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, 2020

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. ☐

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 $37.5 million as of June 30, 2020, 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 19, 2021, the registrant had 463,478,446 ordinary shares, nominal value £0.05 per share, outstanding, which if all held in ADS form, would be represented by 57,934,805 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 2021 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, 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 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. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. 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 will need additional funding to complete development of any future product candidates, or development of other formulations or target indications of ensifentrine, and to commercialize our products, including ensifentrine, if approved;
- 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 heavily on the success of ensifentrine, our only product candidate under development;
- The COVID-19 pandemic has and may continue to adversely impact our business;
- 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, 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 may be unable to obtain orphan drug designation from the FDA or EU for ensifentrine for the treatment of cystic fibrosis, and even if we do obtain such designations, we may be unable to obtain or maintain the benefits associated with orphan drug designation, including the potential for orphan drug exclusivity;
- 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;
- If we fail to enter into new strategic relationships for ensifentrine, our business, research and development and commercialization prospects could be adversely affected;
- 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;
- 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.

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Item 1. Business

OVERVIEW

We are a clinical-stage biopharmaceutical company focused on developing and commercializing innovative therapeutics for the treatment of respiratory diseases with significant unmet medical needs. Our product candidate, ensifentrine, is a first-in-class, inhaled, dual inhibitor of the phosphodiesterase ("PDE") 3 and PDE4 enzymes.

In Phase 2 clinical trials, ensifentrine has demonstrated positive results in chronic obstructive pulmonary disease ("COPD"), asthma and cystic fibrosis ("CF"). In addition, we believe that based on its unique profile, it could be beneficial in the treatment of COVID-19 and it is currently under evaluation in a pilot clinical study.

We are developing ensifentrine in three formulations for the most widely used inhalation devices: nebulizer, 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.

Initially, we are targeting COPD, a common, chronic, progressive, and life-threatening respiratory disease without a cure. If successfully developed, ensifentrine would be the first therapeutic with a novel mode of action for COPD in a decade. We made substantial progress in 2020, including reporting positive data from a large 4-week Phase 2b trial, receiving guidance from the U.S. Food and Drug Administration ("FDA") on our Phase 3 ENHANCE ("Ensifentrine as a Novel inHAled Nebulized COPD thErapy") program and commencing enrollment in the pivotal Phase 3 clinical trials.

Our near term operating focus is the ongoing ENHANCE program, related chemistry, manufacturing and controls, regulatory efforts and early pre-commercial activities. We believe that our cash and cash equivalents as of December 31, 2020, together with funding expected to become available under the Term Loan and from cash receipts from U.K. tax credits, will enable us to fund our planned operating expenses and capital expenditure requirements into 2023.

Overview of COPD and current treatments

COPD is a common, chronic, progressive, and life-threatening respiratory disease without a cure. It damages the airways and lungs, 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 384 million people and is the third leading cause of death, according to the World Health Organization.

The goal of COPD pharmacological therapy is to improve patients' quality of life by reducing symptoms, reducing the quantity and severity of exacerbations (often an escalation of symptoms) and to improve patients' ability to function (GOLD 2020).

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 Medicines Agency ("EMA"): anti-muscarinics, beta-agonists and inhaled corticosteroids ("ICSs"). COPD patients are frequently treated with bronchodilators, including long acting anti-muscarinics ("LAMAs") and long acting beta-agonists ("LABAs"), to relieve airway constriction and make it easier to breathe. In addition, they receive ICSs to prevent exacerbations.

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 has been associated with unfavorable gastrointestinal side-effects such as nausea, emesis, diarrhea, abdominal pain, loss of appetite and weight loss.

COPD treatments are often combined in patients who remain uncontrolled on one or two therapies. These include LAMA/LABA combinations or LAMA/LABA/ICS combinations. Unfortunately, clinical data suggests that 40-60% of patients on dual or triple therapy still experience significant symptoms of COPD, including breathlessness. These chronic recurring symptoms limit their daily activities and impair quality of life. Despite receiving maximum therapy, it is estimated that more than 1.2 million patients in the U.S. alone remain symptomatic. For these patients, there are no available inhaled therapies that offer treatment options beyond standard LAMA / LABA and ICS combinations. New treatment options are urgently needed to help improve lung function, symptoms, and overall quality of life in these patients.

Ensifentrine

Ensifentrine is a first-in-class, inhaled, dual PDE3 and PDE4 inhibitor. This dual inhibition enables it to act as a bronchodilator and an anti-inflammatory agent in a single compound. Importantly, this 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 or approved by the FDA nor the EMA for the treatment of respiratory diseases that acts both as a bronchodilator and anti-inflammatory agent. If successfully developed and approved, ensifentrine has the potential to be the first novel class of bronchodilator in COPD in over 40 years and the only bronchodilator option as an add-on to existing dual / triple therapy.

Ensifentrine has demonstrated significant and clinically meaningful improvements in both lung function and COPD symptoms, including breathlessness, in our prior Phase 2 clinical studies in patients with moderate to severe COPD. In addition, ensifentrine showed further improved lung function and reduced lung volumes in patients taking standard short- and long-acting bronchodilator therapy, including maximum bronchodilator treatment with dual/ triple therapy.

Safety profile

Ensifentrine has demonstrated a safety profile similar to placebo in clinical trials involving more than 1,300 people to date. 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.

