharmaceuticals, Inc., or Ligand, which acquired Vernalis Development Limited, or Vernalis, in October 2018.

We currently rely on third-party manufacturers and suppliers for production of the active pharmaceutical ingredient ensifentrine and its derived formulated products. Our dependence on these third parties may impair the advancement of our research and development programs and the development of ensifentrine. Moreover, we intend to rely on third parties to produce commercial supplies of ensifentrine, if approved, and commercialization could be stopped, delayed or made less profitable if those third parties fail to obtain the necessary approvals from the FDA or comparable regulatory authorities, fail to provide us with sufficient quantities of product in a timely manner or fail to do so at acceptable quality levels or prices or fail to otherwise complete their duties in compliance with their obligations to us or other parties.

We do not own facilities for manufacturing ensifentrine and its derived formulated products. Instead, we rely on and expect to continue to rely on third-party contract manufacturing organizations ("CMOs"), for the supply of cGMP- or GMP-grade clinical trial materials and commercial quantities of ensifentrine and its derived formulated products, if approved. While we may contract with other CMOs in the future, we currently have one CMO for the manufacture of ensifentrine drug substance and one CMO for each formulation of ensifentrine. The facilities used to manufacture ensifentrine and its derived formulated products must be approved by the FDA pursuant to inspections that will be conducted after we submit an NDA to the FDA, and by comparable foreign regulatory authorities for approvals outside the United States. While we provide sponsor oversight of manufacturing activities, we do not and will not directly control the manufacturing process of, and are or will be essentially dependent on, our CMOs for compliance with cGMP and similar foreign requirements for the manufacture of ensifentrine and its derived formulated

products. If a CMO cannot successfully manufacture material that conforms to our specifications and the regulatory requirements of the FDA or a comparable foreign regulatory authority, it will not be able to secure or maintain regulatory approval for the manufacture of ensifentrine and its derived formulated products in its manufacturing facilities. In addition, we have little direct control over the ability of a CMO to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of ensifentrine and its derived formulated products or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would delay our development program and significantly impact our ability to develop, obtain regulatory approval for or market ensifentrine and its derived formulated products, if approved. In addition, any failure to achieve and maintain compliance with these laws, regulations and standards could subject us to the risk that we may have to suspend the manufacture of ensifentrine and its derived formulated products or that obtained approvals could be revoked. Furthermore, third-party providers may breach existing agreements they have with us because of factors beyond our control. They may also terminate or refuse to renew their agreement because of their own financial difficulties or business priorities, at a time that is costly or otherwise inconvenient for us. If we were unable to find an adequate replacement or another acceptable solution in time, our clinical trials could be delayed or our commercial activities could be harmed. In addition, the fact that we are dependent on our suppliers, CMOs and other third parties for the manufacture, storage and distribution of ensifentrine and its derived formulated products means that we are subject to the risk that ensifentrine and its derived formulated products may have manufacturing defects that we have limited ability to prevent, detect or control.

We rely on and will continue to rely on CMOs to purchase from third-party suppliers the materials necessary to produce ensifentrine and its derived formulated products and the inhalation and nebulization devices to deliver ensifentrine. We do not and will not have any direct control over the process or timing of the acquisition and delivery of these supplies by any CMO or its third-party suppliers, or the quality or quantity of such supplies. These supplies could be interrupted from time to time and, if interrupted, we cannot be certain that alternative supplies could be obtained within a reasonable timeframe, at an acceptable cost or quality, or at all. There are a limited number of suppliers for the raw materials that we may use to manufacture ensifentrine and for the drug delivery devices (e.g. nebulizers) that we use for clinical trials with ensifentrine, and we will need to assess alternate suppliers to prevent a possible disruption to our clinical trials, and if approved, ultimately to commercial sales. Although we generally do not begin a clinical trial unless we believe we have on hand, or will be able to obtain, a sufficient supply of ensifentrine to complete the clinical trial, any significant delay in the supply of ensifentrine drug products, or the raw material components needed to produce, or devices needed to deliver, ensifentrine, for an ongoing clinical trial due to our CMOs or their third-party suppliers could considerably delay completion of our clinical trials, product testing and potential regulatory approval of ensifentrine. If our CMOs, their third-party supplies, or we are unable to purchase these supplies after regulatory approval has been obtained for ensifentrine, the commercial launch of ensifentrine would be delayed or there would be a shortage in supply, which would impair our ability to generate revenues from the sale of ensifentrine. In addition, growth in the costs and expenses of these supplies may impair our ability to cost-effectively manufacture ensifentrine. Additionally, CMOs are experiencing labor constraints which could impact their ability to manufacture and deliver ensifentrine.

We rely and will continue to rely on CMOs and third-party suppliers to comply with and respect the proprietary rights of others in conducting their contractual obligations for us. If a CMO or third-party suppliers fails to acquire the proper licenses or otherwise infringes third-party proprietary rights in the course of providing services to us, we may have to find alternative CMOs or third-party suppliers, or defend against claims of infringement, either of which would significantly impact our ability to develop, obtain regulatory approval for, or market ensifentrine and any of its derived formulated products, if approved.

Risks Related to Intellectual Property and Information Technology

We rely on patents and other intellectual property rights to protect ensifentrine, the enforcement, defense and maintenance of which may be challenging and costly. Failure to enforce or protect these rights adequately could harm our ability to compete and impair our business.

Our commercial success depends in part on obtaining and maintaining patents and other forms of intellectual property rights for ensifentrine, formulations of ensifentrine, polymorphs, salts and analogs of ensifentrine, methods used to manufacture ensifentrine, methods for manufacturing of final drug product for different inhalation devices such as nebulizer, DPI, pMDI, and the methods for treating patients with respiratory diseases using ensifentrine alone or in combination with other available products, or on in-licensing such rights. The registrations of the assignment of each of these patents and patent applications with the relevant authorities in certain jurisdictions in which the patent and patent applications are registered have been granted, but there is no assurance that any

additional registrations will be effected in a timely manner or at all. Failure to protect or to obtain, maintain or extend adequate patent and other intellectual property rights could adversely affect our ability to develop and market ensifentrine.

The patent prosecution process is expensive and time-consuming, and we or our licensors, licensees or collaborators may not be able to prepare, file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions. It is also possible that we or our licensors, licensees or collaborators will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Moreover, depending on the terms of any future in-licenses to which we may become a party, in some circumstances we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology in-licensed from third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Further, the issuance, scope, validity, enforceability and commercial value of our and our current or future licensors', licensees' or collaborators' patent rights are highly uncertain. Our and our licensors' pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. The patent examination process may require us or our licensors, licensees or collaborators to narrow the scope of the claims of our or our licensors', licensees' or collaborators' pending and future patent applications, which may limit the scope of patent protection that may be obtained. We cannot provide assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found. If such prior art exists, it can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if such patents cover ensifentrine, third parties may initiate an opposition, interference, re-examination, post-grant review, inter partes review, nullification or derivation action in court or before patent offices, or similar proceedings challenging the validity, enforceability or scope of such patents, which may result in the patent claims being narrowed or invalidated. Our and our licensors', licensees' or collaborators' patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications, and then only to the extent the issued claims cover the technology.

Because patent applications are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we or our licensors were the first to file any patent application related to ensifentrine. Furthermore, if third parties have filed such patent applications on or before March 15, 2013, the date on which the U.S. patent filing system changed from a first-to-invent to a first-to-file standard, an interference proceeding can be initiated by such third parties to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. If third parties have filed such applications after March 15, 2013, a derivation proceeding can be initiated by such third parties to determine whether our invention was derived from theirs. Even where we have a valid and enforceable patent, we may not be able to exclude others from practicing our invention where the other party can show that they used the invention in commerce before our filing date or the other party benefits from a compulsory license.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent which might adversely affect our ability to develop, manufacture and market ensifentrine.

We cannot guarantee that any of our or our licensors' patent searches or analyses, including but not limited to the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of ensifentrine in any jurisdiction. For example, U.S. applications filed before November 29, 2000 and certain U.S. applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States 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. Therefore, patent applications covering ensifentrine could have been filed by others without our knowledge. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover ensifentrine or the use of ensifentrine. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market ensifentrine. We may incorrectly determine that ensifentrine is not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market ensifentrine. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market ensifentrine.

If we fail to identify and correctly interpret relevant patents, we may be subject to infringement claims. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we fail in any such dispute, in addition to being forced to pay damages, we may be temporarily or permanently prohibited from commercializing ensifentrine. We might, if possible, also be forced to redesign ensifentrine so that we no longer infringe the third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

We may be involved in lawsuits to protect or enforce patents covering ensifentrine, which could be expensive, time consuming and unsuccessful, and issued patents could be found invalid or unenforceable if challenged in court.

To protect our competitive position, we may from time to time need to resort to litigation in order to enforce or defend any patents or other intellectual property rights owned by or licensed to us, or to determine or challenge the scope or validity of patents or other intellectual property rights of third parties. As enforcement of intellectual property rights is difficult, unpredictable, time consuming and expensive, we may fail in enforcing our rights — in which case our competitors may be permitted to use our technology without being required to pay us any license fees. In addition, however, litigation involving our patents carries the risk that one or more of our patents will be held invalid (in whole or in part, on a claim-by-claim basis) or held unenforceable. Such an adverse court ruling could allow third parties to commercialize ensifentrine, and then compete directly with us, without payment to us. If we in-license intellectual property rights, our agreements may give our licensors the first right to control claims of third-party infringement, or to defend validity challenges. Therefore, these patents and patent applications may not be enforced or defended in a manner consistent with the best interests of our business.

If we were to initiate legal proceedings against a third party to enforce a patent covering one of our products, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States or in Europe, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the U.S. Patent and Trademark Office, or USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on ensifentrine. Patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without infringing our patents or other intellectual property rights.

Furthermore, 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. If securities analysts, industry commentators or investors perceive these results to be negative, it could have an adverse effect on the price of our ADSs.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a negative impact on the success of our business.

Our commercial success depends, in part, upon our ability, and the ability of our future collaborators, to develop, manufacture, market and sell our product candidates without alleged or actual infringement, misappropriation or other violation of the patents and proprietary rights of third parties. There have been many lawsuits and other proceedings involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and reexamination proceedings before the USPTO and corresponding foreign patent offices. The various markets in which we plan to operate are subject to frequent and extensive litigation regarding patents and other intellectual property rights. In addition, many companies in intellectual property-dependent industries, including the biopharmaceutical and pharmaceutical industries, have employed intellectual property litigation as a means to gain an advantage over their competitors. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing ensifentrine. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us. As the biotechnology and pharmaceutical industries expand

and more patents are issued, the risk increases that ensifentrine may be subject to claims of infringement of the intellectual property rights of third parties.

We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to ensifentrine and any future product candidates, including interference or derivation proceedings, post grant review and inter partes review before the USPTO or similar adversarial proceedings or litigation in other jurisdictions. Similarly, we or our licensors or collaborators may initiate such proceedings or litigation against third parties, for example, to challenge the validity or scope of intellectual property rights controlled by third parties. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, and the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our compositions, formulations, or methods of treatment, prevention or use, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires or is finally determined to be invalid or unenforceable. Such licenses may not be available on reasonable terms, or at all, or may be non-exclusive thereby giving our competitors access to the same technologies licensed to us.

If we fail in any such dispute, we may be forced to pay damages, including the possibility of treble damages in a patent case if a court finds us to have willfully infringed certain intellectual property rights. We or our licensees may be temporarily or permanently prohibited from commercializing ensifentrine or from selling, incorporating, manufacturing or using our products in the United States and/or other jurisdictions that use the subject intellectual property. We might, if possible, also be forced to redesign ensifentrine so that we no longer infringe the third-party intellectual property rights, which may result in significant cost or delay to us, or which redesign could be technically infeasible. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

In addition, if the breadth or strength of protection provided by our or our licensors' or collaborators' patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

Although we are not currently experiencing any claims challenging the inventorship of our patents or ownership of our intellectual property, we may in the future be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. While it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. For example, the assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, or we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. 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.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, such perceptions could have a substantial adverse effect on the price of our ADSs. Such litigation or proceedings could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because

of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have an adverse effect on our ability to compete in the marketplace.

If we fail to comply with our obligations under our existing and any future intellectual property licenses or loan agreements with third parties, we could lose rights that are important to our business.

We are party to a license agreement with Ligand, under which we in-license certain intellectual property and were assigned certain patents and patent applications related to our business. We may enter into additional license agreements in the future. We expect that any future license agreements would impose various diligence, milestone payment, royalty, insurance and other obligations on us. We also recently entered into a term Loan Agreement with Oxford Finance LLC and Hercules Capital, Inc. The term loan is secured by a lien on substantially all of the assets of Verona Pharma, Inc. and Verona Pharma plc, other than intellectual property, provided that a lien on intellectual property will be granted on the earlier of (i) the funding date of any term loan that would cause the aggregate principal amount of outstanding term loans drawn pursuant to the loan agreement to exceed $50.0 million and (ii) prior to Verona Pharma, Inc. or Verona Pharma plc entering into a permitted royalty financing, as defined in the Loan Agreement. Verona Pharma, Inc. or Verona Pharma plc have also granted Oxford and Hercules a negative pledge with respect to their intellectual property. For further description of the Loan Agreement, see the section titled Risk Factors – Risks Related to our Business and Industry. Any uncured, material breach under these agreements could result in our loss of rights to practice the patent rights and other intellectual property under these agreements, and could compromise our development and commercialization efforts for ensifentrine or any future product candidates. Under our agreement with Ligand, we may not abandon any of the assigned patents or allow any of the assigned patents to lapse without consent from Ligand, which is not to be unreasonably delayed or withheld. If we do not obtain such consent in a timely manner or at all and such assigned patent rights lapse or are abandoned, our agreement with Ligand may be terminated in its entirety. For example, if we decide for commercial reasons to let an assigned patent lapse in a country of little commercial importance, but Ligand does not provide consent and such patent rights lapse, we may lose all intellectual property rights covering ensifentrine in multiple markets. Moreover, our future licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights.

We may not be successful in maintaining the necessary rights to ensifentrine or obtaining other intellectual property rights important to our business through acquisitions and in-licenses.

We currently own and have in-licensed rights to intellectual property, including patents, patent applications and know-how, relating to ensifentrine, and our success will likely depend on maintaining these rights. Because our programs may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license, maintain or use these proprietary rights. In addition, ensifentrine may require specific formulations to work effectively and the rights to these formulations may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes, or other third-party intellectual property rights that we identify as necessary for ensifentrine. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies also are pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We may also be unable to license or acquire third-party intellectual property rights on a timely basis, on terms that would allow us to make an appropriate return on our investment, or at all. Even if we are able to obtain a license to intellectual property of interest, we may not be able to secure exclusive rights, in which case others could use the same rights and compete with us. If we are unable to successfully obtain a license to third-party intellectual property rights necessary for the development of ensifentrine or a development program on acceptable terms, we may have to abandon development of ensifentrine or that development program.

We will need to obtain FDA approval of any proposed product names, and any failure or delay associated with such approval may adversely affect our business.

Any proprietary name we intend to use for our product candidates will require approval from the FDA regardless of whether we have secured a formal trademark registration from the USPTO. The FDA reviews proposed product names, considering both the potential for the name to lead to medical errors due to confusion with other product names and whether the proposed name is overly fanciful, misleadingly implies unique effectiveness or composition, or contributes to overstatement of product efficacy, minimization of risk, broadening of product indications or unsubstantiated superiority. We are working with the FDA on identifying an appropriate brand name for ensifentrine

that is acceptable to the FDA. If we experience delays in identifying an acceptable name, such delays could adversely affect the launch of ensifentrine, if approved, including delaying certain elements of product manufacturing.

If the FDA objects to any of our proposed product names, we may be required to adopt an alternative name for our product candidates. If we adopt an alternative name, we could lose the benefit of any existing trademark applications for such product candidate, and may be required to expend significant additional resources in an effort to identify a suitable product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. We may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our ability to commercialize our product candidates.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our competitive position may be adversely affected.

We have registered trademarks in some territories and made applications to register the trademarks in other territories for potential trade names for our business and proposed drug products. We may not be able to obtain trademark protection for our trade names in territories that we consider of significant importance to us. If we register trademarks, our trademark applications may be rejected during trademark registration proceedings. Although we will be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, any of our trademarks or trade names, whether registered or unregistered, may be challenged, opposed, infringed, cancelled, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition by potential collaborators or customers in our markets of interest. Over the long-term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. If other entities use trademarks similar to ours in different jurisdictions, or have senior rights to ours, it could interfere with our use of our current trademarks throughout the world.

If we do not obtain protection under the Hatch-Waxman Amendments and similar non-U.S. legislation for extending the term of patents covering ensifentrine and any other product candidates, our ability to compete effectively could be impaired.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. The issued patents covering the composition of matter for ensifentrine expired in 2020, and our other issued patents will expire in 2031 to 2041, subject to any patent extensions that may be available for such patents. If patents are issued on our pending patent applications, the resulting patents are projected to expire on dates ranging from 2031 to 2044. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering ensifentrine are obtained, once the patent life has expired for a product, we may be open to competition from competitive medications, including generic medications. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Depending upon the timing, duration and conditions of the FDA marketing approval of ensifentrine, 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, referred to as the Hatch-Waxman Amendments, and similar legislation in the EU. The Hatch-Waxman Amendments permit 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. However, 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. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced, possibly materially.

We enjoy only limited geographical protection with respect to certain patents and may face difficulties in certain jurisdictions, which may diminish the value of our intellectual property rights in those jurisdictions.

We generally file our first patent application, or priority filing, at the United Kingdom Intellectual Property Office. International applications under the Patent Cooperation Treaty, or PCT, are usually filed within 12 months after the priority filing. Based on the PCT filing, national and regional patent applications may be filed in additional jurisdictions where we believe a product candidate may be marketed or manufactured. We have so far not filed for

patent protection for ensifentrine in all national and regional jurisdictions where such protection may be available. Filing, prosecuting and defending patents in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, we may decide to abandon national and regional patent applications before grant. The grant proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications might in some jurisdictions be refused by the relevant patent offices, while granted by others. For example, unlike other countries, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. Furthermore, generic drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' patents, requiring us or our licensors to engage in complex, lengthy and costly litigation or other proceedings. Generic drug manufacturers may develop, seek approval for and launch generic versions of our products. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology.

Competitors may use our or our licensors' or collaborators' technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we or our licensors or collaborators have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our product candidates, and our and our licensors' or collaborators' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or rules and regulations in the United States and the EU, and many companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition from others in those jurisdictions.

Some countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

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. The following examples are illustrative:

- Others may be able to make compounds that are the same as or similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed;
- The patents of third parties may impair our ability to develop or commercialize our product candidates;
- We or our licensors or any future strategic collaborators might not have been the first to conceive or reduce to practice the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed;
- We or our licensors or any future collaborators might not have been the first to file patent applications covering certain of our inventions;

- 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 pending patent applications will not lead to issued patents;
- Issued patents that we own or have exclusively licensed may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- Our competitors 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;
- Third parties performing manufacturing or testing for us using our product candidates or technologies could use the intellectual property of others without obtaining a proper license; and
- We may not develop additional technologies that are patentable.