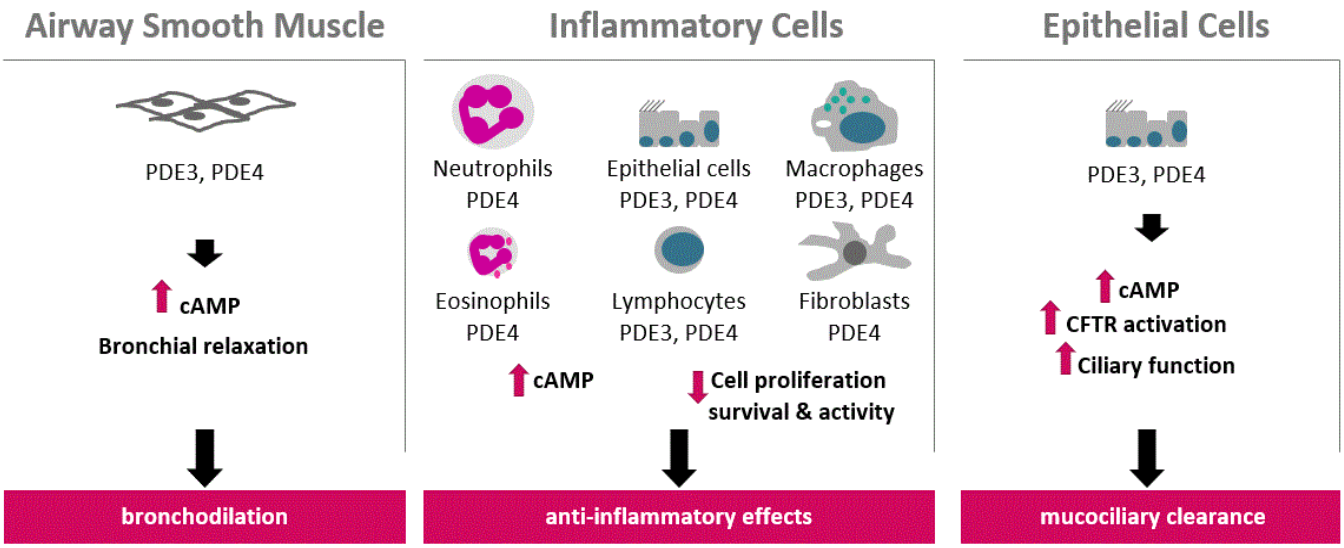
Differentiated profile

By 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 is also designed 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 and are 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, asthma and CF.

Ensifentrine: Differentiated profile as dual bronchodilator and anti-inflammatory

Ensifentrine impacts 3 key mechanisms in respiratory disease



We believe ensifentrine has the potential to address the large unmet need in treating COPD with its improvement in COPD symptoms and meaningful improvement in quality of life.

Clinical data

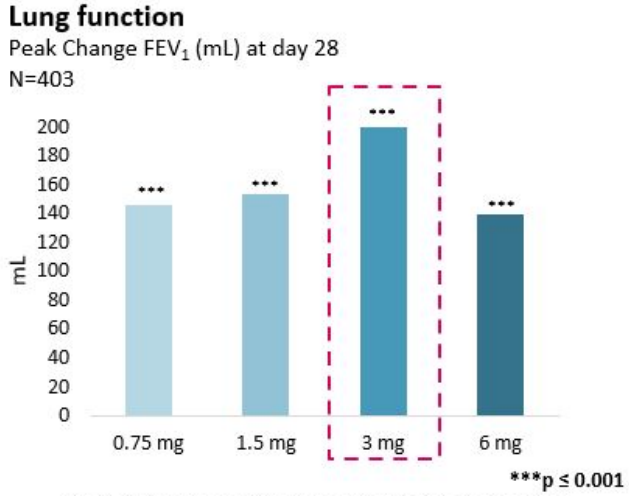
Ensifentrine has demonstrated improvements in lung function, symptoms and quality of life with or without background therapy in two 4-week, Phase 2b dose-ranging clinical trials in moderate to severe COPD patients. In both studies ensifentrine was well tolerated at all doses with an adverse event profile similar to placebo:

- In March 2018, we reported positive top-line results with ensifentrine as monotherapy from our first Phase 2b trial in 403 patients. The trial evaluated four doses of nebulized ensifentrine (0.75 mg, 1.5 mg, 3 mg and 6 mg) or placebo twice daily over 4 weeks. Patients withheld use of regular long-acting bronchodilator therapy for the duration of the study. The trial met its primary endpoint of improved lung function with ensifentrine demonstrating a clinically and statistically significant increase in peak forced expiratory volume in 1 second ("FEV_1") at week 4 compared to placebo. In addition, clinically relevant secondary endpoints were met including significant progressive improvements in COPD symptoms.
- In January 2020, we reported positive top-line results with ensifentrine added on to background therapy from our second Phase 2b trial in 413 patients. This trial evaluated four doses of nebulized ensifentrine (0.375 mg, 0.75 mg, 1.5 mg and 3 mg) or placebo added on to treatment with once-daily tiotropium (Spiriva® Respimat®), a commonly used LAMA bronchodilator, in symptomatic patients with moderate to severe COPD who required additional treatment. The trial met its primary endpoint of improved lung function, with ensifentrine plus tiotropium demonstrating a clinically and statistically significant dose-dependent improvement in peak FEV_1 and FEV_1 over 12 hours with ensifentrine at week 4, compared to placebo plus tiotropium. Additionally, clinically meaningful and statistically significant improvements in health-related quality of life were observed with ensifentrine added on to tiotropium.

Ensifentrine: Efficacy demonstrated in two large Phase 2b trials

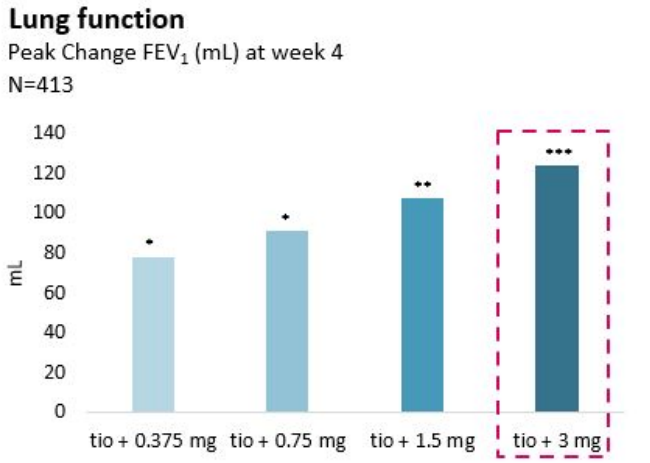
Improvements in lung function seen at Phase 3 trial dose

Study 203: *Ensifentrine Monotherapy*



*Peak Change from Day 1 in Baseline in FEV_1 (mL) on Day 28, Week 4, Primary endpoint met; placebo corrected

Study 205: *Ensifentrine + Tiotropium*



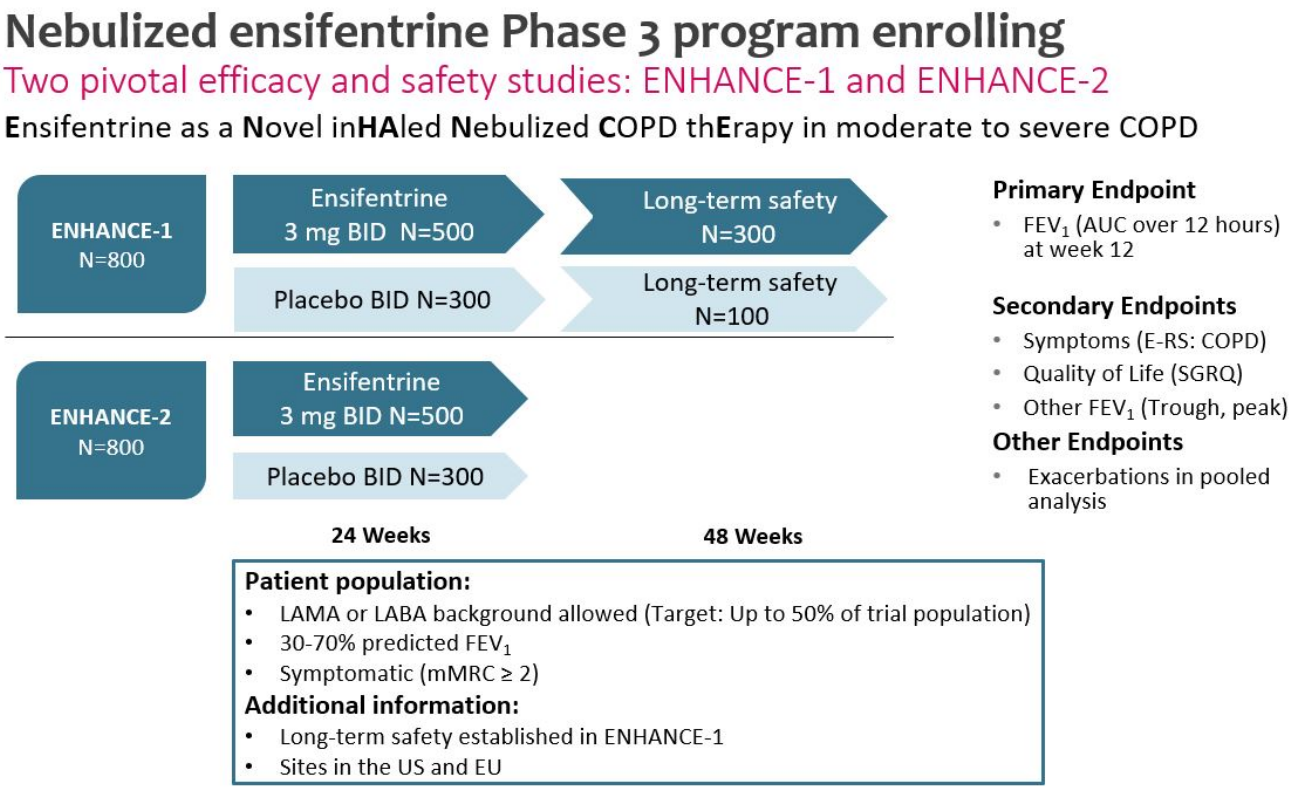
Primary endpoint met; placebo corrected

In May 2020, the FDA provided guidance on key features of our pivotal Phase 3 clinical program in response to our End-of-Phase 2 briefing package for nebulized ensifentrine as a maintenance treatment for COPD. This included clarity on the dose, primary and secondary endpoints, patient population and program design.

In September 2020, we initiated our ENHANCE Phase 3 trials to evaluate the efficacy and safety of nebulized ensifentrine in patients with moderate to severe COPD. The two randomized, double-blind, placebo-controlled studies (ENHANCE-1 and ENHANCE-2) will evaluate ensifentrine as monotherapy and added onto a single bronchodilator.

Each study is expected to enroll approximately 800 moderate to severe, symptomatic COPD patients at sites primarily in the U.S. and Europe. The two study designs will replicate measurements of efficacy and safety data over 24 weeks but ENHANCE-1 will also evaluate longer-term safety in 400 patients over 48 weeks. The primary endpoint is improvement in lung function measured by FEV_1 over 12 hours with ensifentrine after 12 weeks of treatment. Key secondary endpoints include measurements of COPD symptoms and health-related quality of life through 24 weeks assessed via the validated patient reported outcome tools, E-RS: COPD and SGRQ. Additional lung function endpoints including peak and morning trough FEV_1 will also be assessed. Exacerbations will be analyzed by individual study and in a pooled analysis.

We are in the early stages of recruiting patients and based on our recruitment projections, we expect to complete enrollment in both Phase 3 studies in the second half of 2021. Longer term, based on forecasted recruitment, we expect to report top-line data from ENHANCE-2 in the first half of 2022 and ENHANCE-1 in the second half of 2022.



Formulations

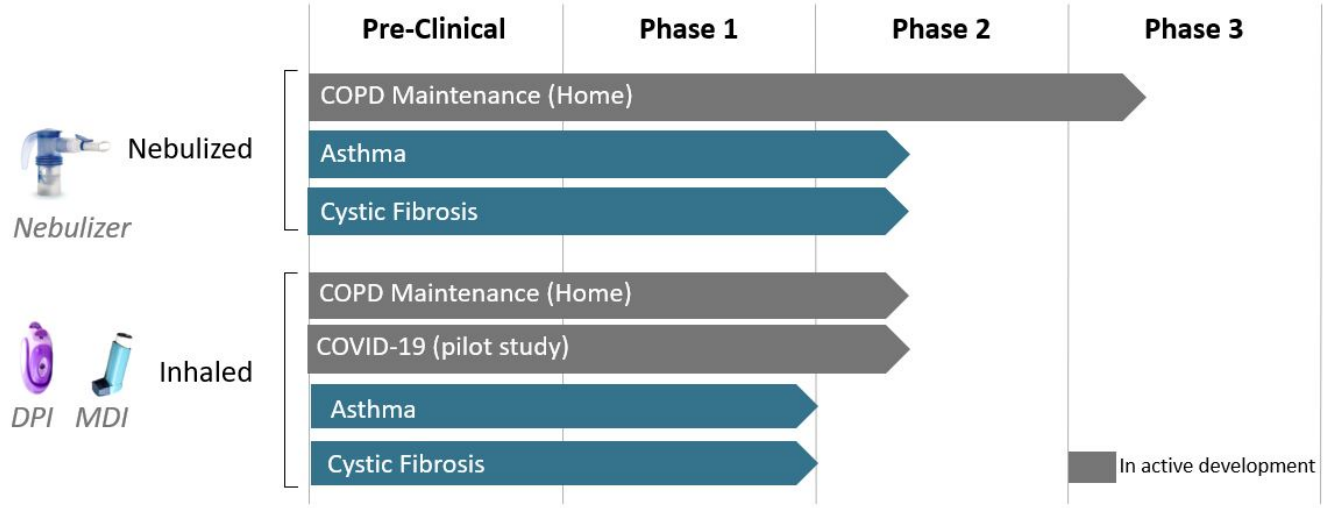
Verona Pharma has developed formulations of ensifentrine for the three most widely used inhalation devices: nebulizer, DPI and pMDI. The nebulized formulation of ensifentrine is designed to be suitable for use in a standard jet nebulizer, not a proprietary device. Delivery of COPD medications by nebulizer 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 may 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 in the approximately $9.6 billion U.S. market for maintenance COPD therapies.