Changes in patent laws or patent jurisprudence could diminish the value of patents in general, thereby impairing our ability to protect ensifentrine or any future product candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological complexity and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time consuming and inherently uncertain. In addition, the America Invents Act, or the AIA, which was passed on September 16, 2011, resulted in significant changes to the U.S. patent system.

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO, after that date but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by the third party. This requires us to be cognizant of the time from invention to filing of a patent application, but circumstances could prevent us from promptly filing patent applications on our inventions.

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and providing opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action.

Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. It is not clear what, if any, impact the AIA will have on the operation of our business. However, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' or collaboration partners' patent applications and the enforcement or defense of our or our licensors' or collaboration partners' issued patents.

Additionally, the U.S. Supreme Court has ruled on several patent cases in recent years 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 decisions by Congress, the 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 our existing patents and patents that we might obtain in the future. Similarly, the complexity and uncertainty of European patent laws has also increased in recent years. In addition, the European patent system is relatively stringent in the type of amendments that are allowed during prosecution. Complying with these laws and regulations could limit our ability to obtain new patents in the future that may be important for our business.

Finally, a Unitary Patent and Unified Patent Court (UPC) system were implemented in Europe on June 1, 2023. This new regime may present uncertainties for our ability to protect and enforce our patent rights against competitors in Europe. Under the UPC, all European patents, including those issued prior to ratification of the European Patent Package, by default automatically fall under the jurisdiction of the UPC. The UPC provides our competitors with a

new forum to centrally revoke our European patents, and allows for the possibility of a competitor to obtain pan-European injunctions. It will be several years before we will understand the scope of patent rights that will be recognized and the strength of patent remedies that will be provided by the UPC. Under the EU Patent Package, we will have the right to opt our patents out of the UPC over the first seven years of the court's existence, but doing so may preclude us from realizing the benefits of the new unified court.

Confidentiality agreements with employees and others may not adequately prevent disclosure of trade secrets and protect other proprietary information.

We consider proprietary trade secrets and confidential know-how and unpatented know-how to be important to our business. We may rely on trade secrets or confidential know-how to protect our technology, especially where patent protection is believed to be of limited value. However, trade secrets and confidential know-how are difficult to maintain as confidential.

To protect this type of information against disclosure or appropriation by competitors, our policy is to require our employees, consultants, contractors and advisors to enter into confidentiality agreements with us. We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. We cannot guarantee that our trade secrets and other proprietary and confidential information will not be disclosed or that competitors will not otherwise gain access to our trade secrets. However, current or former employees, consultants, contractors and advisors may unintentionally or willfully disclose our confidential information to competitors, and confidentiality agreements may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. Enforcing a claim that a third party obtained illegally and is using trade secrets and/or confidential know-how is expensive, time consuming and unpredictable. The enforceability of confidentiality agreements may vary from jurisdiction to jurisdiction. Furthermore, if a competitor lawfully obtained or independently developed any of our trade secrets, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret.

Failure to obtain or maintain trade secrets and confidential know-how trade protection could adversely affect our competitive position. Moreover, our competitors may independently develop substantially equivalent proprietary information and may even apply for patent protection in respect of the same. If successful in obtaining such patent protection, our competitors could limit our use of our trade secrets and/or confidential know-how.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees, including our senior management, were previously employed at universities or at other biopharmaceutical companies, including our competitors or potential competitors. Some of these employees executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we try to ensure that our employees 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 these employees have used or disclosed confidential information or intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we successfully prosecute or defend against such claims, litigation could result in substantial costs and distract management.

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.

Periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result

in abandonment or lapse of the patent or patent application, resulting in 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. If we or our licensors or collaboration partners fail to maintain the patents and patent applications covering our product candidates, our competitors might be able to enter the market, which would hurt our competitive position and could impair our ability to successfully commercialize any product candidate.

Our information technology systems, and those of our manufacturers, suppliers and other third parties that we use to conduct our pre-clinical and clinical trials or otherwise collaborate with, may fail or suffer security breaches, which could distract our operations and cause delays in our research and development work, and may adversely affect our business, operations and financial performance.

In the ordinary course of our business, we and our manufacturers, suppliers and third parties that we use to conduct our pre-clinical and clinical trials or otherwise collaborate with, collect and store sensitive data, including intellectual property, clinical trial data, proprietary business information and personally identifiable information (collectively, "Confidential Information") of our clinical trial subjects and employees, in our and third-party data centers and on our and third-party networks. The secure processing, maintenance and transmission of Confidential Information is critical to our operations. Our information technology and other internal infrastructure systems, including corporate firewalls, servers, leased lines and connection to the Internet, and that of our manufacturers, suppliers and other third parties that we use to conduct our pre-clinical and clinical trials or otherwise collaborate with, face the risk of systemic failure that could disrupt our operations. A significant disruption in the availability of these information technology and other internal infrastructure systems could cause interruptions in our collaborations and delays in our research and development work.

Further, our information technology systems and those of our third-party service providers, strategic partners and other contractors or consultants are vulnerable to damage, attack or interruption from computer viruses, malware (e.g ransomware), misconfigurations, "bugs" or other vulnerabilities, natural disasters, terrorism, war, telecommunication and electrical failures, hacking, cyberattacks, phishing attacks and other social engineering schemes, malicious code, employee theft or misuse, human error, fraud, denial or degradation of service attacks, sophisticated nation-state and nation-state-supported actors or unauthorized access or use by persons inside our organization, or persons with access to systems inside our organization. Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. As a result of a continued hybrid working environment, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage or disrupt, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. There can also be no assurance that our and our manufacturers', suppliers' and other critical third parties' cybersecurity risk management program and processes, including policies, controls or procedures, will be fully implemented, complied with or effective in protecting our systems, networks and Confidential Information.

Despite security measures that we and our critical third parties (e.g., collaborators) implement, our information technology and infrastructure may be vulnerable to attacks by hackers or internal bad actors, breaches due to human error, technical vulnerabilities, malfeasance or other disruptions. We and certain of our service providers are from time to time subject to cyberattacks and security incidents. Although to our knowledge we have not experienced any significant security breach to date, any such breach could compromise our networks and the Confidential Information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal data, regulatory penalties, disrupt our operations, damage our reputation, and cause a loss of confidence in us and our ability to conduct clinical trials, which could adversely affect our reputation and delay clinical development of our product candidates. Any adverse impact to the availability, integrity or confidentiality of our or third-party systems or Confidential Information can result in legal claims or proceedings (such as class actions), regulatory investigations and enforcement actions, fines and penalties, negative reputational impacts that cause us to lose existing or future customers, and/or significant incident response, system restoration or remediation and future

compliance costs. Any losses, costs or liabilities may not be covered by, or may exceed the coverage limits of, any or all applicable insurance policies.

Risks Related to Employee Matters and Managing Growth

Our future growth and ability to compete depends on our ability to retain our key personnel and recruit additional qualified personnel.

Our success depends upon the contributions of our key management, scientific and technical personnel, many of whom have been instrumental for us and have substantial experience with ensifentrine and related technologies. Our key management individuals include our chief executive officer, David Zaccardelli, our chief financial officer, Mark Hahn, our general counsel, Claire Poll, our chief medical officer, Kathleen Rickard, our senior vice president, regulatory affairs, Caroline Diaz, our chief commercial officer, Christopher Martin, and our chief development officer, Tara Rheault. The loss of key personnel could delay our commercialization and research and development activities. In addition, the competition for qualified personnel in the biopharmaceutical and pharmaceutical field is intense, and our future success depends upon our ability to attract, retain and motivate highly skilled scientific, technical and managerial employees. We face competition for personnel from other companies, universities, public and private research institutions and other organizations. If our recruitment and retention efforts are unsuccessful in the future, it may be difficult for us to achieve our product candidate development objectives, raise additional capital and implement our business strategy.

We expect to expand our development, regulatory, commercial, sales, marketing, reimbursement and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of commercial operations and sales, marketing, reimbursement and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Risks Related to Our ADSs

Certain of our shareholders, members of our board of directors, and senior management who own our ordinary shares (including ordinary shares represented by ADSs) may be able to exercise significant control over us.

Depending on the level of attendance at our general meetings of shareholders, these shareholders either alone or voting together as a group may be in a position to determine or significantly influence the outcome of decisions taken at any such general meeting. Any shareholder or group of shareholders controlling more than 50% of the share capital present and voting at our general meetings of shareholders may control any shareholder resolution requiring a simple majority, including the appointment of board members, certain decisions relating to our capital structure, and the approval of certain significant corporate transactions. Among other consequences, this concentration of ownership may have the effect of delaying or preventing a change in control and might therefore negatively affect the market price of our ADSs and ordinary shares.

Because we do not anticipate paying any cash dividends on our ADSs or ordinary shares in the foreseeable future, capital appreciation, if any, will be our ADS holders' and shareholders' sole source of gains and they may never receive a return on their investment.

Under current English law, a company's accumulated realized profits must exceed its accumulated realized losses (on a non-consolidated basis) before dividends can be paid. Therefore, we must have distributable profits before issuing a dividend. We have not paid dividends in the past on our ordinary shares. We intend to retain earnings, if any, for use in our business and do not anticipate paying any cash dividends in the foreseeable future. As a result, capital appreciation, if any, on our ADSs or ordinary shares will be our ADS holders' and shareholders' sole source of gain for the foreseeable future, and they will suffer a loss on their investment if they are unable to sell their ADSs or ordinary shares at or above the price at which they were purchased. Investors seeking cash dividends should not purchase our ADSs or ordinary shares.

Holders of our ADSs may not have the same voting rights as the holders of our ordinary shares and may not receive voting materials in time to be able to exercise their right to vote.

Holders of our ADSs are not able to exercise voting rights attaching to the ordinary shares evidenced by our ADSs on an individual basis. Holders of our ADSs have appointed a depositary as their representative to exercise the voting rights attaching to the ordinary shares represented by their ADSs. Holders of our ADSs may not receive voting materials in time to instruct the depositary to vote, and it is possible that they, or persons who hold their ADSs through brokers, dealers or other third parties, will not have the opportunity to exercise a right to vote. Furthermore, the depositary will not be liable for any failure to carry out any instructions to vote, for the manner in which any vote is cast or for the effect of any such vote. As a result, holders of our ADSs may not be able to exercise voting rights and may lack recourse if their ADSs are not voted as requested. In addition, holders of our ADSs will not be able to call a shareholders' meeting.

Holders of our ADSs may not receive distributions on our ordinary shares represented by our ADSs or any value for them if it is illegal or impractical to make them available to them.

The depositary for our ADSs has agreed to pay to holders of our ADSs the cash dividends or other distributions it or the custodian receives on our ordinary shares or other deposited securities after deducting its fees and expenses. Holders of our ADSs will receive these distributions in proportion to the number of our ordinary shares their ADSs represent. However, in accordance with the limitations set forth in the deposit agreement entered into with the depositary, it may be unlawful or impractical to make a distribution available to holders of our ADSs. We have no obligation to take any other action to permit the distribution of our ADSs, ordinary shares, rights or anything else to holders of our ADSs. This means that holders of our ADSs may not receive the distributions we make on our ordinary shares or any value from them if it is unlawful or impractical to make the distributions available to them. These restrictions may have a material adverse effect on the value of our ADSs.

Holders of our ADSs may be subject to limitations on transfer of their ADSs.

ADSs are transferable on the books of the depositary. However, the depositary may close its transfer books at any time or from time to time when it deems expedient in connection with the performance of its duties. In addition, the depositary may refuse to deliver, transfer or register transfers of ADSs generally when our books or the books of the depositary are closed, or at any time if we or the depositary deems it advisable to do so because of any requirement of law or of any government or governmental body, or under any provision of the deposit agreement, or for any other reason in accordance with the terms of the deposit agreement. These limitations on transfer may have a material adverse effect on the value of our ADSs.

The rights of our shareholders may differ from the rights typically offered to shareholders of a U.S. corporation.

We are incorporated under English law. The rights of holders of ordinary shares and, therefore, certain of the rights of holders of ADSs, are governed by English law, including the provisions of the Companies Act 2006, and by our Articles of Association. These rights differ in certain material respects from the rights of shareholders in typical U.S. corporations. As a result, investors in our ordinary shares or ADSs may not have the same protections or rights as they would if they had invested in a U.S. corporation. This may make our ADSs less attractive to such investors, which could harm the value of our ADSs.

Claims of U.S. civil liabilities may not be enforceable against us.

We are incorporated under English law. Substantially all of our assets are located outside the United States. The majority of our senior management and board of directors reside outside the United States. As a result, it may not be possible for investors to effect service of process within the United States upon such persons or to enforce judgments obtained in U.S. courts against them or us, including judgments predicated upon the civil liability provisions of the U.S. federal securities laws.

The United States and the United Kingdom do not currently have a treaty providing for recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters. Consequently, a final judgment for payment given by a court in the United States, whether or not predicated solely upon U.S. securities laws, would not automatically be recognized or enforceable in the United Kingdom. In addition, uncertainty exists as to whether U.K. courts would entertain original actions brought in the United Kingdom against us or our directors or senior management predicated upon the securities laws of the United States or any state in the United States. Any final and conclusive monetary judgment for a definite sum obtained against us in U.S. courts would be treated by the courts of the United Kingdom as a cause of action in itself and sued upon as a debt at common law so that no retrial of the issues would be necessary, provided that certain requirements are met. Whether these requirements are met in respect of a judgment based upon the civil liability provisions of the U.S. securities laws, including whether the

award of monetary damages under such laws would constitute a penalty, is an issue for the court making such decision. If an English court gives judgment for the sum payable under a U.S. judgment, the English judgment will be enforceable by methods generally available for this purpose. These methods generally permit the English court discretion to prescribe the manner of enforcement.

As a result, U.S. investors may not be able to enforce against us or our senior management, board of directors or certain experts named herein who are residents of the United Kingdom or countries other than the United States any judgments obtained in U.S. courts in civil and commercial matters, including judgments under the U.S. federal securities laws.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, shareholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our ADSs.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inadequate internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our ADSs.

Risks Related to Taxation

Changes in our tax rates, unavailability of certain tax credits or reliefs or exposure to additional tax liabilities or assessments could affect our profitability, and audits by tax authorities could result in additional tax payments for prior periods.

New income, sales use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, or interpreted, changed, modified or applied adversely to us, any of which could adversely affect our business operations and financial performance. We are currently unable to predict whether such changes will occur and, if so, the ultimate impact on our business. To the extent that such changes have a negative impact on us, including as a result of related uncertainty, these changes may materially and adversely impact our business, financial condition, results of operations and cash flows.

We carry out research and development activities including, but not limited to, developing ensifentrine for various indications and delivery methods, and as a result we currently benefit in the U.K. from the HM Revenue and Customs, or HMRC, small and medium sized enterprises research and development relief, or SME R&D Relief, which currently provides relief against U.K. Corporation Tax.

Broadly, SME R&D Relief comprises two elements, (a) allowing qualifying SMEs to deduct a total of 186% of their qualifying expenditure from their yearly profit for U.K. Corporation Tax purposes (the deduction is given by allowing an additional 86% deduction plus the usual 100% deduction), or the SME R&D Additional Deduction and, (b) where there are not sufficient profits for U.K. Corporation Tax purposes to fully utilize the SME R&D Additional Deduction, the excess ("surrenderable losses") can be carried forward to offset against future taxable profits, or a tax credit currently equal to 10% of such surrenderable loss can be claimed in cash, or the SME R&D Tax Credit.

Based on criteria established by HMRC a portion of expenditure incurred in relation to our research and development activities including, but not limited to, operating clinical trials, manufacturing, consultant and salary and related costs, is eligible for the SME R&D Additional Deduction. Our consequential surrenderable losses are currently eligible for the SME R&D Tax Credit, in accordance with HMRC criteria.

In the financial statements for the years ended December 31, 2023 and December 31, 2022, we recorded SME R&D Tax Credits of $2.3 million and $8.6 million, respectively. Based on the HMRC criteria, we expect to receive these SME R&D Tax Credits in the year ending December 31, 2024.

Changes to the U.K.'s SME R&D Relief regime may adversely affect our financial condition. At the 2023 Autumn Statement, the U.K. Government confirmed that it would introduce a single R&D relief regime which merges the current "RDEC" and SME R&D Relief scheme. The proposed credit rate under the draft legislation is 20% of

qualifying expenditure, with the credit itself subject to U.K. corporation tax. The credit will therefore be reduced by the applicable rate of U.K. corporation tax (the main rate of which is currently 25%), although the notional tax rate that applies to loss-making companies will be set at the lower rate of 19% for the purposes of the new R&D relief regime. Therefore, under the proposed regime and current rates of U.K. corporation tax, profitable businesses subject to the main rate of U.K. corporation tax will effectively receive a credit of 15% of qualifying expenditure whilst loss-making businesses will receive a credit of 16.2%. The proposed legislation also contains restrictions on R&D relief which can be claimed where a company contracts R&D activity to a third party or makes payments for externally provided workers so that, broadly, a taxpayer will only be able to claim relief where the work is performed in the U.K. It is proposed that the only expenditure allowable outside the U.K. would be for activities which are necessary due to geographical, environmental or social conditions not present or replicable in the U.K. The proposed legislation also contains new rules relating to subcontracting of R&D activities to a third party.

In addition, it is proposed that for accounting periods beginning on or after 1 April 2024, the R&D intensive loss-making SME scheme threshold (broadly, the proportion of qualifying R&D expenditure compared to total expenditure) will be 30%. Therefore, loss-making SMEs with qualifying R&D expenditure of 30% or more of its total expenditure may claim an enhanced deduction of 86% and a repayable credit of 14.5%.

It is proposed that the new U.K. R&D tax relief regime will apply to accounting periods starting on or after 1 April 2024. The legislation for the new regime is not yet finalized and therefore the impact on our financial position cannot be fully known, however the proposed changes to the scheme and/or any further changes could have a material adverse effect on our financial position, results of operations or cash flows.

If we were classified as a passive foreign investment company, it would result in adverse U.S. federal income tax consequences to U.S. holders.

Based on the composition of our income and assets and the value of our assets in the taxable year ended December 31, 2023, we believe that we are a Passive Foreign Investment Company ("PFIC") for U.S. federal income tax purposes for our taxable year ended December 31, 2023. However, no assurances regarding our PFIC status can be provided for any past taxable years, the taxable year ending December 31, 2024, or any future taxable years. If we are classified as a PFIC for any taxable year during which a U.S. Holder (as defined below) holds our ordinary shares or ADSs, certain adverse U.S. federal income tax consequences could apply to such U.S. Holder, including (i) the treatment of all or a portion of any gain on disposition of our ordinary shares or ADSs as ordinary income, (ii) the application of a deferred interest charge on such gain and the receipt of certain dividends, and (iii) the obligation to comply certain reporting requirements. We cannot provide any assurances that we will furnish to any U.S. Holder information that may be necessary to comply with the aforementioned reporting and tax payment obligations.

A non-U.S. corporation will generally be considered a passive foreign investment company, or PFIC, for any taxable year in which (i) 75% or more of its gross income consists of passive income or (ii) 50% or more of the average quarterly value of its assets consists of assets that produce, or are held for the production of, passive income. For purposes of these tests, passive income includes dividends, interest, gains from the sale or exchange of investment property and certain rents and royalties. In addition, for purposes of the above calculations, a non-U.S. corporation that directly or indirectly owns at least 25% by value of the shares of another corporation is treated as holding and receiving directly its proportionate share of the assets and income of such corporation. The determination of whether we are a PFIC is a fact-intensive determination made on an annual basis applying principles and methodologies that in some circumstances are unclear and subject to varying interpretation. Under the income test, our status as a PFIC depends on the composition of our income which will depend on the transactions we enter into and our corporate structure. The composition of our income and assets is also affected by the spending of the cash we raise in any offering. Each U.S. Holder should consult its own tax advisors with respect to the potential adverse U.S. tax consequences to it if we are a PFIC.

A "U.S. Holder" is a holder who, for U.S. federal income tax purposes, is a beneficial owner of our ordinary shares or ADSs and who is a citizen or individual resident of the United States; a corporation, or other entity taxable as a corporation, created or organized in or under the laws of the United States, any state therein or the District of Columbia; an estate the income of which is subject to U.S. federal income taxation regardless of its source; or a trust that (i) is subject to the supervision of a U.S. court and all substantial decisions of which are subject to the control of one or more "United States persons" (within the meaning of Section 7701(a)(30) of the Code), or (ii) has a valid election in effect to be treated as a United States person.

If we are classified as a PFIC in any year with respect to which a U.S. Holder owns our ordinary shares or ADSs, we will continue to be treated as a PFIC with respect to such U.S. Holder in all succeeding years during which the U.S. Holder owns our ordinary shares or ADSs, regardless of whether we continue to meet the PFIC test described above, unless the U.S. Holder makes a specified election once we cease to be a PFIC.

If a U.S. Holder is treated as owning at least 10% of our ordinary shares or ADSs, such holder may be subject to adverse U.S. federal income tax consequences.

If a U.S. Holder (as defined above) is treated as owning, directly, indirectly or constructively, at least 10% of the value or voting power of our ordinary shares or ADSs, such U.S. Holder may be treated as a "United States shareholder" with respect to each "controlled foreign corporation" or "CFC" in our group, if any. Because our group includes one or more U.S. subsidiaries, certain of our non-U.S. subsidiaries could be treated as CFCs, regardless of whether we are treated as a CFC. A United States shareholder of a CFC may be required to annually report and include in its U.S. taxable income its pro rata share of "Subpart F income," "global intangible low-taxed income" and investments in U.S. property by such CFCs, regardless of whether such CFC make any distributions. An individual that is a United States shareholder with respect to a CFC generally would not be allowed certain tax deductions or foreign tax credits that would be allowed to a United States shareholder that is a U.S. corporation. Failure to comply with these reporting obligations may subject a United States shareholder to significant monetary penalties and may prevent the statute of limitations with respect to such shareholder's U.S. federal income tax return for the year for which reporting was due from starting. We cannot provide any assurances that we will assist our investors in determining whether we or any of our non-U.S. subsidiaries are treated as a CFC or whether such investor is treated as a United States shareholder with respect to any of such CFCs. Further, we cannot provide any assurances that we will furnish to any United States shareholder information that may be necessary to comply with the reporting and tax paying obligations described in this risk factor. U.S. Holders should consult their tax advisors regarding the potential application of these rules to their investment in our ordinary shares or ADSs.

General Risks

The price of our ADSs may be volatile and may fluctuate due to factors beyond our control.

The trading market for publicly traded emerging biopharmaceutical and drug discovery and development companies has been highly volatile and is likely to remain highly volatile in the future. The market price of our ADSs may fluctuate significantly due to a variety of factors, including:

- positive or negative results from, or delays in, clinical trials of ensifentrine;
- developments in our competitors' businesses;
- delays in entering into collaborations and strategic relationships with respect to development or commercialization of ensifentrine or entry into collaborations and strategic relationships on terms that are not deemed to be favorable to us;
- technological innovations or commercial product introductions by us or competitors;
- changes in government regulations;
- developments concerning proprietary rights, including patents and litigation matters;
- public concern relating to the commercial value or safety of ensifentrine;
- financing or other corporate transactions;
- publication of research reports or comments by securities or industry analysts or commentators;
- general market conditions in the pharmaceutical industry or in the economy as a whole;
- the loss of any of our key scientific or senior management personnel;
- sales of our ADSs by us, our senior management or board members, and significant holders of our ADSs; or
- other events and factors, many of which are beyond our control.

These and other market and industry factors may cause the market price and demand for our ADSs to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from readily selling their ADSs and may otherwise negatively affect the liquidity of our ADSs. In addition, the stock market in general, and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. 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 the holders of our ADSs were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our senior management would be diverted from the operation of our business. Any adverse determination in litigation could also subject us to significant liabilities.

Future sales, or the possibility of future sales, of a substantial number of our ADSs or ordinary shares could adversely affect the price of our ADSs.

Future sales of a substantial number of our ADSs or ordinary shares, or the perception that such sales will occur, could cause a decline in the market price of our ADSs. Sales in the United States of our ADSs and ordinary shares held by our directors, officers and affiliated shareholders are subject to restrictions. If these shareholders sell substantial amounts of ordinary shares or ADSs in the public market, or the market perceives that such sales may occur, the market price of our ADSs and our ability to raise capital through an issue of equity securities in the future could be adversely affected.

Unstable market and economic conditions may have serious adverse consequences on our business and financial condition and the price of our ADSs. The global economy, including credit and financial markets, has recently experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, rising interest and inflation rates, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. If the equity and credit markets continue to deteriorate or the United Kingdom or the United States enters a recession, it may make any necessary debt or equity financing more difficult to obtain in a timely manner or on favorable terms, more costly or more dilutive. In addition, there is a risk that one or more of our CROs, suppliers or other third-party providers may not survive an economic downturn or recession. As a result, our business, results of operations and price of our ADSs may be adversely affected.

If securities or industry analysts or commentators publish inaccurate or unfavorable research, about our business, the price of our ADSs and ordinary shares and our trading volume could decline.

The trading market for our ADSs and ordinary shares depends in part on the research and reports that securities or industry analysts or commentators publish about us or our business. If one or more of the analysts who cover us downgrade our ADSs or if they or other industry commentators publish inaccurate or unfavorable research or comments about our business, the price of our ADSs and ordinary shares would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, demand for our ADSs could decrease, which might cause the price of our ADSs and ordinary shares and trading volume to decline.

We have incurred and expect to continue to incur increased costs as a result of operating as a public company in the United States, and our senior management are required to devote substantial time to new compliance initiatives and corporate governance practices.

As a U.S. public company, we have incurred and expect to continue to incur significant legal, accounting and other expenses that we did not incur prior to becoming a U.S. public company, including in connection with our transition to large accelerated filer as of December 31, 2023. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of Nasdaq and other applicable securities rules and regulations impose various requirements on non-U.S. reporting public companies, including the establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our senior management and other personnel have devoted and will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will continue to increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our senior management on our internal control over financial reporting and an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To prepare for and maintain compliance with Section 404(b), we have implemented a process of documenting and evaluating our internal control over financial reporting. In this regard, we have dedicated, and will need to continue to dedicate, internal resources, engage outside consultants and pursue a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting, which is both costly and challenging. Despite our efforts, there is a risk that we will not be able to conclude that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Business interruptions could adversely affect our operations.

Our operations are potentially vulnerable to interruption by fire, severe weather conditions, power loss, telecommunications failure, terrorist activity, public health crises and pandemic diseases, such as COVID-19, and other natural and man-made disasters or events beyond our control. Our facilities are located in regions that experience severe weather from time to time. We have not undertaken a systematic analysis of the potential consequences to our business and financial results from a major tornado, flood, fire, earthquake, power loss, terrorist activity, public health crisis, pandemic diseases or other disasters and do not have a recovery plan for such disasters. In addition, we do not carry sufficient insurance to compensate us for actual losses from interruption of our business that may occur, and any losses or damages incurred by us could harm our business. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

Item 1B. Unresolved Staff Comments

None.

Item 1C. Cybersecurity

Cybersecurity Risk Management and Strategy

We have developed and implemented a cybersecurity risk management program intended to protect the confidentiality, integrity, and availability of our critical systems and information.

We design and assess our program based on the National Institute of Standards and Technology Cybersecurity Framework ("NIST CSF").This does not imply that we meet any particular technical standards, specifications, or requirements, only that we use the NIST CSF as a guide to help us identify, assess, and manage cybersecurity risks relevant to our business.

Our cybersecurity risk management program is integrated into our overall enterprise risk management program, and shares common methodologies, reporting channels and governance processes that apply across the enterprise risk management program to other legal, compliance, strategic, operational, and financial risk areas.

Our cybersecurity risk management program includes:

- risk assessments designed to help identify material cybersecurity risks to our critical systems, information, products, services, and our broader enterprise IT environment;
- an information technology team principally responsible for managing (1) our cybersecurity risk assessment processes, (2) our security controls, and (3) our response to cybersecurity incidents;
- the use of external advisors and service providers, where appropriate, to assess, test or otherwise assist with aspects of our security controls;
- cybersecurity awareness training of our employees, contractors, incident response personnel, and senior management;
- a cybersecurity incident response plan that includes procedures for responding to cybersecurity incidents and alignment with the broader corporate business continuity plan; and
- a third-party risk management process for service providers, suppliers, and vendors that have access to our critical systems and information.

We have not identified risks from known cybersecurity threats, including as a result of any prior cybersecurity incidents, that have materially affected or are reasonably likely to materially affect us, including our operations, business strategy, results of operations, or financial condition. For more information, see the section titled "Risk Factor— Our business and operations may suffer in the event of information technology system failures, cyberattacks or deficiencies in our cybersecurity."

Cybersecurity Governance

Our Board considers cybersecurity risk as part of its risk oversight function and has delegated to the Audit Committee (Committee) oversight of cybersecurity and other information technology risks. The Committee oversees management's implementation of our cybersecurity risk management program.

The Committee receives quarterly reports from management on our cybersecurity risks. In addition, management updates the Committee, as necessary, regarding any material cybersecurity incidents, as well as any incidents with lesser impact potential.

The Committee reports to the full Board regarding its activities, including those related to cybersecurity. The full Board also receives briefings from management on our cyber risk management program. Board members receive presentations on cybersecurity topics from our Vice President, Digital and Information Technology, internal security staff or external experts as part of the Board's continuing education on topics that impact public companies.

Our management team, including our Vice President, Digital and Information Technology and Chief Financial Officer, is responsible for assessing and managing our material risks from cybersecurity threats. The team has primary responsibility for our overall cybersecurity risk management program and supervises both our internal cybersecurity personnel and our retained external cybersecurity consultants. Our management team's experience includes decades of managing public pharmaceutical companies, including their related information technology and cybersecurity risk management programs.

Our management team supervises efforts to prevent, detect, mitigate, and remediate cybersecurity risks and incidents through various means, which may include briefings from internal security personnel; threat intelligence and other information obtained from governmental, public or private sources, including external consultants engaged by us; and alerts and reports produced by security tools deployed in the IT environment.

Item 2. Properties

Our corporate headquarters is in leased office space at 3 More London Riverside, London, U.K. The leases for these offices expire in the first quarter of 2025. We also have office space at 33 Park of Commerce, Suite 300, Savannah, Georgia, 31405, which expires in the fourth quarter of 2025, and 8529 Six Forks Road, Suite 400, Raleigh, North Carolina, 27615, which expires in the fourth quarter of 2027. We believe that these facilities are adequate to meet our current and near term needs.

Item 3. Legal Proceedings

From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. We are not currently subject to any material legal proceedings.

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 and Holders

Prior to October 30, 2020, our ordinary shares were traded on the AIM Market of the London Stock Exchange under the symbol "VRP". We canceled the admission of the ordinary shares to trading on AIM on October 30, 2020 and our ordinary shares are now not publicly traded. Our American Depositary Shares ("ADSs") have been publicly traded on the Nasdaq Global Market under the symbol "VRNA" since April 27, 2017.

Each ADS represents eight ordinary shares of Verona Pharma plc.

As of February 27, 2024, we had 423 registered holders of ordinary voting shares. 99.9% of our voting ordinary shares are held in ADS form. The 0.1% balance of our ordinary voting shares are held as unlisted voting ordinary shares. We also have 48,088,896 unlisted non-voting ordinary shares.

Dividends

We have never declared or paid any dividends on our common stock. We anticipate that we will retain all of our future earnings, if any, for use in the operation and expansion of our business and do not anticipate paying cash dividends in the foreseeable future.

Recent Sales of Unregistered Securities

None.

Item 6. [Reserved]

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with the Consolidated Financial Statements and the related notes to those statements included later in this Annual Report on Form 10-K. In addition to historical financial information, the following discussion contains forward-looking statements that reflect our plans, estimates, beliefs and expectations that involve risks and uncertainties. Our actual results and the timing of events could differ materially from those discussed in these forward-looking statements. Important factors that could cause or contribute to these differences include those discussed below and elsewhere in this Annual Report on Form 10-K, particularly in Part I, Item 1A. "Risk Factors" and the section entitled "Cautionary Note Regarding Forward-Looking Statements."

In this Item 7, we discuss the results of operations for the years ended December 31, 2023 and 2022 and comparisons of the year ended December 31, 2023 to the year ended December 31, 2022. Discussion and analysis of our 2021 fiscal year specifically, as well as the year-over-year comparison of our 2022 financial performance to 2021, are located in Part II, Item 7 - Management's Discussion and Analysis of Financial Condition and Results of Operations in our Annual Report on Form 10-K for the fiscal year ended December 31, 2022, filed with the SEC on March 7, 2023.

Overview

We are a clinical-stage biopharmaceutical company focused on developing and commercializing innovative therapeutics for the treatment of chronic respiratory diseases with significant unmet medical needs. Our product candidate, ensifentrine, is an investigational, first-in-class, inhaled, selective, small molecule and dual inhibitor of the enzymes phosphodiesterase 3 and 4 ("PDE3" and "PDE4"), combining bronchodilator and non-steroidal anti-inflammatory activities in one compound.

Initially, we are developing inhaled ensifentrine for the maintenance treatment of chronic obstructive pulmonary disease ("COPD"), a common, chronic, progressive, and life-threatening respiratory disease without a cure. If successfully developed and approved, ensifentrine is expected to be the first inhaled therapeutic with a novel mode of action for the maintenance treatment of COPD in over 20 years.

In August 2023, the U.S. Food and Drug Administration ("FDA") accepted for review our New Drug Application ("NDA") seeking approval of ensifentrine for the maintenance treatment of COPD and assigned a Prescription Drug User Fee Act ("PDUFA") target action date of June 26, 2024. The FDA stated it is not currently planning to hold an advisory committee meeting to discuss the application.

Based on the results from our successful Phase 3 ENHANCE ("Ensifentrine as a Novel inHAled Nebulized COPD thErapy") program, we believe ensifentrine, if approved, has the potential to change the treatment paradigm for COPD. Ensifentrine met the primary endpoint in both the ENHANCE-1 and ENHANCE-2 trials demonstrating statistically significant and clinically meaningful improvements in measures of lung function. In addition, other endpoint data demonstrated that ensifentrine substantially reduced the rate and risk of COPD exacerbations in ENHANCE-1 and ENHANCE-2. Ensifentrine was well tolerated in both trials.

We recently presented additional analyses of data from the ENHANCE trials at international scientific conferences:

- In October 2023, we gave four presentations on pooled and subgroup analyses from ENHANCE-1 and ENHANCE-2 covering data related to exacerbations, lung function, symptoms and quality of life endpoints and use of daily medication, at CHEST Annual Meeting 2023. The data are published in the CHEST Annual Meeting online supplement.

- Also at CHEST Annual Meeting, we launched a disease awareness campaign highlighting that despite suffering symptoms that have a substantial impact on everyday life, many COPD patients struggle to fully disclose to their healthcare provider the true extent or severity of their symptoms. This campaign was designed to encourage healthcare providers to find out how patients are coping with COPD.

- In September 2023, we gave a presentation on an analysis of the ENHANCE-1 24-week exacerbation data at ERS International Congress 2023. The abstract is published in the peer reviewed publication, *European Respiratory Journal.*

If approved, we intend to commercialize inhaled ensifentrine for the maintenance treatment of COPD in the United States ("U.S."). Ensifentrine is not considered a drug device combination because patients use a readily available standard jet nebulizer to take ensifentrine. Outside the U.S., we intend to license ensifentrine to companies with expertise and experience in developing and commercializing products in those regions. To that end, we have entered into a strategic collaboration with Nuance Pharma Limited, a Shanghai-based specialty pharmaceutical company ("Nuance Pharma"), to develop and commercialize ensifentrine in Greater China.

In Phase 2 clinical trials, ensifentrine has demonstrated positive results in patients with COPD, asthma and cystic fibrosis ("CF"). Two additional formulations of ensifentrine have been evaluated in Phase 2 trials for the treatment of COPD: dry powder inhaler ("DPI") and pressurized metered-dose inhaler ("pMDI").

We have incurred recurring losses and negative cash flows from operations since inception, and have an accumulated deficit of $388.4 million as of December 31, 2023. We expect to incur additional losses and negative cash flows from operations until our product candidates potentially gain regulatory approval and reach commercial profitability, if at all.

We anticipate significant expenses in connection with our ongoing activities, if and as we:

- establish a sales, marketing and distribution infrastructure, ramp up production to commercial scale with our manufacturing and other Chemistry, Manufacturing and Controls activities to potentially commercialize any products for which we may obtain regulatory approval;
- continue the clinical development of our DPI and pMDI formulations of ensifentrine and research and development of other formulations of ensifentrine, as well as a fixed-dose combination of ensifentrine and a long-acting muscarinic antagonist;
- initiate and conduct further clinical trials for ensifentrine for the treatment of non-CF bronchiectasis, acute COPD, CF or any other indication;
- initiate and progress pre-clinical studies relating to other potential indications of ensifentrine;
- seek to discover and develop additional product candidates;
- seek regulatory approvals for any of our product candidates that successfully complete clinical trials;
- maintain, expand and protect our intellectual property portfolio;
- seek to discover and develop or in-license additional respiratory product candidates;

- add clinical, scientific, operational, financial and management information systems and personnel, including personnel to support our product development and potential future commercialization efforts and to support our continuing operations as a U.S. public company; and
- experience any delays or encounter any issues from any of the above, including but not limited to failed studies, complex results, safety issues or other regulatory challenges.

On December 27, 2023, we entered into a term loan facility (the "2023 Term Loan") of up to $400.0 million with Oxford Finance LLC ("Oxford"), as collateral agent, and certain funds managed by Oxford and Hercules Capital, Inc. At closing $50.0 million was funded with up to four additional advances of an aggregate $350.0 million available subject to meeting certain regulatory and commercial milestones. The 2023 Term Loan replaced the our existing $150.0 million facility with Oxford Finance Luxembourg S.A R.L. Refer to Note 5 - Debt to our Consolidated Financial Statements and related notes included elsewhere in this Annual Report for additional details.