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.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.

Verona Pharma has 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 dosing 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

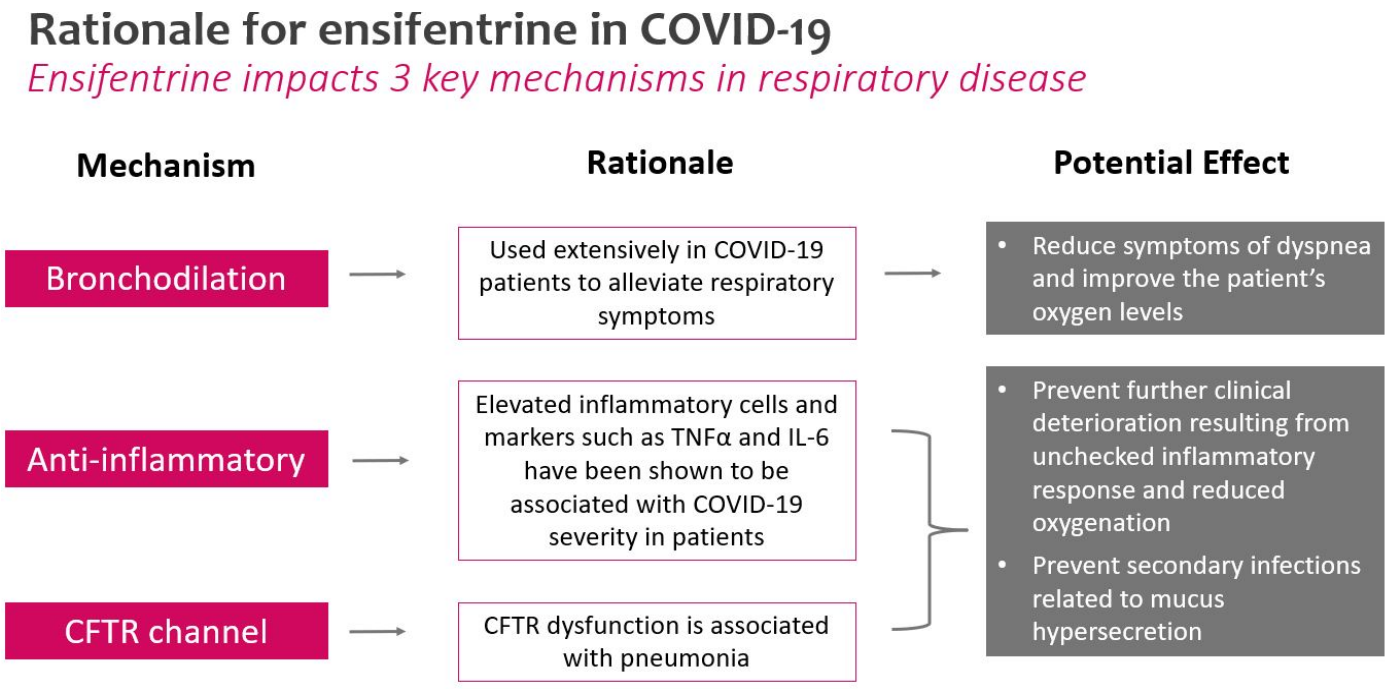
The following table summarizes our development programs.



Potential additional indications for ensifentrine

COVID-19

While our initial focus is COPD, we are also evaluating ensifentrine as a potential treatment option for COVID-19. Clinical data from prior studies of ensifentrine in other respiratory diseases demonstrated that ensifentrine improved lung function, reduced cellular markers of inflammation in the lungs and reduced symptoms of cough and sputum. We believe these results, if replicated in COVID-19 patients, could improve patient outcomes from COVID-19 by reducing dyspnea, targeting viral-induced inflammation in the lung, improving patient's oxygen levels and preventing secondary infections related to mucus hypersecretion.



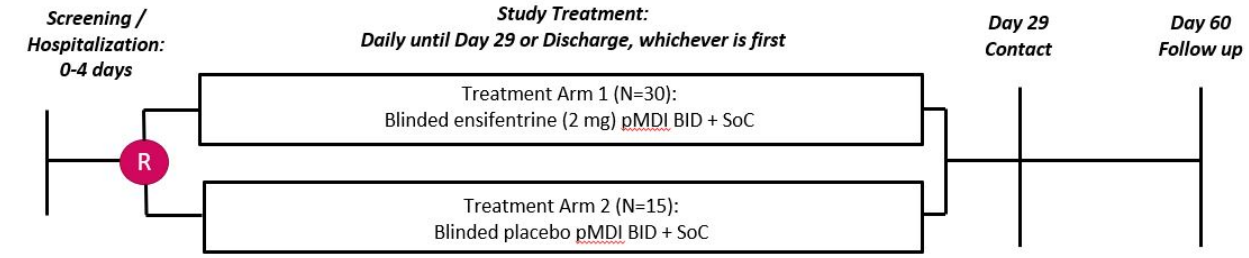
In January 2021, we completed enrollment (n=45) in a pilot study to evaluate pMDI ensifentrine in a randomized, double-blind, placebo-controlled pilot clinical study for the treatment of U.S. patients hospitalized with COVID-19.

The study will evaluate the effect of ensifentrine on key outcomes in patients hospitalized with COVID-19 including facilitation of recovery from the viral infection, clinical status improvement, reduction in supplemental oxygen use and progression to mechanical ventilation. We expect to report top-line results in the second quarter of 2021.