We believe that our cash and cash equivalents as of December 31, 2023 and funding expected to become available under the 2023 Term Loan will enable us to fund our planned operating expenses and capital expenditure requirements through at least the end of 2026 including the planned commercial launch of ensifentrine in the U.S., if approved. The remaining advances under the 2023 Term Loan are contingent upon the achievement of certain clinical and regulatory milestones and other specified conditions. See "Liquidity and capital resources" for additional information.

Significant agreements

Ligand agreement

In 2006 we acquired Rhinopharma and assumed contingent liabilities owed to Ligand UK Development Limited ("Ligand") (formerly Vernalis Development Limited). We refer to the assignment and license agreement as the Ligand Agreement.

Ligand assigned to us all of its rights to certain patents and patent applications relating to ensifentrine and related compounds (the "Ligand Patents") and an exclusive, worldwide, royalty-bearing license under certain Ligand know-how to develop, manufacture and commercialize products (the "Ligand Licensed Products") developed using Ligand Patents, Ligand know-how and the physical stock of certain compounds.

We are obligated to pay a milestone payment of £5.0 million on obtaining the first approval of any regulatory authority for the commercialization of a Ligand Licensed Product, low single digit royalties based on the future sales performance of all Ligand Licensed Products and a portion equal to a mid-twenty percent of any consideration received from any sub-licensees for the Ligand Patents and for Ligand know-how. Royalties payable are based on the future sales performance so the amount payable is unlimited.

At the time each contingency is resolved, we will record the contingent consideration payment (or payable) in connection with the Ligand Agreement as an expense.

In March 2022, we entered into an Amendment Agreement (the "Amendment") with Ligand whereby the Ligand Agreement was amended to clarify certain ambiguous terms in the Ligand Agreement. Pursuant to the Amendment:

- we agreed to pay to Ligand (i) $2.0 million within five business days of the date of the Amendment and (ii) $15.0 million upon the first commercial sale of ensifentrine by us or a sub-licensee, which amount is payable in cash or, at the our discretion, by the issuance of Company equity of equivalent value, as determined based on the volume-weighted average price of the our American Depositary Shares on the Nasdaq Global Market over the ten (10) trading days including and prior to such milestone event;
- the Ligand Agreement shall expire on March 24, 2042 unless terminated earlier by either party in accordance with its terms;
- upon termination of the Ligand Agreement, any Sub-licensee (as defined in the Amendment) shall have the right to enter into a direct license agreement with Ligand for the portion of the Program IP (as defined in the Amendment) that was sub-licensed by such Sub-licensee;
- the Milestone Payment may be paid in cash or, at our discretion, by issuing to Ligand shares in the Company of equivalent value; and

- each party's right to terminate the Ligand Agreement is conditioned upon such party obtaining a final judgment of the English High Court declaring that the other party is in material breach of its obligations under the Ligand Agreement.

We accounted for the $2.0 million payment at execution of the Amendment as selling, general and administrative expense in the consolidated statements of operations and comprehensive loss as the payment is related to a contract modification.

Nuance agreement

We entered into a collaboration and license agreement (the "Nuance Agreement") with Nuance Pharma effective June 9, 2021 (the "Nuance Effective Date") under which we granted Nuance Pharma the exclusive rights to develop and commercialize ensifentrine in Greater China (China, Taiwan, Hong Kong and Macau). In return, we received an unconditional right to consideration aggregating $40.0 million consisting of $25.0 million in cash and an equity interest valued at $15.0 million as of the Effective Date in Nuance Biotech, the parent company of Nuance Pharma. We are eligible to receive future milestone payments of up to $179.0 million, triggered upon achievement of certain clinical, regulatory, and commercial milestones as well as tiered double-digit royalties on net sales in Greater China. We will recognize these milestones when it is probable that a significant revenue reversal would not occur.

As of December 31, 2023, the $15.0 million equity interest was recorded as Equity interest on the Consolidated Balance Sheet, included elsewhere in this Annual Report. The Equity interest is recorded at cost as we have elected to use the measurement alternative for equity investments without readily determinable fair values. We will evaluate this investment for indicators of impairment quarterly. We evaluate this investment for indicators of impairment quarterly. We did not identify events or changes in circumstances that may have a significant effect on the fair value of the investment during the year ended December 31, 2023.

Nuance Pharma will be responsible for all costs related to clinical development and commercialization of ensifentrine in Greater China. In August 2022, Nuance Pharma, received clearance from China's Center for Drug Evaluation to begin Phase 1 and Phase 3 studies with ensifentrine for COPD in mainland China. Nuance Pharma initiated a Phase 1 trial with ensifentrine in healthy volunteers in March 2023. In April 2023, Nuance Pharma dosed the first subject in its pivotal Phase 3 clinical trial evaluating ensifentrine for the maintenance treatment of COPD in mainland China. A joint steering committee has been established between us and Nuance Pharma to oversee and coordinate the overall conduct of such clinical development and commercialization. We intend to use the joint steering committee to help ensure the clinical development of ensifentrine in Greater China aligns with our overall global development and commercialization strategy.

Under the terms of the Nuance Agreement, at any time until three months prior to the expected submission of the first New Drug Application in Greater China, if (i) a third party is interested in partnering with us, either globally or in territory covering at least the United States or Europe, for the development and/or commercialization of ensifentrine or (ii) we undergo a change of control, we will have an exclusive option right to buy back the license granted to Nuance Pharma and all related assets. The price is agreed to be equal to the aggregate of (i) all prior amounts paid by Nuance Pharma to us in cash under the agreement and (ii) all development and regulatory costs incurred and paid by Nuance Pharma in connection with the development and commercialization of the ensifentrine under the Nuance Agreement multiplied by a single-digit factor range dependent upon achievement of certain milestones, subject to a specified maximum amount.

The Nuance Agreement will continue on a jurisdiction-by-jurisdiction and product-by-product basis until the expiration of royalty payment obligations with respect to such product in such jurisdiction unless earlier terminated by the parties. Either party may terminate the Nuance Agreement for an uncured material breach or bankruptcy of the other party. Nuance Pharma may also terminate the Nuance Agreement at will upon 90 days' prior written notice.

We reviewed the buy-back option and determined that because it is conditional on a third party we do not have the practical ability to exercise it and, accordingly, the contract is accounted for under ASC 606.

On April 13, 2022, we entered into an Agreement for the Manufacture and Supply of ensifentrine ("Nuance Supply Agreement") with Nuance Pharma. We determined that the manufacturing and supply of ensifentrine to Nuance represents a distinct and separate performance obligation, for which consideration to be received is variable based on the quantities to be ordered by Nuance. Revenue earned with the manufacture and supply of the licensed product is, and will be, recognized as the supply is delivered to Nuance. We have determined we are acting as principal in relation to the manufacture and supply under the Agreement. In its capacity as principal, we will recognize the associated revenue on a gross basis. In the year ended December 31, 2022, we recognized $0.5 million in relation to the clinical supply of ensifentrine to Nuance Pharma.

For additional information regarding the Nuance Agreement, see Note 6 - Significant agreements to our Consolidated Financial Statements and related notes included elsewhere in this Annual Report.

Critical accounting estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our Consolidated Financial Statements, which have been prepared in accordance with generally accepted accounting principles in the United States of America ("U.S. GAAP"). The preparation of these financial statements requires us to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent liabilities as of the dates of the balance sheets and the reported amounts of expenses during the reporting periods. In accordance with U.S. GAAP, we evaluate our estimates and judgments on an ongoing basis.

While our significant accounting policies are described in more detail in the notes to our Consolidated Financial Statements included elsewhere in this Annual Report, we believe that the following accounting policy is most critical to the judgments and estimates used in the preparation of our Consolidated Financial Statements.

Research and development costs

Research and development ("R&D") costs are charged to the consolidated statements of operations and comprehensive loss, as incurred. We are required to estimate our expenses resulting from our obligation under contracts with vendors and consultants and clinical site agreements in connection with our R&D efforts. The financial terms of these contracts are subject to negotiations which vary contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts. Our objective is to reflect the appropriate clinical trial expenses in our financial statements by matching those expenses with the period in which services and efforts are expended. We account for these expenses according to the progress of the trials and other development activities measured by patient progression and the timing of various aspects of the trial. We also determine prepaid and accrual estimates through discussions with applicable personnel and outside service providers as to the progress of clinical trials, or other services completed. During the course of a clinical trial, we may adjust our rate of clinical trial expense recognition if actual results differ from its estimates. We make estimates of our prepaid and accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known at that time. 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 may result in us reporting amounts that are too high or too low for any particular period. Our clinical trial prepaid and accrual expense is dependent upon the timely and accurate reporting of study recruitment from contract research organizations and activities carried out by other third-party vendors as well as the timely processing of any change orders from the contract research organizations. As of December 31, 2023 and 2022, accrued expenses related to clinical trial and other development costs was $0.7 million and $12.3 million.

Components of results of operations

We anticipate that our expenses will increase substantially if and as we:

- initiate and conduct clinical trials of ensifentrine for the treatment of non-cystic fibrosis bronchiectasis ("NCFBE"), cystic fibrosis ("CF"), asthma or other indications;
- initiate and conduct other future clinical trials of ensifentrine in other formulations, including in combination with other active ingredients including fixed-dose combinations, for the treatment of COPD or other indications;
- initiate and conduct clinical pharmacology studies with any formulation;
- seek to discover and develop or in-license additional respiratory product candidates;
- conduct pre-clinical studies to support ensifentrine and potentially other future product candidates;
- develop the manufacturing processes and produce clinical and commercial supplies of the ensifentrine active pharmaceutical ingredient and formulated drug products derived from it;
- seek regulatory approvals of ensifentrine;
- grow the commercial infrastructure to support the potential commercialization of ensifentrine, including sales, marketing, operations, reimbursement and distribution infrastructure and scale-up manufacturing capabilities to commercialize ensifentrine, if approved;
- maintain, expand and protect our intellectual property portfolio;
- secure, maintain or obtain freedom to operate for our in-licensed technologies and products;
- add clinical, scientific, operational, financial and management information systems and personnel, including personnel to support our product development and potential future commercialization efforts; and
- expand our operations in the United States, the United Kingdom ("U.K.") and possibly elsewhere.

To date, we have not generated revenue from the sale of any products. All revenue to date has been derived from the receipt of up-front proceeds and supply of ensifentrine under the Nuance Agreement.

In the future, we anticipate generating revenue from a combination of sales of our products, if approved, whether through our own or a third-party sales force, and license fees, milestone payments and royalties in connection with strategic collaborations regarding ensifentrine or other potential products. We expect that any revenue we generate will fluctuate from quarter to quarter. If we or our strategic partners fail to complete the development of ensifentrine in a timely manner or obtain regulatory approval for them, or if we fail to develop our own sales force or find one or more strategic partners for the commercialization of approved products, our ability to generate future revenue, and our financial condition and results of operations would be materially adversely affected.

Operating expenses

Research and development costs

Research and development costs consist of salary and personnel related costs and third party costs for our research and development activities for ensifentrine. Personnel related costs include a share-based compensation charge relating to our stock option plan. The largest component of third party costs is for clinical trials, as well as manufacturing for clinical supplies and associated development, and pre-clinical studies. Research and development costs are expensed as incurred.

As the Phase 3 ENHANCE program has completed study conduct and analysis, we expect our research and development costs to decrease as compared to the prior year same period over the first half of 2024 until we add new compounds or develop ensifentrine further in other delivery methods or indications. Due to the nature of research and development, the expected costs are inherently uncertain and may vary significantly from our current expectations.

Selling, general and administrative costs

Selling, general and administrative costs consist of salary and personnel related costs, including share-based compensation, expenses relating to operating as a public company, including professional fees, insurance and commercial related costs, as well as other operating expenses.

We expect commercial costs to significantly increase as we continue to develop our commercial operations, prepare for a potential launch and, in the event of successful regulatory approval, incur sales force, marketing and other launch related costs. As we develop our knowledge of the market and refine our commercialization plans, expected costs may vary significantly from our current expectations.

Other income/(expense)

Other income/(expense) are driven by interest income and expense, foreign exchange movements on cash and cash equivalents and taxes receivable, and the U.K. research and development tax credits (the "R&D tax credit").

We participate in the U.K. Small and Medium Enterprises research and development tax relief program. The tax credits are calculated as a percentage of qualifying research and development expenditure and are payable in cash by the U.K. government to us. Credits recorded related to the 2022 and 2023 financial years are expected to be received in 2024.

Taxation

We are subject to corporate taxation in the United States and the United Kingdom. We have generated losses since inception and have therefore not paid United Kingdom corporation tax. The income taxes presented in our consolidated statements of operations and comprehensive loss represents the tax impact from our operating activities in the United States, which generates taxable income based on intercompany service arrangements.

United Kingdom losses may be carried forward indefinitely to be offset against future taxable profits, subject to various utilization criteria and restrictions. The amount that can be offset each year is limited to £5.0 million plus an incremental 50% of U.K. taxable profits.

Results of operations for the years ended December 31, 2023 and 2022

The following table shows our statements of operations for the years ended December 31, 2023 and 2022 (in thousands):

	Year ended December 31,		
	2023	2022	Variance
Revenue	$ —	$ 458	$ (458)
Cost of sales	—	(346)	346
Gross profit	—	112	(112)
Operating expenses:			
Research and development (Note 11)	17,216	49,283	(32,067)
Selling, general and administrative	50,353	26,579	23,774
Total operating expenses	67,569	75,862	(8,293)
Operating loss	(67,569)	(75,750)	8,181
Other income/(expense):			
Research and development tax credit	1,104	9,634	(8,530)
Loss on extinguishment of debt	—	(815)	815
Interest income	12,761	2,821	9,940
Interest expense	(2,057)	(521)	(1,536)
Foreign exchange gain/(loss)	1,866	(3,817)	5,683
Total other income, net	13,674	7,302	6,372
Loss before income taxes	(53,895)	(68,448)	14,553
Income tax expense	(474)	(253)	(221)
Net loss	$ (54,369)	$ (68,701)	$ 14,332

Revenue

Revenue of $0.5 million for the year ended December 31, 2022 was related to sales of clinical supply materials to Nuance Pharma.

Cost of sales

Cost of sales of $0.3 million for the year ended December 31, 2022 related to the manufacture of the clinical supply materials sold to Nuance Pharma.

Research and development costs

Research and development costs were $17.2 million for the year ended December 31, 2023, compared to $49.3 million for the year ended December 31, 2022, a decrease of $32.1 million. This decrease was primarily due to a $32.7 million decrease in clinical trial and other development costs as we incurred less costs under the Phase 3 ENHANCE program which completed study conduct and analysis in 2023 whereas in 2022 significant costs were incurred associated with the then ongoing study conduct. The 2023 clinical trial and other development costs also include the impact of $2.2 million of credits received related to the final financial reconciliation of a Phase 3 ENHANCE program supplier. The decrease in clinical trial and other development costs also includes a reversal of $1.5 million of costs which were expensed in the year ended December 31, 2022 related to the resolution of the supplier matter, as discussed in Note 11 - Commitments and contingencies to our Consolidated Financial Statements and related notes included elsewhere in this Annual Report. .

Selling, general and administrative costs

Selling, general and administrative costs were $50.4 million for the year ended December 31, 2023 compared to $26.6 million for the year ended December 31, 2022, an increase of $23.8 million. This increase was driven primarily by a $15.6 million increase in people related costs, inclusive of share-based compensation, an increase of $9.7 million related to the build-out of the commercial and information technology infrastructures in preparation for

commercial launch, marketing and market development expenses, travel and other corporate costs. These increases were partially offset by a non-recurring $2.0 million charge related to the modification of the assignment and license agreement with Ligand UK Development Limited, which was incurred in the three months ended March 31, 2022.

Other income / (expense)

Other income/(expense) for the year ended December 31, 2023 was $13.7 million compared to $7.3 million for the year ended December 31, 2022, an increase of $6.4 million. The increase was primarily attributable to an increase of $9.9 million in interest income from a higher average cash balance and higher interest rates as well as an increase of $5.7 million related to the strengthening of the pound sterling while the pound sterling weakened in 2022. This was partially offset by a $8.5 million decrease in the R&D tax credit due to the decreased activity of the Phase 3 ENHANCE program in 2023 as compared to 2022 as well as the impact of the supplier final reconciliation credits.

Cash flows

The following table summarizes our cash flows for the years ended December 31, 2023 and 2022 (in thousands):

	Year ended December 31,		
	2023	2022	Variance
Cash and cash equivalents at beginning of the year	$ 227,827	$ 148,380	$ 79,447
Net cash used in operating activities	(50,222)	(59,862)	9,640
Net cash used in investing activities	—	(29)	29
Net cash provided by financing activities	92,869	140,818	(47,949)
Effect of exchange rate changes on cash and cash equivalents	1,298	(1,480)	2,778
Cash and cash equivalents at end of the year	$ 271,772	$ 227,827	$ 43,945

Operating activities

Net cash used in operating activities was $50.2 million in the year ended December 31, 2023 compared to $59.9 million during the year ended December 31, 2022, a decrease of $9.6 million. The decrease in cash used in operating activities was primarily due to the decrease in clinical trial and other development costs, partially offset by payments made throughout the twelve months ended December 31, 2023 related to Accounts payable and Accrued expenses balances included on the Consolidated Balance Sheet as of December 31, 2022. This was partially offset by the increase in people related costs and costs associated with the build out of information technology and commercial infrastructure in preparation for the planned commercial launch. Additionally, in the year ended December 31, 2022 we received payment of the 2021 R&D tax credit while at December 31, 2023, our 2022 R&D tax credit of $8.7 million was not yet received.

Financing activities

The decrease in cash provided by financing activities was primarily due to a decrease in proceeds received from equity issuances of $83.4 million partially offset by an increase in net proceeds related to the issuance of debt instruments of $34.8 million.

Liquidity and capital resources

We do not currently have any approved products and have never generated any revenue from product sales. To date, we have financed our operations primarily through the issuances of our equity securities, including warrants, from borrowings under our term loan facilities and from upfront payments received under the Nuance Agreement. See “Significant Agreements” for additional information.

We have incurred recurring losses since inception, including net losses of $54.4 million, and $68.7 million for the years ended December 31, 2023, and 2022, respectively. In addition, as of December 31, 2023, we had an accumulated deficit of $388.4 million. We may continue to incur significant operating losses for the foreseeable future as we expand our research and development efforts, advance our clinical development of ensifentrine in other formulations or for other indications, and seek to obtain regulatory approval for and commercialize ensifentrine in various formulations or indications.

We have no ongoing material financial commitments, such as lines of credit or guarantees, that are expected to affect our liquidity over the next five years, other than leases and our term loan facility.

2023 Financing and Capital Transactions

- Received $10.0 million under the second term loan advance related to a loan and security agreement with Oxford Finance Luxembourg S.À R.L. for an aggregate amount of up to $150.0 million (the "Oxford Term Loan");
- Sold 20,321,384 ordinary shares (equivalent to 2,540,173 ADSs) under the at-the-market offering program entered into in March 2021 (the "2021 ATM Program"), at an average price of approximately $2.88 per share (equivalent to $23.08 per ADS), raising aggregate net proceeds of approximately $56.9 million after deducting issuance costs;
- Replaced the 2021 ATM Program with an open market sale agreement with Jefferies LLC ("Jefferies") to sell our ordinary shares, in the form of ADSs, with aggregate gross proceeds of up to $200.0 million.
- Entered into the 2023 Term Loan with a term loan advance of $50.0 million funded on the closing date and four additional term loan advances aggregating up to $350.0 million, subject to certain terms and conditions. A portion of the proceeds were used to repay, in full, the outstanding indebtedness owed by under the Oxford Term Loan.

Our 2023 Term Loan requires, among others, that we maintain certain financial covenants, and we were in compliance with all of these covenants as of December 31, 2023.

Refer to Note 5 - Debt to our Consolidated Financial Statements and related notes included elsewhere in this Annual Report for additional information regarding the 2023 Term Loan and Note 1 - Organization and description of business operations for additional information regarding the ATM programs.

Funding requirements

We believe that our cash and cash equivalents as of December 31, 2023, together with additional funding expected to become available under the 2023 Term Loan, will enable us to fund our planned operating expenses and capital expenditure requirements through at least the end of 2026, including the planned commercial launch of nebulized ensifentrine for COPD maintenance treatment in the U.S. Future advances under the 2023 Term Loan are contingent upon achievement of certain regulatory and commercial milestones as well as other specified conditions.

We may require additional capital to commercialize ensifentrine, to continue the clinical development of our DPI and pMDI formulations of ensifentrine and to research and develop additional formulations of or with ensifentrine. In addition, we may seek to initiate or conduct preclinical or clinical studies with ensifentrine in additional indications or to discover or in-license and develop additional product candidates. We may need to seek additional funding through public or private financings, debt financing, collaboration or licensing agreements and other arrangements. However, there is no guarantee that we will be successful in securing additional capital on acceptable terms, or at all.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our shareholders and ADS holders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect such holders' rights as a shareholder or ADS holder. Any future debt financing or preferred equity financing, if available, may involve agreements that include security interests in our assets and future revenue streams, covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and may require the issuance of warrants, which could potentially dilute our security holders' ownership interests.

If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our future capital requirements for ensifentrine or any future product candidates will depend on many factors, including:

- the progress, timing and completion of pre-clinical testing and clinical trials for ensifentrine or any future product candidates and the potential that we may be required to conduct additional clinical trials for ensifentrine;
- the number of potential new product candidates we decide to in-license and develop;
- the costs involved in growing our organization to the size needed to allow for the research, development and potential commercialization of ensifentrine or any future product candidates;
- the costs involved in filing patent applications and maintaining and enforcing patents or defending against claims or infringements raised by third parties;
- the time and costs involved in obtaining regulatory approvals for ensifentrine or any future product candidate we develop and any delays we may encounter as a result of evolving regulatory requirements or adverse results with respect to ensifentrine or any future product candidates;
- any licensing or milestone fees we might have to pay during future development of ensifentrine or any future product candidates;
- selling and marketing activities undertaken in connection with the anticipated commercialization of ensifentrine or any future product candidates, if approved, and costs involved in the creation of an effective sales and marketing organization; and
- the amount of revenue, if any, we may derive either directly or in the form of royalty payments from future sales of ensifentrine or any future product candidates, if approved.

Our commercial revenue, if any, will be derived from sales of products that we do not expect to be commercially available until the second half of 2024, if ever. Accordingly, we may need to obtain substantial additional funds to achieve our business objectives.

Recent accounting pronouncements

For a discussion of pending and recently adopted accounting pronouncements, see Note 2 Basis of Presentation and Summary of Significant Accounting Policies to our Consolidated Financial Statements included elsewhere in this Annual Report.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We are not required to provide the information required by this Item 7A until our Quarterly Report on Form 10-Q for the first quarter after the fiscal year in which it is determined that we are no longer a smaller reporting company.

Item 8. Financial Statements and Supplementary Data

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report. An index of those financial statements is found in Item 15 of Part IV of this Annual Report.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

On December 14, 2023, the Audit and Risk Committee of the board of directors dismissed PricewaterhouseCoopers LLP ("PwC") and approved the engagement of Ernst & Young LLP ("EY") to serve as the Company's independent registered public accounting firm ("independent auditor") to audit the Company's Consolidated Financial Statements as of and for the fiscal year ending December 31, 2024, contingent upon the appointment of EY as the Company's independent auditor by the Company's shareholders at its 2024 Annual General Meeting (the "Shareholder Appointment"). Subject to the Shareholder Appointment, EY will replace PwC, the Company's current independent auditor, which is not being nominated for re-appointment by the shareholders and whose term as independent auditor is expected to end following the Company's 2024 Annual General Meeting.

The reports of PwC on the Company's Consolidated Financial Statements as of and for the years ended December 31, 2022 and 2021 did not contain an adverse opinion or a disclaimer of opinion, nor were they qualified or modified as to uncertainty, audit scope or accounting principles.

During the fiscal years ended December 31, 2022 and 2021, and in the subsequent interim period through December 14, 2023, there were (i) no "disagreements" (as that term is defined in Item 304(a)(1)(iv) of Regulation S-K) between the Company and PwC on any matter of accounting principles or practices, financial statement disclosure or auditing scope or procedures, which, if not resolved to the satisfaction of PwC, would have caused PwC to make reference to the matter in its report on the financial statements for such years, and (ii) no "reportable events" (as that term is described in Item 304(a)(1)(v) of Regulation S-K).

The Company provided PwC with a copy of the disclosures contained in its Current Report on Form 8-K filed with the SEC on December 18, 2023 and requested that PwC furnish a letter addressed to the SEC stating whether it agrees with the statements contained herein.

During the Company's two most recent fiscal years ended December 31, 2022 and December 31, 2021, and the subsequent interim period from January 1, 2023 through December 14, 2023, neither the Company nor anyone acting on its behalf consulted with EY regarding either (i) the application of accounting principles to a specified transaction, either completed or proposed, or the type of audit opinion that might be rendered on the Company's Consolidated Financial Statements, and neither a written report nor oral advice was provided to the Company that EY concluded was an important factor considered by the Company in reaching a decision as to the accounting, auditing or financial reporting issue; or (ii) any matter that was either the subject of a "disagreement" (as defined in Item 304(a)(1)(iv) of Regulation S-K and the related instructions thereto) or a "reportable event" (as described in Item 304(a)(1)(v) of Regulation S-K).

Item 9A. Controls and Procedures

Disclosure Controls and Procedures

Limitations on Effectiveness of Controls and Procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a- 15(e) and 15d- 15(e) under the Exchange Act), as of the end of the period covered by this Annual Report. Based on such evaluation, our principal executive officer and principal financial officer have concluded that, as of December 31, 2023, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Our management, including our principal executive officer and principal financial officer, is responsible for establishing and maintaining adequate internal control over our financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act.

Our management conducted an assessment of the effectiveness of our internal control over financial reporting as of December 31, 2023 based on the criteria established in "Internal Control – Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Based on this assessment, our management concluded that, as of December 31, 2023, our internal control over financial reporting was effective.

Attestation Report of the Registered Public Accounting Firm

Our independent registered public accounting firm, PricewaterhouseCoopers LLP, has audited the effectiveness of the Company's internal control over financial reporting as of December 31, 2023, as stated in their report that appears on page F-2 of this Annual Report on Form 10-K.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) identified in management's evaluation pursuant to Rules 13a-15(d) or 15d-15(d) of the

Exchange Act that occurred during the quarter ended December 31, 2023 that materially affected, or are 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

Code of Ethics

Our board of directors has adopted a written Code of Business Conduct and Ethics applicable to all officers, directors and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. We have posted a current copy of our Code of Business Conduct and Ethics on our website at www.veronapharma.com in the "Investors" section under "Corporate Governance." We intend to satisfy the disclosure requirement under Item 5.05 of Form 8-K regarding amendments to, or waivers from, a provision of our Code of Business Conduct and Ethics, as well as Nasdaq's requirement to disclose waivers with respect to directors and executive officers, by posting such information on our website at the address and location specified above. The information contained on our website is not incorporated by reference into this Annual Report.

The remaining information required by this item will be included in our definitive proxy statement for the 2024 Annual General Meeting of Shareholders and is incorporated herein by reference to such proxy statement.

Item 11. Executive Compensation

The information required by this item will be included in our definitive proxy statement for the 2024 Annual General Meeting of Shareholders and is incorporated herein by reference to such proxy statement.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item will be included in our definitive proxy statement for the 2024 Annual General Meeting of Shareholders and is incorporated herein by reference to such proxy statement.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this item will be included in our definitive proxy statement for the 2024 Annual General Meeting of Shareholders and is incorporated herein by reference to such proxy statement.

Item 14. Principal Accountant Fees and Services

The information required by this item will be included in our definitive proxy statement for the 2024 Annual General Meeting of Shareholders and is incorporated herein by reference to such proxy statement.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a)(1) Financial Statements

The following financial statements and the Report of Independent Registered Accounting Firm are filed as part of this Annual Report:

(a)(2) Financial Statement Schedules.

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(a)(3) Exhibits.

The following is a list of exhibits filed as part of this Annual Report.

		Incorporated by Reference to Filings Indicated				
Exhibit Number	Exhibit Description	Form	File No.	Exhibit No.	Filing date	Filed / Furnished Herewith
1.1	Open Market Sale Agreement[SM], dated as of March 19, 2021, between Verona Pharma plc and Jefferies LLC, and as amended	S-3ASR	333-270339	1.2	3/7/2023	
3.1	Articles of Association, as amended and as currently in effect	6-K	001-38067	1	12/30/2020	
4.1	Deposit Agreement	20-F	001-38067	2.1	2/27/2018	
4.2	Form of American Depositary Receipt (included in Exhibit 4.1)	20-F	001-38067	2.2	2/27/2018	
4.3	Form of Warrant issued to each of the investors named in Schedule A thereto	F-1	333-217124	4.3	4/3/2017	
4.4	Warrant Instrument issued to NPlus1 Singer LLP	F-1	333-217124	4.4	4/3/2017	
4.5	Description of Securities	10-K	001-38067	4.5	2/29/2024	*
10.1	Registration Rights Agreement, dated July 29, 2016, by and among Verona Pharma plc and the investors set forth therein	F-1	333-217124	10.1	4/3/2017	
10.2	Registration Rights Agreement, dated July 16, 2020, by and among Verona Pharma plc and the investors set forth therein	6-K	001-38067	2	7/22/2020	
10.3.1†	Intellectual Property Assignment and Licence Agreement between Vernalis Development Limited and Rhinopharma Limited, as predecessor to Verona Pharma plc, dated February 7, 2005	F-1	333-217124	10.2	4/3/2017	

10.3.2	Amendment Agreement by and between Verona Pharma plc and Ligand U.K. Development Limited dated March 23, 2022	8-K	001-38067	10.1	3/30/2022
10.4.3	Renewal Agreement to Lease by and between the Verona Pharma plc and Regus Management (U.K.) Limited dated September 16, 2017#1	20-F	001-38067	4.3.3	2/27/2020
10.4.4	Renewal Agreement to Lease by and between the Verona Pharma plc and Regus Management (U.K.) Limited dated September 16, 2017#2	20-F	001-38067	4.3.4	2/27/2020
10.4.5	Renewal Agreement to Lease by and between the Verona Pharma plc and Regus Management (U.K.) Limited dated September 16, 2017#3	20-F	001-38067	4.3.5	2/27/2020
10.4.6	Renewal Agreement to Lease by and between the Verona Pharma Inc. and Regus Management Group LLC dated July 16, 2019	20-F	001-38067	4.3.6	2/27/2020
10.4.7	Renewal Agreement to Lease by and between the Verona Pharma plc and Regus Management (U.K.) Limited dated November 9, 2021	10-K	001-38067	10.4.7	3/7/2022
10.4.8	Renewal Agreement to Lease by and between the Verona Pharma plc and Regus Management (U.K.) Limited dated December 7, 2021	10-K	001-38067	10.4.8	3/7/2022
10.4.9	Agreement to Lease by and between Verona Pharma, Inc. and Brier Creek Office #4, LLC dated March 6, 2020	10-K	001-38067	10.4.9	3/7/2022
10.5	Agreement of Sublease, dated August 28, 2023, by and between Verona Pharma, Inc. and insightsoftware, LLC	8-K	001-38067	10.1	9/1/2023
10.6#	EMI Option Scheme	F-1	333-217124	10.4	4/3/2017
10.7#	Unapproved Share Option Scheme, as amended	F-1	333-217124	10.5	4/3/2017
10.8#	Verona Pharma plc Second Amended and Restated 2017 Incentive Award Plan	8-K	001-38067	10.1	5/1/2023
10.9#	Employment Agreement, dated January 28, 2020, between Verona Pharma, Inc. and David Zaccardelli, Pharm. D.	20-F	001-38067	4.7	2/27/2020
10.10#	Employment Agreement, dated December 21, 2019, between Verona Pharma plc and Kathleen Rickard	20-F	001-38067	4.8	3/19/2019
10.11#	Employment Agreement, dated October 1, 2016, between Verona Pharma plc and Claire Poll	F-1	333-217124	10.9	4/3/2017
10.12#	Employment Agreement, dated February 1, 2020, between Verona Pharma, Inc. and Mark Hahn	F-1	333-247928	10.12	8/17/2020
10.13#	Form of Indemnification Agreement for board members	F-1/A	333-217124	10.11.1	4/18/2017
10.14#	Form of Indemnification Agreement for executive officers	F-1/A	333-217124	10.11.2	4/18/2017
10.15#	Employee Change in Control Severance Benefit Plan	8-K	001-39067	10.1	8/11/2021

10.16	Relationship Agreement relating to Verona Pharma plc, dated July 29, 2016, by and among Verona Pharma plc, OrbiMed Private Investments VI, LP and NPlus1 Singer Advisory LLP	F-1	333-217124	10.12	4/3/2017	
10.17	Relationship Agreement relating to Verona Pharma plc, dated July 29, 2016, by and among Verona Pharma plc, Abingworth Bioventures VI LP and NPlus1 Singer Advisory LLP	F-1	333-217124	10.13	4/3/2017	
10.18	Relationship Agreement relating to Verona Pharma plc, dated July 29, 2016, by and among Verona Pharma plc, Vivo Ventures Fund VII, L.P., Vivo Ventures VII Affiliates Fund, L.P., Vivo Ventures Fund VI, L.P., Vivo Ventures VI Affiliates Fund, L.P. and NPlus1 Singer Advisory LLP	F-1	333-217124	10.14	4/3/2017	
10.19	Relationship Agreement relating to Verona Pharma plc, dated July 29, 2016, by and among Verona Pharma plc, Vivo Ventures Fund VII, L.P., Vivo Ventures VII Affiliates Fund, L.P., Vivo Ventures Fund VI, L.P., Vivo Ventures VI Affiliates Fund, L.P. and NPlus1 Singer Advisory LLP	6-K	001-38067	1	7/22/2020	
10.20#	Form of Non-Executive Director letter of appointment	10-K	001-38067	10.2	2/25/2021	
10.21†	Collaboration and License Agreement, effective as of June 9, 2021, by and between Verona Pharma plc, Nuance Pharma Limited and Nuance (Shanghai) Pharma Co Ltd	10-Q	001-38067	10.1	8/5/2021	
10.22†	Loan and Security Agreement, dated as of December 27, 2023, by and among Verona Pharma, Inc., Oxford Finance LLC, as collateral agent and as a lender, and the other lenders party thereto	8-K	001-38067	10.1	1/2/2024	
10.23†	Commercial Supply Agreement between The Ritedose Corporation and Verona Pharma plc dated December 20, 2023	10-K	001-38067	10.23	2/29/2024	*
21.1	List of Subsidiaries of Verona Pharma plc					*
16.1	Letter of PricewaterhouseCoopers LLP, dated December 14, 2023.	8-K	001-38067	16.1	12/18/2023	
23.1	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm					*
31.1	Rule 13a-14(a)/15d-14(a) Certification of Chief Executive Officer					*
31.2	Rule 13a-14(a)/15d-14(a) Certification of Chief Financial Officer					*
32.1	Section 1350 Certification of Chief Executive Officer					**
32.2	Section 1350 Certification of Chief Financial Officer					**
97#	Policy for Recovery of Erroneously Awarded Compensation					*
101.INS	Inline XBRL Instance Document					*

101.SCH	Inline XBRL Taxonomy Extension Schema Document	*
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	*
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	*
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	*
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	*
104	Cover Page Interactive Data File (formatted in Inline XBRL and contained in Exhibit 101)	*

* Filed herewith.

** Furnished herewith.

# Indicates management contract or compensatory plan.

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to Regulation S-K, Item 601(b)(10). Such omitted information is not material and the registrant customarily and actually treats such information as private or confidential. Additionally, schedules and attachments to this exhibit have been omitted pursuant to Regulation S-K, Items 601(a)(5).

Item 16. Form 10-K Summary

None

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

VERONA PHARMA PLC

Date: February 29, 2024

By: /s/ David Zaccardelli

David Zaccardelli, Pharm. D.

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 in the capacities and on the dates indicated.

/s/ David Zaccardelli **David Zaccardelli, Pharm. D.**	President and Chief Executive Officer *(principal executive officer)*	February 29, 2024
/s/ Mark W. Hahn **Mark W. Hahn**	Chief Financial Officer *(principal financial and accounting officer)*	February 29, 2024
/s/ David Ebsworth, Ph.D. **David Ebsworth, Ph.D.**	Chairperson of the Board of Directors	February 29, 2024
/s/ Christina Ackermann **Christina Ackermann**	Director	February 29, 2024
/s/ Michael Austwick **Michael Austwick**	Director	February 29, 2024
/s/ James Brady **James Brady**	Director	February 29, 2024
/s/ Ken Cunningham, M.D. **Ken Cunningham, M.D.**	Director	February 29, 2024
/s/ Lisa Deschamps **Lisa Deschamps**	Director	February 29, 2024
/s/ Martin Edwards, M.D. **Martin Edwards, M.D.**	Director	February 29, 2024
/s/ Mahendra Shah, Ph.D. **Mahendra Shah, Ph.D.**	Director	February 29, 2024
/s/ Vikas Sinha **Vikas Sinha**	Director	February 29, 2024
/s/ Anders Ullman, M.D., Ph.D. **Anders Ullman, M.D., Ph.D.**	Director	February 29, 2024

Index

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders of Verona Pharma plc

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of Verona Pharma plc and its subsidiaries (the "Company") as of December 31, 2023 and 2022, and the related consolidated statements of operations and comprehensive loss, of shareholders' equity and of cash flows for the years then ended, including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2023, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2023 and 2022, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2023, based on criteria established in Internal Control - Integrated Framework (2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Annual Report on Internal Control Over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting 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 audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated 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 consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process 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. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become

inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that (i) relates to accounts or disclosures that are material to the consolidated financial statements and (ii) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated 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.