Ensifentrine: Treatment of hospitalized patients with COVID-19

Enrollment complete, top-line results in 2Q21

Pilot Study Objectives	• To evaluate treatment with ensifentrine on key outcomes in patients hospitalized with COVID-19 • Facilitation of recovery from the viral infection, clinical status improvement, supplemental oxygen use and reduction of progression to mechanical ventilation



Pilot Study Details	• Randomized, double-blind, single-center at University of Alabama, Birmingham • 2 mg dose or placebo; delivered twice daily added-on to standard of care • N=45 patients hospitalized with COVID-19 not on mechanical ventilator • Primary endpoint: Proportion of patients who recover from COVID-19 and are not hospitalized on day 29

Cystic fibrosis and asthma

In addition to COPD and COVID-19, we believe ensifentrine has potential applications in other respiratory diseases including CF and asthma.

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. More than 70,000 people worldwide are living with CF 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, taking an average of seven per day, including inhaled and injected treatments to clear mucus and fight infections as well as enzyme pills to digest food. 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, 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 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 300 million people worldwide suffer from asthma and it is the most common chronic disease among children, according to the World Health Organization.

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 bronchodilation that were comparable 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. We currently do not have any agreements for the commercial production of ensifentrine.

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

United States

In the United States, we are preparing to commercialize nebulized ensifentrine ourselves, if approved. Despite the availability of current therapies, it is estimated that 1.2 million patients remain symptomatic following treatment with maximum therapy. 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, which was conducted with U.S. healthcare providers and payers, we anticipate ensifentrine would be used primarily as an add-on to dual or triple therapy regimens and we anticipate the majority of ensifentrine usage would be initiated by pulmonologists. Due to this focused prescriber base, we anticipate needing a field sales force of approximately 100 representatives.

International

COPD effects over 384 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.

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 anti-inflammatory properties in a single compound. As far as we are aware, no other dual PDE3 and PDE4 inhibitor is on the market nor in clinical development. Based on our market research, we expect ensifentrine to be used mainly in addition to existing dual and triple therapies, LAMA / LABA / ICS where no additional treatment options exist for patients who

are symptomatic. Some healthcare providers have indicated that they would use it as earlier line therapy 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 MDI. 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 nebulizers 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® and Lonhala®Magnair®).

In the DPI/MDI 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, Utibron Neohaler®, a combination of a long-acting beta2-agonist and long-acting anti-muscarinic bronchodilator marketed by Novartis International AG, 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 and Chiesi Farmaceutici S.p.A., 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.

Other potential therapies in clinical development for the prevention of COPD exacerbations include injectable biologics. Sanofi's anti-IL4, Dupixent®, AstraZeneca's anti-IL5, Fasenra®, and GlaxoSmithKline's anti-IL5, Nucala®, 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 hold rights in the major markets relating to ensifentrine for treating respiratory disorders.

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, 2020, our patent portfolio consisted of eleven issued U.S. patents, three pending U.S. patent applications, forty-six issued foreign patents and forty-three pending foreign applications including two patent applications made under the Patent Cooperation Treaty. These patents and patent applications include claims directed to new dosage formulations comprising ensifentrine and a crystalline polymorph, as well as methods of making and using ensifentrine in the treatment of respiratory diseases, with expected expiry dates up to 2041.

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 United States 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 United States 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. We refer to the assignment and license agreement as the Ligand Agreement. In 2006, we acquired Rhinopharma and all its rights and liabilities under 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.

Under the Ligand Agreement, we are obligated to pay Ligand a milestone payment of £5.0 million upon the first approval of any regulatory authority for the commercialization of any Licensed Product, and a portion equal to a percentage in the mid-twenties of any consideration received from any of our sublicensees for Ligand Patents or Ligand know-how, excluding royalties. We must also pay Ligand, on a Licensed Product-by-Licensed Product and country-by-country basis, a low single digit percentage royalty based on net sales of each Licensed Product for a period beginning with the first commercial sale of such Licensed Product in a country and ending on the later of the expiration of a certain number of years after such first commercial sale and if applicable the expiration of the last to expire valid claim in the Ligand Patents covering the development, manufacture or commercialization of such Licensed Product in such country. Prior to the first commercial sale of each Licensed Product, such royalties also are due in the same percentages for any named patient sales.

The Ligand Agreement continues until terminated by either party in accordance with its terms. Either party may terminate the Ligand Agreement for an uncured material breach, bankruptcy or insolvency of the other party. 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.

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 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 assessment 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 and formulation studies in compliance with the FDA's good laboratory practice ("GLP") regulations;
- Submission to the FDA of an investigational new drug application ("IND"), which must become effective before human clinical trials may begin;
- 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 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 authorization from the FDA to ship in interstate commerce and administer an investigational new 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 new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which 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. 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. Sponsors typically use the meetings at the end of the Phase 2 trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new drug.

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.

While the IND is active and before approval, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report 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.

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.

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 the 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.

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 supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver from the FDA.

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 new 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 product candidate may be eligible for priority review. 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 intended to expedite the FDA review and approval process, such as priority review and accelerated approval. A product candidate is eligible for priority review if it 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, 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 post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required post-marketing studies 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 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 indication 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 indication 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 marketing 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 marketing 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.

Foreign regulation

In order to market any pharmaceutical 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. Each jurisdiction will apply these regulations in their assessment of clinical trial applications and marketing authorization applications. 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.

In order to market our future products in the EEA (which is comprised of the 27 Member States of the EU plus Norway, Iceland and Liechtenstein) and many other foreign jurisdictions, we must obtain separate regulatory approvals. With respect to the United-Kingdom, the transition period, during which EU pharmaceutical laws continued to apply to the United Kingdom expired on December 31, 2020. The EU and the United Kingdom have concluded a trade and cooperation agreement ("TCA"), which is provisionally applicable since January 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations.

In the EEA, a clinical trial application ("CTA") must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and the IRB, respectively. Once the CTA is approved by the national health authority and the ethics committee has granted a positive opinion in relation to the conduct of the trial in the relevant EU Member State(s), clinical study development may proceed. The requirements and process governing the conduct of clinical studies are to a significant extent harmonized at EU level but could vary from country to country. In all cases, the clinical studies must be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. The way clinical trials are conducted in the EU will undergo a major change when the Clinical Trial Regulation (Regulation (EU) No 536/2014) comes into application, probably in 2022. The Regulation harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which will contain a centralized EU portal and database. During the development of a pharmaceutical product, the European Medicines Agency ("EMA") and national regulators within the EU provide the opportunity for dialogue and guidance on the development program.

In the EEA, medicinal products can only be placed on the market after obtaining a Marketing Authorization ("MA"). There are two types of MAs:

- The Union MA, which is 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 which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of human medicinal products, such as medicines derived from biotechnology processes, advanced therapy medicinal products (such as gene therapy, somatic cell therapy and tissue engineered products), orphan designated medicinal products, products that contain a new active substance indicated for the treatment of certain diseases such as HIV/AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU. Under the centralized procedure the maximum timeframe for the evaluation of a or MA application, by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP; and
- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products 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 EEA, 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 NCA 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 EEA 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.

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 PRIME scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. Such products are generally eligible for accelerated assessment (according to which the timeframe for the evaluation of a MA application is reduced to 150 days, excluding clock stops) and may also benefit from different types of fast track approvals, such as a conditional marketing authorization or a marketing authorization under exceptional circumstances granted on the basis of less comprehensive clinical data than normally required (respectively in the likelihood that the sponsor will provide such data within an agreed timeframe or when comprehensive data cannot be obtained even after authorization).

In the EEA, new products authorized for marketing, or reference products, qualify for eight years of data exclusivity and an additional two years of market exclusivity upon MA. 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 marketing authorization 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 marketing authorization 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.

In the EEA, MA applications 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 is not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. We have received a waiver for pediatric data in COPD. Once the MA is obtained in all Member States of the EU and study results are included in the product information, even when negative, the product is eligible for six months' supplementary extension of the protection under a supplementary protection certificate (if any is in effect at the time of the approval) or, in the case of orphan pharmaceutical products, a two year extension of the orphan market exclusivity is granted.

The criteria for designating an "orphan medicinal product" in the European Union are similar in principle to those in the United States. A medicinal product may be designated as orphan if (1) it 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 European Union when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the European Union to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the European Union, or if such a method exists, the product will be of significant benefit to those affected by the condition. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. The application for orphan drug designation must be submitted before the application for MA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The 10-year market exclusivity 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, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. 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.

Similar to the United States, both marketing authorization holders and manufacturers of pharmaceutical products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the EU Member States. 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 pharmaceutical products and marketing of such products, both before

and after grant of the MA, manufacturing of pharmaceutical 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.

We are also subject to privacy laws in the jurisdictions in which we are established or in which we sell or market our products or run clinical trials. For example, in Europe, we are subject to Regulation (EU) 2016/679 (General Data Protection Regulation ("GDPR") in relation to our collection, control, processing and other use of personal data (i.e. data relating to an identifiable living individual). We process personal data in relation to participants in our clinical trials in the EEA., including the health and medical information of these participants. The GDPR is directly applicable in each EU Member State, however, it provides that EU Member States may introduce further conditions, including limitations which could limit our ability to collect, use and share personal data (including health and medical information), or could cause our compliance costs to increase, ultimately having an adverse impact on our business. The GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing and implement policies as part of its mandated privacy governance framework. It also requires data controllers to be transparent and disclose to data subjects (in a concise, intelligible and easily accessible form) how their personal information is to be used, imposes limitations on retention of personal data; defines for the first time pseudonymized (i.e., key-coded) data; introduces mandatory data breach notification requirements; and sets higher standards for data controllers to demonstrate that they have obtained valid consent for certain data processing activities. We are also subject to EU rules with respect to cross-border transfers of personal data out of the EU and EEA. We are subject to the supervision of local data protection authorities in those EU jurisdictions where we are established or otherwise subject to the GDPR. Fines for certain breaches of the GDPR are significant: up to the greater of €20 million or 4% of total global annual turnover. In addition to the foregoing, a breach of the GDPR could result in regulatory investigations, reputational damage, orders to cease/change our use of data, enforcement notices, as well potential civil claims including class action type litigation where individuals suffer harm. Following the United Kingdom's formal departure from the European Union on January 31, 2020 and the end of the transition period on December 31, 2020, the United Kingdom has become a "third country" for the purposes of EU data protection law. However, the TCA includes a provision, whereby the transfer of personal data from the EU to the United Kingdom will not be considered as a transfer to a "third country" for a period of four months starting from the entry into force of the TCA. This period will be extended by two further months, unless the EU or the United Kingdom objects.

Following the United Kingdom's formal departure from the European Union on January 31, 2020 and the end of the transition period on December 31, 2020, the United Kingdom has become a "third country" for the purposes of EU data protection law. However, the TCA includes a provision, whereby the transfer of personal data from the EU to the United Kingdom will not be considered as a transfer to a "third country" for a period of four months starting from the entry into force of the TCA. This period will be extended by two further months, unless the EU or the United Kingdom objects.

Other U.S. 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, data privacy and security 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 majority of states also have anti-kickback laws, which establish similar prohibitions and in some cases may apply to items or services reimbursed by any third-party payor, including commercial insurers.

The federal false claims and civil monetary penalties 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 67 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.

Violations of fraud and abuse laws, including federal and state anti-kickback and false claims laws, may be punishable by criminal and civil sanctions, including fines and civil monetary penalties, 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. 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.

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, the ACA broadened the reach of certain criminal healthcare fraud statutes created under HIPAA by amending the intent requirement such that 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 ACA imposed, among other things, new annual reporting requirements through the Physician Payments Sunshine Act for covered manufacturers for certain payments and "transfers of value" provided to physicians 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.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and their respective implementing regulations impose obligations relating to the privacy, security and transmission of individually identifiable health information held by covered entities and their business associates. Entities that are found to be in violation of HIPAA, whether as the result of a breach of unsecured PHI, a complaint about privacy practices, or an audit by HHS, may be subject to significant civil, criminal, and administrative fines and penalties and/or additional reporting and oversight obligations. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same requirements, thus complicating compliance efforts.

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 the EEA, 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. 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, the U.S. federal government has delayed or suspended implementation of certain provisions of the ACA. In addition, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. In addition, Congress could consider subsequent legislation to replace those elements of the ACA if so repealed. Further, on December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, ruled that the entire ACA is invalid based primarily on the fact that the Tax Cuts and Jobs Act of 2017 repealed the tax-based shared responsibility payment imposed by the ACA, on certain individuals who fail to maintain qualifying health coverage for all or part of a year, which is commonly referred to as the "individual mandate". Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. The United States Supreme Court is currently reviewing this case, although it is unclear when a will be made. It is also unclear how other efforts to challenge or replace the ACA will impact the law. The ultimate content, timing or effect of any healthcare reform legislation on the U.S. healthcare industry is unclear.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, and additional downward pressure on the price that we receive for any approved product. 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 effect 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. Moreover, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drugs.