Accounting for the modification of a term loan facility

As described in Note 1, 2 and 5 to the consolidated financial statements, on December 27, 2023 (the "2023 Effective Date") the Company entered into a term loan facility of up to $400.0 million (the "2023 Term Loan" or "Loan Agreement"), consisting of a term loan advance in an aggregate amount of $50.0 million funded on the 2023 Effective Date (the "Term A Loan") and four additional term loan advances subject to certain terms and conditions. The 2023 Term Loan replaced the Company's existing $150.0 million facility. The Company received net proceeds from the Term A Loan partially offset by the repayment, in full, of the existing outstanding indebtedness owed by the Company under the previous Term Loan of $20 million. Debt may be considered extinguished when it has been modified and the terms of the new debt instruments and old debt instruments are "substantially different". Based upon management's evaluation of the accounting for the Loan Agreement, management has applied modification accounting to a portion of the Term A Loan in accordance with ASC 470-50 "*Debt-Modifications and Extinguishments*".

The principal considerations for our determination that performing procedures relating to the accounting for the modification of a term loan facility is a critical audit matter are (i) the matter represented a significant transaction, and (ii) a high degree of auditor effort in performing procedures and evaluating audit evidence related to the Company's accounting for the term loan facility modification and extinguishment assessment.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included testing the effectiveness of controls relating to management's accounting for significant transactions in connection with debt modification. These procedures also included, among others, (i) evaluating management's assessment regarding the accounting for the new term facility, in particular with respect to their assessment of modification and extinguishment in accordance with the applicable accounting guidance; and (ii) evaluating the sufficiency of the disclosures in the consolidated financial statements.

/s/ PricewaterhouseCoopers LLP
Reading, United Kingdom
February 29, 2024

We have served as the Company's auditor since 2015.

Verona Pharma plc
Consolidated Balance Sheets
(in thousands, except share and per share amounts)

	December 31, 2023	December 31, 2022
ASSETS		
Current assets:		
Cash and cash equivalents	$ 271,772	$ 227,827
Prepaid expenses	3,617	2,499
Tax incentive receivables	10,954	9,282
Other current assets	3,365	3,388
Total current assets	289,708	242,996
Non-current assets:		
Furniture and equipment, net	24	73
Goodwill	545	545
Equity interest	15,000	15,000
Right-of-use assets	2,847	854
Total non-current assets:	18,416	16,472
Total assets	$ 308,124	$ 259,468
LIABILITIES AND SHAREHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 3,492	$ 2,910
Accrued expenses	3,585	13,752
Current operating lease liabilities	1,180	675
Taxes payable	—	283
Other current liabilities	435	1,409
Total current liabilities	8,692	19,029
Non-current liabilities:		
Term loan	48,374	9,768
Non-current operating lease liabilities	1,775	205
Total non-current liabilities	50,149	9,973
Total liabilities	58,841	29,002
Commitments and contingencies		
Shareholders' equity		
Ordinary £0.05 par value shares: 667,659,630 and 631,338,246 issued, and 643,536,094 and 606,301,054 outstanding, at December 31, 2023 and 2022, respectively	42,771	40,526
Additional paid-in capital	601,063	529,187
Ordinary shares held in treasury	(1,517)	(1,549)
Accumulated other comprehensive loss	(4,601)	(4,601)
Accumulated deficit	(388,433)	(333,097)
Total shareholders' equity	249,283	230,466
Total liabilities and shareholders' equity	$ 308,124	$ 259,468

The accompanying notes are an integral part of these consolidated financial statements.

Verona Pharma plc
Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share amounts)

	Year ended December 31,	
	2023	2022
Revenue	$ —	$ 458
Cost of sales	—	(346)
Gross profit	—	112
Operating expenses:		
Research and development (Note 11)	17,216	49,283
Selling, general and administrative	50,353	26,579
Total operating expenses	67,569	75,862
Operating loss	(67,569)	(75,750)
Other income/(expense):		
Research and development tax credit	1,104	9,634
Loss on extinguishment of debt	—	(815)
Interest income	12,761	2,821
Interest expense	(2,057)	(521)
Foreign exchange gain/(loss)	1,866	(3,817)
Total other income, net	13,674	7,302
Loss before income taxes	(53,895)	(68,448)
Income tax expense	(474)	(253)
Net loss	$ (54,369)	$ (68,701)
Loss per ordinary share — basic and diluted	$ (0.09)	$ (0.13)
Weighted-average shares outstanding - basic and diluted	634,142,660	529,071,526

The accompanying notes are an integral part of these consolidated financial statements.

Verona Pharma plc
Consolidated Statements of Shareholders' Equity
(in thousands except share data)

	Ordinary shares		Additional paid-in capital	Ordinary shares held in treasury	Accumulated other comprehensive loss	Accumulated deficit	Total shareholders' equity
	Number	Amount					
Balance at January 1, 2022	489,177,550	$31,855	$385,070	$ (603)	$ (4,601)	$ (263,716)	$ 148,005
Net loss	—	—	—	—	—	(68,701)	(68,701)
Issuance of ordinary shares, net of issuance costs	114,080,000	6,918	133,279	—	—	—	140,197
Issuance of common shares under at-the-market sales agreement	80,696	5	62	—	—	—	67
Issuance of ordinary shares to treasury	28,000,000	1,748	—	(1,748)	—	—	—
Restricted share units vested	—	—	—	680	—	(680)	—
Share options exercised	—	—	1,250	122	—	—	1,372
Share-based compensation	—	—	14,121	—	—	—	14,121
Common shares withheld for taxes on vested stock awards	—	—	(4,723)	—	—	—	(4,723)
Equity settled share-based compensation reclassified as cash-settled	—	—	128	—	—	—	128
Balance at December 31, 2022	631,338,246	$40,526	$529,187	$ (1,549)	$ (4,601)	$ (333,097)	$ 230,466
Net loss	—	—	—	—	—	(54,369)	(54,369)
Issuance of common shares under at-the-market sales agreement	20,321,384	1,227	55,682	—	—	—	56,909
Issuance of ordinary shares to treasury	16,000,000	1,018	—	(1,018)	—	—	—
Restricted share units vested	—	—	—	967	—	(967)	—
Share options exercised	—	—	1,866	83	—	—	1,949
Share-based compensation	—	—	19,012	—	—	—	19,012
Common shares withheld for taxes on vested stock awards	—	—	(4,389)	—	—	—	(4,389)
Equity settled share-based compensation reclassified as cash-settled	—	—	(295)	—	—	—	(295)
Balance at December 31, 2023	667,659,630	$42,771	$601,063	$ (1,517)	$ (4,601)	$ (388,433)	$ 249,283

The accompanying notes are an integral part of these consolidated financial statements.

Verona Pharma plc
Consolidated Statements of Cash Flows
(in thousands)

	Year ended December 31,	
	2023	**2022**
Operating activities:		
Net loss:	$ (54,369)	$ (68,701)
Adjustments to reconcile net income to net cash used in operating activities:		
Foreign exchange (gain)/loss	(1,866)	3,817
Amortization of debt issuance costs	116	80
Accretion of redemption premium on debt	106	108
Loss on extinguishment of debt	—	815
Share-based compensation	19,012	14,121
Depreciation and amortization	677	636
Changes in operating assets and liabilities:		
Prepaid expenses	(1,118)	1,538
Tax incentive receivables	(1,104)	3,964
Other current assets	777	(1,325)
Accounts payable	486	(7,146)
Accrued expenses	(10,351)	(8,504)
Operating lease liabilities	(591)	(597)
Income taxes	(1,037)	136
Other current liabilities	(960)	1,196
Net cash used in operating activities	(50,222)	(59,862)
Cash flows from investing activities:		
Purchases of furniture and equipment	—	(29)
Net cash used in investing activities	—	(29)
Cash flows from financing activities:		
Proceeds from issuance of ordinary shares	56,909	149,797
Payment of offering costs in connection with the issuance of ordinary shares	—	(9,533)
Proceeds from Oxford Term Loan	9,996	10,000
Proceeds from 2023 Term Loan, net of repayment of Oxford Term Loan and debt issuance costs incurred	28,712	—
Payment of debt issuance costs	(12)	(245)
Repayment of SVB Term Loan	—	(5,000)
SVB Term Loan repayment costs	—	(850)
Payments of withholding taxes from share-based awards	(4,685)	(4,723)
Proceeds from exercise of share options	1,949	1,372
Net cash provided by financing activities	92,869	140,818
Effect of exchange rate changes on cash and cash equivalents	1,298	(1,480)
Net change in cash and cash equivalents	43,945	79,447
Cash and cash equivalents at beginning of the year	227,827	148,380
Cash and cash equivalents at end of the year	$ 271,772	$ 227,827
Supplemental disclosure of cash flow information:		
Income taxes paid	$ 1,245	$ 120
Interest paid	$ 2,006	$ 348

The accompanying notes are an integral part of these consolidated financial statements.

Note 1 - Organization and description of business operations

Verona Pharma plc is incorporated and domiciled in the United Kingdom. Verona Pharma plc has one wholly-owned subsidiary, Verona Pharma, Inc., a Delaware corporation (together with Verona Pharma plc the "Company"). The address of the registered office is 1 Central Square, Cardiff, CF10 1FS, United Kingdom.

The Company is a clinical-stage biopharmaceutical group focused on developing and commercializing innovative therapeutics for the treatment of respiratory diseases with significant unmet medical needs. The Company's American Depositary Shares ("ADSs") are listed on the Nasdaq Global Market ("Nasdaq") and trade under the symbol "VRNA".

In August 2023, the U.S. Food and Drug Administration ("FDA") accepted for review the Company's New Drug Application ("NDA") seeking approval of ensifentrine for the maintenance treatment of chronic obstructive pulmonary disease ("COPD") and assigned a Prescription Drug User Fee Act ("PDUFA") target action date of June 26, 2024. The FDA stated it is not currently planning to hold an advisory committee meeting to discuss the application. The Company is preparing for a potential commercial launch in 2024, subject to approval of the NDA.

In conjunction with the submission of the NDA in June 2023, the Company paid a $3.2 million PDUFA application fee to the FDA. The Company requested a small business waiver of this application fee which was approved by the FDA and refunded in the three months ended December 31, 2023.

Liquidity

The Company has incurred recurring losses and negative cashflows from operations since inception, and has an accumulated deficit of $388.4 million as of December 31, 2023. The Company expects to incur additional losses and negative cash flows from operations until its products potentially gain regulatory approval and reach commercial profitability, if at all.

The Company expects that its cash and cash equivalents as of December 31, 2023, will be sufficient to fund its operating expenses and capital expenditure requirements for at least the next 12 months from the date of issuance.

In August 2022, the Company completed an upsized public offering of 14,260,000 ADSs, each representing eight ordinary shares of the Company, nominal value £0.05 per share, at a price to the public of $10.50 per ADS, which includes the exercise in full by the underwriters of their option to purchase an additional 1,860,000 ADSs. The aggregate net proceeds from the offering were $140.2 million after deducting underwriting discounts and commissions and estimated offering expenses payable.

During the year ended December 31, 2022, the Company sold 80,696 ordinary shares (equivalent to 10,087 ADSs) under its at the market offering program entered into in March 2021 (the "2021 ATM Program"), at an average price of approximately $0.86 per share (equivalent to $6.86 per ADS), raising aggregate net proceeds of $0.1 million after deducting issuance costs. As of December 31, 2022, there remained $99.2 million of ordinary shares, in the form of ADSs, available for sale under the 2021 ATM Program.

During the year ended December 31, 2023, the Company sold 20,321,384 ordinary shares (equivalent to 2,540,173 ADSs) under the 2021 ATM Program, at an average price of approximately $2.88 per share (equivalent to $23.08 per ADS), raising aggregate net proceeds of $56.9 million after deducting issuance costs.

In March 2023, through a registration statement on Form S-3, the Company replaced the 2021 ATM Program, with an open market sale agreement with Jefferies LLC ("Jefferies") to sell its ordinary shares, in the form of ADSs, with aggregate gross proceeds of up to $200.0 million, from time-to-time, through an "at the market" equity offering program under which Jefferies will act as sales agent (the "2023 ATM Program"). Jefferies is entitled to a commission at a rate of up to 3.0% of the gross proceeds.

In December 2023, the Company entered into a term loan facility (the "2023 Term Loan") of up to $400.0 million with Oxford Finance LLC ("Oxford"), as collateral agent, and certain funds managed by Oxford and Hercules Capital, Inc. At closing $50.0 million was funded with up to four additional advances of an aggregate $350.0 million available subject to the Company meeting certain regulatory and commercial milestones. The 2023 Term Loan replaced the Company's existing $150.0 million facility with Oxford Finance Luxembourg S.A R.L. Refer to Note 5 - Debt for additional details.

The Company's commercial revenue, if any, will be derived from sales of products that are not expected to be commercially available until the second half of 2024, if ever. Additionally, the Company may enter into out-licensing transactions from time to time but there can be no assurance that the Company can secure such transactions in the future. Accordingly, the Company may need to obtain substantial additional funds to achieve its business

objectives including to further advance clinical and regulatory activities, to fund launch related costs and to create an effective sales and marketing organization to commercialize ensifentrine, if approved. Any such funding will need to be obtained through public or private financings, debt financing, collaboration or licensing arrangements or other arrangements. However, there is no guarantee the Company will be successful in securing additional capital on acceptable terms, or at all.

Note 2 - Basis of Presentation and Summary of Significant Accounting Policies

Basis of presentation and consolidation

The Consolidated Financial Statements include the accounts of Verona Pharma plc and its wholly-owned subsidiary Verona Pharma, Inc. All inter-company balances and transactions have been eliminated.

The Consolidated Financial Statements have been prepared in accordance with accounting principles generally accepted in the United States ("U.S. GAAP") and the following accounting policies have been consistently applied.

Use of estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reporting periods. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the accrual and prepayment of research and development expenses and the fair value of share-based compensation. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known. Actual results could differ from the Company’s estimates.

Business combinations

The Company applies the acquisition method to account for business combinations. The consideration transferred for the acquisition of a subsidiary is the fair value of the assets transferred, the liabilities incurred to the former owners of the acquiree and the equity interests issued by the Company. The consideration transferred includes the fair value of any asset or liability resulting from a contingent consideration arrangement. The excess of the cost of acquisition over the fair value of the Company's share of the identifiable net assets acquired is recorded as goodwill.

Identifiable assets acquired and liabilities and contingent liabilities assumed in a business combination are measured initially at their fair values at the acquisition date. Acquisition-related costs are expensed as incurred and included in administrative expenses.

Cash and cash equivalents

The Company considers all highly liquid investments purchased with original maturities of ninety days or less at acquisition to be cash equivalents. Cash and cash equivalents includes deposits held at call with banks, and in money market funds investing in U.S. and U.K. government debt and liquid securities from highly rated institutions.

Equity interest

As part of the Nuance Agreement, the Company received an equity interest in Nuance Biotech, the parent company of Nuance Pharma (see Note 6 - Significant Agreements). As Nuance Biotech’s securities are not publicly traded, the equity interest’s fair value is not readily determinable. The Company therefore follows guidance from ASC 321-10-35-2 and uses the fair value measurement alternative and measures the securities at cost, which is deemed to be the value indicated by the last observable transaction in Nuance Biotech's stock, subject to impairment. The valuation will be adjusted for any observable price changes in orderly transactions for an identical or similar investment in Nuance Biotech, or if there is an indicator of impairment.

Furniture and equipment, net

Furniture and equipment comprise office furniture, computer equipment and leasehold improvements and are stated at cost less accumulated depreciation. Depreciation on furniture and equipment is calculated on a straight-line basis over the expected useful economic lives, generally two to five years. Depreciation on leasehold improvements is over the lesser of the economic life of the asset or the term of the lease.

Goodwill

Goodwill consists of goodwill related to the acquisition of Rhinopharma. Goodwill is not amortized but periodically tested for impairment.

Impairment of long-lived assets

The Company reviews long-lived assets for impairment annually or whenever events or changes in circumstances indicate that the carrying amount of assets may not be fully recoverable.

Debt and debt issuance costs

Upon issuance of a new debt instrument, the Company recognizes a liability equal to the proceeds received, less any allocation of proceeds to other instruments issued with the debt, other elements of the transaction, or features within the debt instrument itself. The proceeds generally approximate the present value of interest and principal payments of the debt.

In situations where, for economic or legal reasons related to the Company's financial difficulties, the borrower grants a concession to the Company that it would not otherwise consider, the related loan is classified as a troubled debt restructuring. If a restructuring does not constitute a troubled debt restructuring, it will be evaluated to consider if it should be accounted for as an extinguishment or as a modification.

Debt may be considered extinguished when it has been modified and the terms of the new debt instruments and old debt instruments are "substantially different" (as defined in the debt modification guidance in ASC 470-50 "Debt-Modifications and Extinguishments").

Debt issuance costs relating to the Company's debt instruments are recorded in Term loan on the Consolidated Balance Sheets as a direct reduction of the carrying amount of the related debt; these costs are deferred and amortized to interest expense using the effective interest method, over the respective terms of the related debt.

Revenue recognition

The Company's revenue consists of revenue from the Company's strategic agreements for the development and commercialization of ensifentrine. The terms of the agreements may include non-refundable upfront fees, payments based upon achievement of milestones and eventually revenue from the commercialized product. These agreements usually have both fixed and variable consideration. Non-refundable upfront fees are considered fixed, while milestone payments and revenue from the commercialized product are identified as variable consideration.

In determining the appropriate amount of revenue to be recognized as it fulfills its obligations under agreements within the scope of ASC Topic 606, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation.

A performance obligation is a promise in a contract to transfer a distinct good or service to the customer and is the unit of account in ASC Topic 606. The Company's performance obligations may include intellectual property rights, (which include the license, patents and developmental and regulatory data) and manufacturing and supply. Management are required to judge when performance obligations are satisfied and consequently when revenue is recognized.

The Company allocates the total transaction price to each performance obligation based on the estimated relative standalone selling prices of the promised goods or service underlying each performance obligation.

For arrangements with licenses of intellectual property that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty has been allocated has been satisfied. If the right to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable, upfront fees allocated to the right when the right is transferred to the customer, and the customer can use and benefit from the right.

At the inception of the arrangement, the Company evaluates whether the development milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely

amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company, such as approvals from regulators, are not considered probable of being achieved until those approvals are received.

Research and development costs

Research and development ("R&D") costs are expensed as incurred. Research and development expenses include salaries, share-based compensation and benefits of employees, and other costs related to the Company's R&D activities, including pre-approval manufacturing costs, contracts with clinical research organizations and contract manufacturers. The Company is required to estimate its expenses resulting from its obligations under contracts with vendors and consultants and clinical site agreements in connection with its R&D efforts. The financial terms of these contracts are subject to negotiations which vary contract to contract and may result in payment flows that do not match the periods over which materials or services are provided to the Company under such contracts. The Company's objective is to reflect the appropriate clinical trial expenses in its Consolidated Financial Statements by matching those expenses with the period in which services and efforts are expended. The Company accounts for these expenses according to the progress of the trials and other development activities. Judgment is applied in determining assumptions related to patient progression and the timing of various aspects of the trial used to measure progress. The Company determines prepaid and accrual estimates through discussions with applicable personnel and outside service providers as to the progress of clinical trials, or other services completed. During the course of a clinical trial, the Company adjusts its rate of clinical trial expense recognition if actual results differ from its estimates. The Company makes estimates of its prepaid and accrued expenses as of each balance sheet date in its Consolidated Financial Statements based on facts and circumstances known at that time. Although the Company does not expect its estimates to be materially different from amounts actually incurred, its understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in the Company reporting amounts that are too high or too low for any particular period. The Company's clinical trial prepaid and accrual expense is dependent upon the timely and accurate reporting of study recruitment from contract research organizations and activities carried out by other third-party vendors as well as the timely processing of any change orders from the contract research organizations.