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 of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2020, 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. 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.

We expect that additional state and federal 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 one approved or additional price increases.

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, 2020, we had 25 full-time and 2 part 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.

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. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.

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 $65.1 million and $40.6 million for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, we had an accumulated deficit of $207.1 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 expect to continue to incur significant operating losses for the foreseeable future as we expand our research and development efforts, advance our clinical development of ensifentrine, and seek to obtain regulatory approval for and commercialize ensifentrine. We anticipate that our expenses will increase substantially as we:

- conduct Phase 3 clinical trials of nebulized ensifentrine for the treatment of chronic obstructive pulmonary disease (“COPD”);
- initiate and conduct clinical trials of ensifentrine for the treatment of cystic fibrosis (“CF”), asthma, COVID-19 or other indications;

- initiate and conduct other future clinical trials in other formulations, 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;
- potentially establish a sales, marketing 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 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 and pre-clinical studies and clinical trials of ensifentrine. We are continuing development of ensifentrine, and we have not completed development of any product candidate or any drugs.

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, discovering and developing additional product candidates, obtaining regulatory approval for ensifentrine and any future product candidates that successfully complete clinical trials, establishing manufacturing and marketing capabilities and ultimately selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of many 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 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 of any future product candidates, or development of other formulations or target indications of ensifentrine, and to commercialize our products, including ensifentrine, if approved. If we are unable to raise capital when needed, 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 our ongoing Phase 2 and Phase 3 clinical trials of ensifentrine, and develop ensifentrine 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, we estimate that our existing cash resources and short-term investments will not be sufficient to commercialize ensifentrine. We will require additional funds to conduct any post-marketing studies to support the commercial positioning of ensifentrine for the treatment of COPD, if regulatory approval is received. 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.

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

- the costs, progress and results of our ongoing Phase 3 clinical trials for the maintenance treatment of COPD;
- the costs, timing and outcome of the regulatory 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 CF, asthma, COVID-19 or other indications;
- 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 for the maintenance treatment of COPD and potentially 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 heavily 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 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, which we do not expect will occur for at least the next several years, if ever, will depend heavily on the successful development and eventual commercialization of ensifentrine, if approved, which may never occur. Ensifentrine will require additional clinical development, management of clinical, pre-clinical and manufacturing activities, regulatory approval in multiple jurisdictions, 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 EMA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for ensifentrine or any future product candidate. We have not submitted an NDA to the FDA, a Marketing Authorization Application to the EMA or comparable applications to other regulatory authorities and do not expect to be in a position to do so in the foreseeable future. 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 planned 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;
- the applicable regulatory authorities may not accept data generated at our clinical trial sites;
- if we submit an NDA to the FDA, and it 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, or REMS, 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 plan to seek regulatory approval to commercialize ensifentrine both in the United States and the EU, and potentially in additional foreign 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.

The COVID-19 pandemic has and may continue to adversely impact our business, including our preclinical studies and clinical trials.

The COVID-19 pandemic has spread to multiple countries, including countries where we have operations or planned or ongoing preclinical studies and clinical trials. Governments from many countries have established stay at home measures including, among other things, the prohibition of public gatherings and restrictions on domestic and international travel. The pandemic and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. In response to the spread of COVID-19, we have closed our principal office in the U.K. and our office in the U.S. with all employees continuing their work outside of our offices. In addition, whilst we successfully initiated our Phase 3 program in the third quarter of 2020, we are investigating the potential impact of the COVID-19 pandemic on the program cost and timelines.

- If the COVID-19 pandemic continues for a significant length of time, we may experience additional disruptions that could severely impact our business, preclinical studies and clinical trials, including in particular the cost and timelines of our Phase 3 program and:
- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials in certain countries;
- delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- disruption to manufacturers that could affect the supply of drug product for our clinical trials or difficulty sourcing key components necessary for the manufacture of ensifentrine drug substance and drug product;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials, including the potential for COVID-19 test shortages and interruption in global shipping that may affect the transport of clinical trial materials;
- changes in local regulations as part of a response to the COVID-19 pandemic which may require us to undertake additional testing or change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue such clinical trials altogether;

- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others, or interruption of clinical trial subject visits and study procedures, the occurrence of which could affect the integrity of clinical trial data;
- risk that participants enrolled in our clinical trials will contract COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- interruptions or delays in preclinical studies due to restricted or limited operations at our third party research and development services;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees;
- diversion of or limitations on employee resources that would otherwise be focused on the operations of our business and the conduct of our clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;
- higher clinical trial insurance costs and/or delays in operations at insurance agencies, which may impact timelines for the issuance of insurance coverage policies and local coverage determinations delays; and
- refusal of the FDA, the EMA or comparable foreign regulatory authorities to accept data from clinical trials in affected geographies.

Health regulatory agencies globally may also experience disruptions in their operations as a result of the COVID-19 pandemic. The FDA, EMA and comparable foreign regulatory agencies may have slower response times or be under-resourced to review or meet to discuss our regulatory submissions, or to continue to monitor our clinical trials and, as a result, review, inspection and other timelines may be materially delayed.

The COVID-19 pandemic continues to rapidly evolve. The extent to which the pandemic impacts our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the pandemic, travel restrictions and social distancing, business closures or business disruptions, the availability and efficacy of vaccines, and the effectiveness of other actions taken to contain and treat the disease.

While the potential economic impact brought by and the duration of the COVID-19 pandemic may be difficult to assess or predict, the widespread pandemic has resulted in, and may continue to result in, significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, the recession or market correction resulting from the spread of COVID-19 could materially affect our business.

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 for ensifentrine, but we have not yet demonstrated our ability to successfully complete any Phase 3 or other pivotal clinical trials, obtain regulatory approvals, manufacture a commercial-scale product or arrange for a third party to do so on our behalf or conduct 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. If we raise additional capital through debt financing, the terms of any new debt could further restrict our ability to operate our business.

In November 2020, we and Verona Pharma, Inc. ("Verona U.S.") entered into a loan and security agreement (the "Loan Agreement"), with Silicon Valley Bank ("SVB"), pursuant to which a term loan facility in an aggregate

amount of up to $30.0 million (the "Term Loan") is available to us in three tranches. We received the first tranche of $5.0 million at closing. Only upon satisfaction of certain clinical milestones relating to ensifentrine and subject to customary terms and conditions will the following be available to the Company: (i) the second tranche will allow us to borrow an additional amount up to $10.0 million through June 30, 2022, and (ii) the third tranche will allow us to borrow an additional amount up to $15.0 million through June 30, 2023.