Share-based compensation

The Company has a share-based compensation plan under which various types of equity-based awards may be granted, including stock options, restricted stock units ("RSUs") and performance restricted stock units ("PRSUs"). The fair value of share options and RSUs, which are subject to milestone or service conditions with graded vesting, are recognized as compensation expense on a straight-line basis using the graded-vesting method; forfeitures are recognized as they occur.

The fair value of PRSUs, which are subject to certain performance and service conditions, will be recognized over the remaining service period using the graded-vesting method once the performance conditions are determined to be probable of occurring.

The Company uses the fair-value based method to determine compensation for all arrangements under which employees receive shares. The fair value of stock options is estimated on the date of grant using the Black-Scholes valuation model that uses assumptions for expected volatility, expected dividends, expected term, and the risk-free interest rate. Expected volatility is based on the historical volatility of the Company's ordinary shares over the expected term of the options. The expected term of options granted is derived using the simplified method, which computes the expected term as the average of the sum of the vesting term plus the contract term. Historically the risk-free rate has been based on the appropriate U.K. government debt yield. After delisting its Ordinary shares from AIM on October 30, 2020, the Company used U.S. government debt yields.

The fair-value of RSUs and PRSUs is calculated using the closing price of the Company's ordinary shares on the date of grant.

Details of the assumptions used are set out in Note 7 - Share-based compensation to the Consolidated Financial Statements.

Other income - United Kingdom R&D tax credits

Research and development tax credit relates to R&D tax credits receivable in the U.K. As a company that carries out extensive research and development activities, the Company is subject to the U.K. R&D Small and Medium Enterprise ("SME") Program. Qualifying expenditures largely comprise employment costs for research staff, consumables, a proportion of relevant, permitted sub-contract costs and certain internal overhead costs incurred as part of research projects for which it does not receive income.

Tax credits related to the SME Program are received as cash and are recorded as other income, as they are akin to grant income, in the Consolidated Statements of Operations and Comprehensive Loss.

Income taxes

The Company accounts for income taxes in accordance with ASC 740, "Income Taxes" ("ASC 740"). ASC 740 prescribes the use of the liability method, whereby deferred tax assets and liability account balances are determined based on differences between financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse.

The Company provides a valuation allowance, if necessary, to reduce deferred tax assets to their estimated realizable value. ASC 740 establishes a single model to address accounting for uncertain tax positions. ASC 740 clarified the accounting for income taxes by prescribing the minimum recognition threshold a tax position is required to meet before being recognized in the financial statements. The Company has no uncertain tax positions.

Comprehensive loss

The Company accounts for comprehensive loss in accordance with ASC 220, "Income Statement - Reporting Comprehensive Income". Comprehensive loss represents all changes in shareholders' equity during the period except those resulting from investments by, or distributions to, shareholders.

Segment Reporting

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company has one operating and reportable segment, pharmaceutical development.

Reporting and functional currencies

The Consolidated Financial Statements are reported in U.S. dollars, which is also the functional currency of the Company's subsidiary. Transactions in foreign currencies are remeasured into the Company's functional currency at the rate of exchange prevailing at the date of the transaction. Any monetary assets and liabilities arising from these transactions are remeasured into our functional currency at exchange rates prevailing at the balance sheet date or on settlement. Resulting gains and losses are recorded in foreign exchange gain/(loss) in our Consolidated Statements of Operations.

Treasury shares

In the year ended December 31, 2020, the Company incorporated a trust to facilitate the acquisition of shares, by or for the benefit of employees and former employees. In the years ended December 31, 2023 and December 31, 2022 the Company issued 16.0 million ordinary shares (equivalent to 2.0 million ADSs) and 28.0 million (equivalent to 3.5 million ADSs), respectively, to the trust to cover expected shares issued upon the vesting of share awards to employees.

The Company has the indirect ability to control the trust as trustees are required to act in accordance with the trust deed and because the Company controls the issuance of shares to cover awards. As a consequence, the trust is consolidated into the Company's Consolidated Financial Statements. The shares that were issued to the trust that have not been issued to employees to satisfy vesting of share awards are included in the Consolidated Balance Sheets as Ordinary shares held in treasury.

Fair value of financial instruments

US GAAP defines fair value and requires companies to establish a framework for measuring fair value and disclosure about fair value measurements using a three-tier approach. These tiers include: Level 1, defined as observable inputs such as quoted prices in active markets; Level 2, defined as inputs other than quoted prices in active markets that are either directly or indirectly observable; and Level 3, defined as unobservable inputs in which little or no market data exists, therefore requiring an entity to develop its own assumptions.

Our financial instruments include cash equivalents, equity interest, other assets, accounts payable and accrued expenses and other liabilities. Fair value estimates of these instruments are made at a specific point in time, based on relevant market information. These estimates may be subjective in nature and involve uncertainties and matters of significant judgement and therefore cannot be determined with precision. The carrying amounts of the other instruments are considered to be representative of their fair values because of their short-term nature.

Concentration of credit risk

Financial instruments that potentially subject the Company to concentration of credit risk consist of principally cash and cash equivalents, bank deposits and certain receivables.

The Company holds cash and cash equivalents with highly rated financial institutions and in highly rated money market funds. Our deposits at these institutions may exceed insured limits, however the Company has not experienced any significant credit losses in these accounts and does not believe the Company is exposed to any significant credit risk on these instruments.

Lease accounting

The Company determines if an arrangement is a lease at inception. ROU assets and liabilities are recognized at the commencement date based on the present value of lease payments over the term of the lease. For this purpose, the Company considers only payments that are fixed and determinable at the time of commencement.

As the Company's leases do not provide an implicit rate, the Company determines the incremental borrowing rate in calculating the present value of lease payments. The ROU assets also include any lease payments made prior to commencement and are recorded net of any lease incentives received.

The Company's lease terms may include options to extend or terminate the lease. When it is reasonably certain the Company will exercise such options the lease will be recognized as a liability and a corresponding ROU asset also recognized.

Operating leases are included in Right-of-use assets and in Current and Non-current operating lease liabilities on the Company's Consolidated Balance Sheets.

Recently adopted accounting standards

In June 2016, the FASB issued ASU 2016-13, Financial Instruments-Credit Losses (Topic 326)-Measurement of Credit Losses on Financial Instruments. This guidance replaces the current incurred loss impairment methodology.

Under this model, on initial recognition and at each reporting period, an entity is required to recognize an allowance that reflects its current estimate of credit losses expected to be incurred over the life of the financial instrument based on historical experience, current conditions and reasonable and supportable forecasts. The guidance requires a modified retrospective transition approach through a cumulative-effect adjustment to retained earnings as of the beginning of the period of adoption. This update became effective for the Company on January 1, 2023 and the adoption of this update did not have a material impact on the Company's financial statements and related disclosures.

Recently issued accounting standards not yet adopted

In December 2023, the FASB issued ASU No. 2023-09, Improvements to Income Tax Disclosures, which requires disaggregated information about a reporting entity's effective tax rate reconciliation as well as information on income taxes paid. The standard is intended to benefit investors by providing more detailed income tax disclosures that would be useful in making capital allocation decisions. The amendments in this ASU are effective for annual periods beginning on January 1, 2025, and should be applied on a prospective basis with the option to apply the standard retrospectively. Early adoption is permitted. This ASU will have no impact on the Company's Consolidated Balance Sheets or Consolidated Statements of Operations and Comprehensive Loss. The Company is currently evaluating the impact to its income tax disclosures.

In November 2023, the FASB issued ASU No. 2023-07, Improvements to Reportable Segment Disclosures, which improves reportable segment disclosure requirements, primarily through enhanced disclosures about significant segment expenses. In addition, the amendments enhance interim disclosure requirements, clarify circumstances in which an entity can disclose multiple segment measures of profit or loss, provide new segment disclosure requirements for entities with a single reportable segment, and contain other disclosure requirements. The purpose of the amendments is to enable investors to better understand an entity's overall performance and assess potential future cash flows. The amendments in this ASU are effective for annual periods beginning on January 1, 2024 and interim periods beginning on January 1, 2025, and should be applied on a retrospective basis for all periods presented. This ASU will have no impact on the Company's Consolidated Balance Sheets or Consolidated Statements of Operations and Comprehensive Loss. The Company is currently evaluating the impact to its segment disclosures.

Note 3 - Property leases

The Company's Right-of-use assets ("ROU") relate to rented office space in London, Georgia and two in North Carolina with leases ending in 2025, 2025, 2024 and 2027, respectively.

In the year ended December 31, 2023, the Company entered into a lease arrangement in North Carolina for office space and extended its existing London lease. As a result of these two agreements, the Company recognized a lease liability and a corresponding ROU asset of $2.7 million. Additionally, the supplemental noncash ROU asset obtained in exchange for operating lease liabilities is $2.7 million.

In the year ended December 31, 2022, the Company entered into a lease arrangement in Georgia for office space and extended its existing London lease recognizing a lease liability and a corresponding ROU asset of $0.7 million.

To calculate lease liabilities the Company used a weighted average discount rate of 11% and 4% for the years ended December 31, 2023 and December 31, 2022, respectively. The weighted average remaining lease term as of December 31, 2023 and December 31, 2022 was 3.3 years and 1.5 years, respectively.

Minimum annual payments over the remaining lease periods as of December 31, 2023 are as follows (in thousands):

2024	$	1,175
2025		842
2026		788
2027		784
Total minimum future lease payments	$	3,589
Less: imputed interest		(634)
Total operating lease liabilities	$	2,955

The total operating lease expense included in selling, general and administrative costs was $0.7 million for the year ended December 31, 2023.

Note 4 - Accrued expenses

Accrued expenses consisted of the following (in thousands):

	December 31,			
	2023		2022	
Clinical trial and other development costs	$	752	$	12,314
Professional fees, listing and general corporate costs		2,039		1,364
People related costs		794		74
Total accrued expenses	$	3,585	$	13,752

Note 5 - Debt

In November 2020, the Company entered into a term loan facility of up to $30.0 million (the "SVB Term Loan"), consisting of advances of $5.0 million funded at closing and $10.0 million and $15.0 million contingent upon achievement of certain clinical development milestones and other specified conditions.

On October 14, 2022 (the "2022 Effective Date"), the Company entered into a loan and security agreement with Oxford Finance Luxembourg S.À R.L. for an aggregate amount of up to $150.0 million (the "Oxford Term Loan"). The Oxford Term Loan provided for an initial term loan advance in an aggregate amount of $10.0 million funded on the 2022 Effective Date (the "Oxford Term A Loan"), and up to four additional term loan advances in an aggregate amount of $140.0 million, contingent upon the achievement of certain clinical and regulatory development milestones as well as other specified conditions. The proceeds from the Oxford Term Loan were used for general corporate and working capital purposes, and a portion of the proceeds of the Oxford Term A Loan were used to repay in full the existing outstanding indebtedness owed under the SVB Term Loan. On March 24, 2023, the Company received $10.0 million under the second term loan advance (the "Oxford Term B Loan").

On December 27, 2023 (the "2023 Effective Date"), the Company entered into a term loan facility of up to $400.0 million (the "2023 Term Loan" or "Loan Agreement"), consisting of a term loan advance in an aggregate

amount of $50.0 million funded on the 2023 Effective Date (the "Term A Loan") and four additional term loan advances subject to certain terms and conditions, as discussed below, in the amounts of $100.0 million (the "Term B Loan"), $75.0 million (the "Term C Loan"), $75.0 million (the "Term D Loan") and $100.0 million (the "Term E Loan"). The 2023 Term Loan was entered into with Oxford Finance LLC, a Delaware limited liability company ("Oxford"), as collateral agent, and certain funds managed by Oxford and Hercules Capital, Inc. party thereto (collectively, the "Lenders"). The net proceeds of the 2023 Term Loan will be used for general corporate and working capital purposes.

The Company received net proceeds from the Term A Loan of $28.4 million which primarily consisted of the Term A Loan proceeds of $50.0 million partially offset by the repayment, in full, of the existing outstanding indebtedness owed by the Company under the Oxford Term Loan of $20.0 million, lender and third-party fees related to the Loan Agreement of $1.4 million and interest amounts of $0.2 million.

Based upon the Company's accounting evaluation of the Loan Agreement, as well as the Oxford entities involved and terms of both the 2023 Term Loan and the Oxford Term Loan, the Company has applied modification accounting to the portion of the Term A Loan associated with Oxford. As such, no gain or loss is recorded upon the modification with the unamortized debt issuance costs at the 2023 Effective Date from the Oxford Term Loans included as amounts the outstanding amount under the 2023 Term Loan. Additionally, certain fees included in the net proceeds were expensed based on the applicable guidance under ASC 470.

The portion of the Term A Loan associated with Hercules Capital, Inc. has been accounted for as the issuance of new debt with the applicable accounting applied under ASC 470.

The Term B Loan will be available, subject to customary terms and conditions, during the period commencing on the date the Company receives approval from the United States Food and Drug Administration for its New Drug Application for ensifentrine through and including the earliest of (i) the date that is 30 days immediately following the date the Company receives such approval and (ii) September 15, 2024. The Term C Loan will be available, subject to customary terms and conditions (including the prior borrowing of the Term B Loan), during the period commencing on the later of (i) September 15, 2025 and (ii) prior to September 30, 2025, the achievement by the Company of a specified net sales milestone. The Term D Loan will be available, subject to customary terms and conditions (including the prior borrowing of the Term C Loan), during the period commencing on the later of (i) February 15, 2026 and (ii) prior to March 31, 2026, the achievement by the Company of a specified net sales milestone. The Term E Loan will be available, subject to customary terms and conditions (including the prior borrowing of the Term D Loan) prior to June 1, 2028 at the Lenders sole discretion and upon the Company's request.

The 2023 Term Loan will mature on December 1, 2028. Each advance under the Loan Agreement accrues interest at a floating per annum rate (the "Basic Rate") equal to (a) the greater of (i) the 1-Month CME Term SOFR (as defined in the Loan Agreement) reference rate on the last business day of the month that immediately precedes the month in which the interest will accrue and (ii) 5.34%, plus (b) 5.85%. Notwithstanding the foregoing, (i) in no event shall the Basic Rate (x) for the Term A Loan be less than 11.19% and (y) for each other 2023 Term Loan be less than the Basic Rate on the business day immediately prior to the funding date of such 2023 Term Loan, (ii) the Basic Rate for the Term A Loan for the period from the Effective Date through and including December 31, 2023 was 11.19% and (iii) the Basic Rate for each 2023 Term Loan shall not increase by more than 2.00% above the applicable Basic Rate as of the funding date of each such 2023 Term Loan. The 2023 Term Loan provides for interest-only payments on a monthly basis until the payment date immediately preceding June 1, 2028. Thereafter, amortization payments will be payable monthly in equal installments of principal plus monthly payments of accrued interest.

Upon repayment (whether at maturity, upon acceleration or by prepayment or otherwise), the Borrower shall make a final payment to the Lenders in the amount of 2.50% to 3.50% of the aggregate 2023 Term Loan advanced, depending on when a 2023 Term Loan is repaid (the "Final Payment"). The Borrower may prepay the 2023 Term Loan in full or in part provided that the Borrower (i) provides ten (10) days' prior written notice to Oxford and the Lenders, (ii) pays on the date of such prepayment (A) all outstanding principal plus accrued and unpaid interest, (B) a prepayment fee of 2.00% of the 2023 Term Loan advanced if paid on or before December 27, 2025; 1.50% of the 2023 Term Loan advanced if paid after December 27, 2025 and before December 27, 2026; 1.00% of the 2023 Term Loan advanced if paid after December 27, 2026, (C) the Final Payment and (D) all other sums, if any, that shall become due and payable under the Loan Agreement, including interest at the default rate with respect to any past due amounts. Amounts outstanding during an event of default are payable upon the Required Lenders' (as defined in the Loan Agreement) demand and shall accrue interest at an additional rate of 5.00% per annum and (iii) any partial prepayment of the 2023 Term Loans shall be in a denomination that is a whole number multiple of $5.0 million.

The 2023 Term Loan is secured by a lien on substantially all of the assets of the Company, other than intellectual property, provided that a lien on intellectual property will be granted on the earlier of (i) the funding date of any 2023 Term Loan that would cause the aggregate principal amount of outstanding 2023 Term Loan drawn pursuant to the Loan Agreement to exceed $50.0 million and (ii) prior to the Borrower or the Company entering into a Permitted Royalty Financing (as defined in the Loan Agreement). The Company has also granted Oxford and the Lenders a negative pledge with respect to its intellectual property.

The Loan Agreement contains customary representations and warranties, covenants and events of default, including two financial covenants: (i) commencing on July 1, 2025, the Borrower is required to maintain certain levels of cash in the United States subject to control agreements in favor of Oxford; provided that such liquidity covenant shall not apply at any given time if the market capitalization of the Company at such time is at least $3.0 billion and (ii) commencing on September 30, 2025, the Borrower and the Company are required to maintain quarterly trailing six-month net product revenue from the sale of ensifentrine; provided that such revenue covenant will be waived at any time (x) the Borrower and the Company's unrestricted cash balance on the last calendar day of each month during such quarter is equal to or greater than the product of 1.25 multiplied by the aggregate principal amount of outstanding 2023 Term Loan on such date, (y)(1) the Borrower and the Company's unrestricted cash balance on the last calendar day of each month during such quarter is equal to or greater than the product of 0.5 multiplied by the aggregate principal amount of outstanding 2023 Term Loan on such date and (2) the average of the daily VWAP of the Company's American Depositary Shares for each of the five trading days preceding the last trading day of each month during such quarter multiplied by the total number of issued and outstanding American Depositary Shares of the Company is at least $1.5 billion, or (z) the average of the daily VWAP of the Company's American Depositary Shares for each of the five trading days preceding the last trading day of each month during such quarter multiplied by the total number of issued and outstanding American Depositary Shares of the Company is at least $3.0 billion. The Loan Agreement also contains other customary provisions, such as expense reimbursement, as well as indemnification rights for the benefit of Oxford and the Lenders.

As of December 31, 2023 the interest rate was approximately 11% per annum and there was no material difference between the carrying value and the estimated fair value of the 2023 Term Loan.

Future principal payments, which exclude the end of term charge, in connection with the 2023 Term Loan as of December 31, 2023 are as follows (in thousands):

2024	$ —
2025	—
2026	—
2027	—
2028	50,000
Total	$ 50,000

Note 6 - Significant agreements

Ligand agreement

In 2006 the Company acquired Rhinopharma and assumed contingent liabilities owed to Ligand UK Development Limited ("Ligand") (formerly Vernalis Development Limited). The Company refers to the assignment and license agreement as the Ligand Agreement.

Ligand assigned to the Company all of its rights to certain patents and patent applications relating to ensifentrine and related compounds (the "Ligand Patents") and an exclusive, worldwide, royalty-bearing license under certain Ligand know-how to develop, manufacture and commercialize products (the "Ligand Licensed Products") developed using Ligand Patents, Ligand know-how and the physical stock of certain compounds.

The Company is obligated to pay a milestone payment of £5.0 million on obtaining the first approval of any regulatory authority for the commercialization of a Ligand Licensed Product, low single digit royalties based on the future sales performance of all Ligand Licensed Products and a portion equal to a mid-twenty percent of any consideration received from any sub-licensees for the Ligand Patents and for Ligand know-how. Royalties payable are based on the future sales performance so the amount payable is unlimited.

At the time each contingency is resolved, the Company will record the contingent consideration payment (or payable) in connection with the Ligand Agreement as an expense.

In March 2022, the Company entered into an Amendment Agreement (the "Amendment") with Ligand whereby the Ligand Agreement was amended to clarify certain ambiguous terms in the Ligand Agreement. Pursuant to the Amendment:

- the Company agreed to pay to Ligand (i) $2.0 million within five business days of the date of the Amendment and (ii) $15.0 million upon the first commercial sale of ensifentrine by the Company or a sub-licensee, which amount is payable in cash or, at the Company's discretion, by the issuance of Company equity of equivalent value, as determined based on the volume-weighted average price of the Company's American Depositary Shares on the Nasdaq Global Market over the ten (10) trading days including and prior to such milestone event;
- the Ligand Agreement shall expire on March 24, 2042 unless terminated earlier by either party in accordance with its terms;
- upon termination of the Ligand Agreement, any Sub-licensee (as defined in the Amendment) shall have the right to enter into a direct license agreement with Ligand for the portion of the Program IP (as defined in the Amendment) that was sub-licensed by such Sub-licensee;
- the milestone payment may be paid in cash or, at the Company's discretion, by issuing to Ligand shares in the Company of equivalent value; and
- each party's right to terminate the Ligand Agreement is conditioned upon such party obtaining a final judgment of the English High Court declaring that the other party is in material breach of its obligations under the Ligand Agreement.

The Company accounted for the $2.0 million payment at execution of the Amendment as selling, general and administrative expense in the consolidated statements of operations and comprehensive loss as the payment is related to a contract modification.

Nuance agreement

The Company entered into a collaboration and license agreement (the "Nuance Agreement") with Nuance Pharma Limited ("Nuance Pharma") effective June 9, 2021 (the "Nuance Effective Date"), under which the Company granted Nuance Pharma the exclusive rights to develop and commercialize ensifentrine in Greater China (China, Taiwan, Hong Kong and Macau). In return, the Company received an unconditional right to consideration aggregating $40.0 million consisting of $25.0 million in cash and an equity interest, valued at $15.0 million as of the Nuance Effective Date, in Nuance Biotech, the parent company of Nuance Pharma. The Company is eligible to receive future milestone payments of up to $179.0 million triggered upon achievement of certain clinical, regulatory, and commercial milestones, as well as tiered double-digit royalties as a percentage of net sales of the products in Greater China. The Company will recognize these milestones when it is probable that a significant revenue reversal would not occur.

As of December 31, 2023, the $15.0 million equity interest was recorded as Equity interest on the Consolidated Balance Sheet. The equity interest is recorded at cost as the Company has elected to use the measurement alternative

for equity investments without readily determinable fair values. The Company evaluates this investment for indicators of impairment quarterly. The Company did not identify events or changes in circumstances that may have a significant effect on the fair value of the investment during the year ended December 31, 2023.

Under the terms of the Nuance Agreement, at any time until three months prior to the expected submission of the first New Drug Application in Greater China, if (i) a third party is interested in partnering with the Company, either globally or in territory covering at least the United States or Europe, for the development and/or commercialization of ensifentrine or (ii) the Company undergoes a change of control, the Company will have an exclusive option right to buy back the license granted to Nuance Pharma and all related assets. The price is agreed to be equal to the aggregate of (i) all prior amounts paid by Nuance Pharma to the Company in cash under the agreement and (ii) all development and regulatory costs incurred and paid by Nuance Pharma in connection with the development and commercialization of ensifentrine under the Nuance Agreement multiplied by a single-digit factor range dependent upon achievement of certain milestones, subject to a specified maximum amount.

The Nuance Agreement will continue on a jurisdiction-by-jurisdiction and product-by-product basis until the expiration of royalty payment obligations with respect to such product in such jurisdiction unless earlier terminated by the parties. Either party may terminate the Nuance Agreement for an uncured material breach or bankruptcy of the other party. Nuance Pharma may also terminate the Nuance Agreement at will upon 90 days' prior written notice.

The Company reviewed the buy-back option and determined that because it is conditional on a third party the Company does not have the practical ability to exercise it and, accordingly, the contract is accounted for under ASC 606.

On April 13, 2022, the Company formalized the Agreement for the Manufacture and Supply of ensifentrine ("Nuance Supply Agreement") with Nuance Pharma. The Company determined that the manufacturing and supply of ensifentrine to Nuance represents a distinct and separate performance obligation, for which consideration to be received is variable based on the quantities to be ordered by Nuance. Revenue earned with the manufacture and supply of the licensed product is, and will be, recognized as the supply is delivered to Nuance. The Company has determined it is acting as principal in relation to the manufacture and supply under the Agreement. In its capacity as principal, the Company will recognize the associated revenue on a gross basis. In the year ended December 31, 2022, the Company recognized $0.5 million of revenue in relation to the clinical supply of ensifentrine to Nuance Pharma.

Note 7 - Share-based compensation

The Company operates various share based incentive plans for its staff and issues ordinary shares or ADSs when share-based awards are exercised.

The Company records share-based compensation expense related to share options and RSUs granted to employees and directors. The expense is included in Research and development and Selling, general and administrative costs, based on the nature of individual employees' functions, and represents the relevant year's allocation of the expense. The costs of share-based compensation to employees are recognized in the Consolidated Statements of Operations and Comprehensive Loss, together with a corresponding increase in equity over the vesting period.

Options are issued with an exercise price of the closing market price on the day before the grant and generally vest over a period of one to four years and the contractual life of all options is ten years.

The following table shows the allocation of share-based compensation between research and development and selling, general and administrative costs (in thousands):

	December 31,	
	2023	2022
Research and development	$ 4,228	$ 5,420
Selling, general and administrative	14,784	8,701
Total share-based compensation	$ 19,012	$ 14,121

EMI Option Plan and Pre-IPO Option Plan

The EMI Option Plan and the Pre-IPO Option Plan were adopted by our board of directors on September 18, 2006, and July 24, 2012, respectively. The total number of shares that may be issued under these plans is the current number of outstanding options over 114,000 ordinary shares, or 14,250 ADSs, for the EMI Option Plan and 1,320,000 ordinary shares, or 165,000 ADSs, for the Pre-IPO Option Plan.

No further awards have been granted under either plan since the 2017 Incentive Award Plan was adopted, and no further awards will be granted under them.

2017 Incentive Award Plan

The 2017 Incentive Award Plan was adopted by our board of directors and became effective on April 26, 2017, in order to grant share based compensation to certain of the Company's directors and employees. It provides for the grant of stock options, RSUs, and other share-based awards to Company's directors, officers, employees and non-employee directors.

Share option activity

The number of options, the weighted average grant date fair value per stock option, and the weighted average exercise price are all shown below on a per ordinary shares basis. The Company's ADSs that are listed on the Nasdaq Global Market each represent eight ordinary shares.

The following table shows share option activity and includes the options outstanding from all three plans:

	Number of share options	Weighted average exercise price [(1)]	Weighted average remaining contractual term (years)	Aggregate intrinsic value (thousands)
Outstanding at January 1, 2022	12,695,200	$ 1.38	6.5	
Granted	9,024,000	0.90		
Forfeited	(620,016)	1.04		
Exercised	(1,822,688)	0.75		
Outstanding at December 31, 2022	19,276,496	$ 1.22	7.2	$ 39,412
Granted	7,376,000	2.46		
Forfeited	(464,680)	0.89		
Expired	(240,000)	3.07		
Exercised	(1,258,192)	1.55		
Outstanding at December 31, 2023	24,689,624	$ 1.56	7.4	$ 24,022
Exercisable at December 31, 2023	12,904,640	$ 1.30	5.8	$ 15,574

[(1)] The exercise prices relate to the equivalent price for an ordinary share, calculated as one eighth of the ADS price.

The following summarizes the aggregate intrinsic value and cash receipts related to stock option exercise activity for the years ended December 31:

($ in thousands)	2023	2022
Aggregate intrinsic value of stock options exercised	$ 1,861	$ 2,413
Cash receipts from stock options exercised	$ 1,949	$ 1,372

Determining the fair value of share options

The total fair values of the options, estimated using the Black-Scholes option-pricing model for equity-settled compensation, amounted to $13.2 million for options granted in the year ended December 31, 2023 and $5.9 million for instruments granted in the year ended December 31, 2022. The cost is amortized over the vesting period of the options on a straight-line basis using the graded-vesting method. The following assumptions were used for the Black-Scholes valuation of share options granted in 2023 and 2022.

Expected volatility

Volatility is calculated using historical daily averages of the Company's share price over a period that is in line with the expected life of the options.

Fair value of ordinary shares

Prior to delisting from the AIM in October 2020, the fair value of ordinary shares was based on the closing share price of the Company's shares on AIM on the evening before the date of grant. Subsequently, the fair value has been based on the closing price of ADSs traded on Nasdaq on the evening before the date of grant.

Risk-free interest rate

The risk-free interest rate has been based on U.K. Government debt yield for the relevant term at the time of grant up until October 20, 2020 when the company delisted from AIM. After this, appropriate U.S Treasury yield rates were used.

Expected term

As the Company does not have sufficient history to estimate its expected term, the Company applied the simplified method of estimating the expected term of the options, as described in the SEC's Staff Accounting Bulletins 107 and

110. The expected term, calculated under the simplified method, is applied to all stock options which have similar contractual terms. Using this method, the expected term is determined using the average of the vesting period and the contractual life of the stock options granted.

Expected dividend

There are no expected dividends.

A summary of the weighted-average assumptions applicable to the share options granted in the applicable years is as follows:

	December 31,	
	2023	2022
Risk-free interest rate	3.40% - 4.69%	2.09% - 4.20%
Expected lives, years	5-7	5-7
Expected volatility	80.64% - 87.26%	82.50% - 84.27%
Expected dividend yield	— %	— %
Grant date fair value (per share)	$1.69 - $3.27	$0.34 - $1.33

Restricted stock units activity

The following table shows RSU activity:

	Number of RSUs	Weighted average grant date fair value	Weighted average remaining contractual term (years)
Outstanding at January 1, 2022	38,347,352	$ 0.97	1.2
Granted	12,877,864	1.07	
Forfeited	(1,006,264)	1.03	
Vested	(15,676,608)	0.96	
Outstanding at December 31, 2022	34,542,344	$ 1.01	1.2
Granted	3,596,872	1.66	
Forfeited	(303,648)	1.10	
Vested	(18,332,944)	0.99	
Outstanding at December 31, 2023	19,502,624	$ 1.14	1.2

The intrinsic value of RSUs that vested in the years ended December 31, 2023 and 2022, was $41.5 million and $14.3 million, respectively.

As of December 31, 2023, total compensation cost related to share options and RSUs granted but not yet recognized was $20.0 million. This cost will be amortized to expense over a weighted average remaining period of 1.9 years and will be adjusted for subsequent forfeitures.

Performance Restricted Stock Units ("PRSUs")

The Company began issuing PRSUs during 2023. PRSUs will begin to vest upon achievement of certain performance goals and are subject to continued service. The fair value of PRSUs will be recognized over the remaining service period using the graded-vesting method once the performance conditions are determined to be probable of occurring. Due to the presence of the performance conditions, which are not yet considered probable under the applicable accounting framework, the Company recognized no compensation expense for the PRSUs in 2023.

A summary of the Company's PRSU activity for the year ended December 31, 2023 is as follows:

	Number of PRSUs	Weighted average grant date fair value	Aggregate Intrinsic Value (thousands)
Outstanding at January 1, 2023	—	$ —	
Granted	10,790,144	1.66	
Forfeited	(60,000)	1.66	
Outstanding at December 31, 2023	10,730,144	$ 1.66	$ 26,665

The total compensation cost not yet recognized as of December 31, 2023 related to non-vested PRSUs was $17.8 million, which will be recognized over a weighted-average period of approximately one year, once the performance condition is achieved.

Note 8 - Benefit plans

The Company maintains a 401(k) defined contribution retirement plan in the U.S. and a defined contribution plan in the U.K. for its employees and executive directors. The assets of the plans are held separately from those of the Company in independently administered funds.

The retirement plan cost represents the contributions payable by the Company to the plans during the year. Defined contribution costs during the years ended December 31, 2023 and 2022 amounted to $0.6 million and $0.3 million, respectively.

Note 9 - Taxation

Verona Pharma plc operates in the United Kingdom and Verona Pharma, Inc. in the United States and they are subject to income taxes in those countries. For the year ended December 31, 2023 the U.K. corporation tax is charged at 23.5% and the U.S. Federal Income tax rate is 21%.

The components of (profit)/loss before income taxes are as follows (in thousands):

	December 31,	
	2023	2022
United States	$ (7,429)	$ (3,868)
United Kingdom	61,324	72,316
Total	$ 53,895	$ 68,448

The components of income tax expense are as follows (in thousands):

	December 31,	
	2023	2022
United States	$ 474	$ 253
United Kingdom	—	—
Total current tax expense	$ 474	$ 253
United States	$ —	$ —
United Kingdom	—	—
Total deferred tax expense	—	—
Total income tax expense	$ 474	$ 253

A reconciliation of the U.K. statutory income tax rate to our effective income tax rate is as follows (in percentages):

	December 31,	
	2023	2022
U.K. tax rate	23.5 %	19.0 %
Non-deductible expenses	(8.0)%	(1.8)%
Research and development incentive	(4.1)%	(8.0)%
Share options exercised	5.4 %	2.1 %
Change in deferred tax valuation allowance	(18.1)%	(11.6)%
Other differences	0.4 %	(0.1)%
Effective income tax rate	(0.9)%	(0.4)%

Components of the Company's deferred tax assets and liabilities are as follows (in thousands):

	December 31,	
	2023	2022
Deferred tax liabilities:		
Contingent liability [1]	$ (53,851)	$ (34,565)
Total deferred tax liabilities	(53,851)	(34,565)
Deferred tax assets:		
Net operating losses	54,012	38,893
IPR&D asset [1]	47,793	32,700
Future exercisable shares	7,548	11,964
Other	21	(516)
Total deferred tax assets	109,374	83,041
Less: valuation allowance	(55,523)	(48,476)
Deferred tax assets, net of valuation allowance	$ —	$ —
Movements in the deferred tax valuation allowance		
Valuation allowance at January 1	$ 48,476	$ 30,252
Change in tax rates	(851)	—
Increase in valuation allowance	7,898	18,224
Valuation allowance at December 31	$ 55,523	$ 48,476

[1] These relate to the difference in the tax base of the IP R&D asset and assumed contingent liability and the financial reporting base, which is nil under U.S. GAAP.

Management has reviewed cumulative tax losses and projections of future taxable losses and determined that it is not more likely than not that they will be realized. Accordingly, valuation allowances have been provided over deferred tax assets.

At December 31, 2023 and December 31, 2022, the Company had U.K. net operating losses ("NOLs") of $216.0 million and $155.6 million, respectively. The NOLs can be carried forward indefinitely to be offset against future taxable profits, but this is restricted to an annual £5 million allowance after which there will be a 50% restriction in the profits that can be covered by losses brought forward.

The Company files separate income tax returns in the U.K. and the U.S. All necessary income tax filings have been completed for all years up to and including December 31, 2022. The Company's R&D Tax Incentive Claim for the year ended December 31, 2022 is currently under routine review by HMRC. No material adjustments are expected to be made to the claimed amount as a result of this review. No interest or penalties were recognized in the Consolidated Statements of Operations and Comprehensive Loss or Consolidated Balance Sheets. As of December 31, 2023, the Company has no uncertain tax positions.

Note 10 - Net loss per share

Net loss per share is calculated on an ordinary share basis. The Company's ADSs that are listed on the Nasdaq Global Market each represent eight ordinary shares. The following table shows the computation of basic and diluted earnings per share for 2023 and 2022 (in thousands, except share and per share amounts):

	December 31,	
	2023	2022
Numerator:		
Net loss	$ (54,369)	$ (68,701)
Net loss available to ordinary shareholders - basic and diluted	$ (54,369)	$ (68,701)
Denominator:		
Weighted-average shares outstanding - basic and diluted	634,142,660	529,071,526
Net loss per share - basic and diluted	$ (0.09)	$ (0.13)

During the years ended December 31, 2023 and 2022, outstanding share options, RSUs and PRSUs of 54.9 million and 53.8 million, respectively, were not included in the computation of diluted earnings per ordinary share, because to do so would be antidilutive.

Note 11 - Commitments and contingencies

In the three months ended March 31, 2023, the Company accrued up to the maximum exposure of $6.9 million related to a matter with a supplier and also had certain invoices in the amount of $1.5 million in accounts payable to the same supplier. Both items were settled in June 2023 for $2.1 million. This resulted in a net reversal of $6.3 million in the three months ended June 30, 2023 and a net reversal of $1.5 million in the year ended December 31, 2023 in Research and development costs in the Consolidated Statement of Operations and Comprehensive Loss.

Note 12 - Related party transactions and other shareholder matters

In the years ended December 31, 2023 and 2022 there were no related party transactions.

CORPORATE INFORMATION

EXECUTIVE OFFICERS

David Zaccardelli, Pharm.D.
President & Chief Executive Officer

Mark W. Hahn
Chief Financial Officer

Kathleen Rickard, M.D.
Chief Medical Officer

Andrew Fisher
General Counsel

BOARD OF DIRECTORS

David Ebsworth, Ph.D
Chairperson of the Board, Verona Pharma and
Non-Executive Director of Sartorius AG

David Zaccardelli, Pharm.D.
President & CEO Verona Pharma

Christina Ackermann
Formerly EVP, Ophthalmic Pharmaceuticals at Bausch + Lomb Inc

Michael Austwick
Formerly CEO of Vectura Ltd

James Brady
Formerly CFO of MedImmune, a division of AstraZeneca AB

Ken Cunningham, M.D.
Non-Executive Chair of Medherant Ltd

Lisa Deschamps
CEO of AviadoBIO Ltd

Martin Edwards, M.D
Formerly Senior Partner, Novo Holdings A/S

Mahendra Shah, Ph.D
Senior Fellow, Vivo Capital LLC

Vikas Sinha
CFO of ElevateBio, Inc

Anders Ullman, M.D., Ph.D.
Formerly Head of R&D and Chief Medical Officer of Sobi AB

SHAREHOLDER INFORMATION

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ANNUAL GENERAL MEETING OF SHAREHOLDERS
April 26, 2024
Details to be notified in the Proxy Statement

An Annual Report, a Proxy Statement and a form of Proxy (or ADS voting instructions) will be furnished to each shareholder and ADS holder as of the record date of March 13, 2024

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STOCK EXCHANGE
Verona Pharma plc's American Depositary Shares* are listed and traded on the Nasdaq Global Market under the ticker symbol "VRNA"

*Each ADS listed on the Nasdaq Global Market represents 8 ordinary shares