The Term Loan is secured by a lien on substantially all of our and Verona U.S.'s assets, other than the equity interests of Verona U.S. and other than intellectual property, provided that such lien on substantially all assets includes any rights to payments and proceeds from the sale, licensing or disposition of intellectual property. We have also granted SVB a negative pledge with respect to our intellectual property.

The Loan Agreement contains customary covenants and representations, including but not limited to financial reporting obligations and limitations on dividends, indebtedness, collateral, investments, distributions, transfers, mergers or acquisitions, taxes, corporate changes, deposit accounts, and subsidiaries. The Loan Agreement also contains other customary provisions, such as expense reimbursement, non-disclosure obligations as well as indemnification rights for the benefit of SVB. The Loan Agreement includes a minimum cash covenant triggered when our consolidated cash and cash equivalents drop below $45.0 million at any time after the occurrence of certain clinical and/or regulatory event. Upon such trigger, we would be required cash collateralize an amount equal to the outstanding obligations to SVB plus the amount of any prepayment penalty and a final payment which would be due in the event the Loan Agreement were prepaid in full with respect to the Term Loans advanced as of such time. Any such cash collateralization could have a material adverse impact on our liquidity and financial condition.

The events of default under the Loan Agreement include, but are not limited to: (i) insolvency, liquidation, bankruptcy or similar events; (ii) failure to pay any debts due under the Loan Agreement or other loan documents on a timely basis; (iii) failure to observe certain covenants under the Loan Agreement; (iv) occurrence of a material adverse effect; (v) material misrepresentation by us; (vi) occurrence of any default under any other agreement involving material indebtedness; and (vii) certain material money judgments. If we default under the Loan Agreement, SVB may accelerate all of our repayment obligations and take control of our and Verona U.S.'s pledged assets, potentially requiring us to renegotiate our agreement on terms less favorable to us or to immediately cease operations. Further, if we are liquidated, the lenders' right to repayment would be senior to the rights of our ADS holders or shareholders to receive any proceeds from the liquidation. Any declaration by SVB of an event of default could significantly harm our business and prospects and could cause the price of our ADSs to decline. 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, or 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, 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 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, including the withdrawal of the United Kingdom from the EU;
- 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, or natural disasters including earthquakes, typhoons, floods and fires, or public health emergencies, such as the COVID-19 pandemic.

The United Kingdom's withdrawal from the EU may have a negative effect on global economic conditions, financial markets and our business, which could reduce the price of our ADSs.

Following a national referendum and enactment of legislation by the government of the United Kingdom, the United Kingdom formally withdrew from the EU on January 31, 2020 and entered into a transition period during which it continued its ongoing and complex negotiations with the EU relating to the future trading relationship between the parties. The transition period ended on December 31, 2020, before which the United Kingdom and the European Commission reached an agreement on the future trading relationship between the parties (the "UK-EU Trade and Cooperation Agreement" or "TCA"). On December 30, 2020, the U.K. Parliament approved the European Union (Future Relationship) Bill, thereby ratifying the TCA. The TCA is subject to formal approval by the European Parliament and the Council of the European Union before it comes into effect and has been applied provisionally since January 1, 2021. Significant political and economic uncertainty remains about whether the terms of the relationship will differ materially from the terms before withdrawal.

These developments, or the perception that any of them could occur, have had and may continue to have a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Asset valuations, currency exchange rates and credit ratings may be especially subject to increased market volatility. Any of these factors could have a significant adverse effect on our business, financial condition, results of operations and prospects.

Further, the United Kingdom's withdrawal from the EU has resulted in the relocation of the EMA from the United Kingdom to the Netherlands. This relocation has caused, and may continue to cause, disruption in the administrative and medical scientific links between the EMA and the U.K. Medicines and Healthcare products Regulatory Agency, including delays in granting clinical trial authorization or marketing authorization, disruption of importation and export of active substance and other components of new drug formulations, and disruption of the supply chain for clinical trial product and final authorized formulations. The cumulative effects of the disruption to the regulatory framework may add considerably to the development lead time to marketing authorization and commercialization of products in the EU and/or the United Kingdom.

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

Owing to the international scope of our operations, fluctuations in exchange rates, particularly between the pound sterling and the U.S. dollar, may adversely affect us. Although we are based in the United Kingdom, we source research and development, manufacturing, consulting and other services from the United States and the EU. Further, potential future revenue may be derived from abroad, particularly from the United States. 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 involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

Our only product candidate, ensifentrine, is in clinical development. 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 desired safety and efficacy, 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. 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. Our future clinical trial results may not be successful.

We may experience delays in our ongoing 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;
- delays in or failure to obtain institutional review board ("IRB"), or ethics committee approval 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, or natural disasters including earthquakes, typhoons, floods and fires;
- 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 treat in a particular trial, which may delay enrollment.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials. 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 or any clinical trial of ensifentrine is terminated, the commercial prospects of ensifentrine may be harmed, and our ability to generate product revenues from ensifentrine, if any, will be delayed. Moreover, any delays in completing our clinical trials will increase our costs, slow down the development and approval process of ensifentrine 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 ensifentrine and could impair our ability to commercialize ensifentrine. 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.

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, or cGMP, 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 good clinical practice, or 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.

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, EMA 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 17 Phase 1 and 2 clinical trials of ensifentrine. In these trials, some patients have experienced mild to moderate adverse reactions, including headache, cough, worsening of COPD, nasopharyngitis 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, EMA 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 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 for multiple indications, including asthma, CF, COVID-19 or other respiratory diseases.

Part of our strategy is to continue to develop ensifentrine in indications other than COPD, such as CF, asthma and COVID-19. Although our research and development efforts to date have suggested that ensifentrine has the potential to treat CF, asthma and COVID-19, 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, 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 including COVID-19. 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 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 EMA 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 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 clinical and other 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 other reasons, not be sufficient to support the submission of an NDA in the United States, an MMA in the EU, or other comparable submission to obtain regulatory approval in other countries;
- the FDA, the EMA 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;
- the approval policies or regulations of the FDA, the EMA 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 EMA or any other regulatory authority.

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.

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 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 ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the FDA 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 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, including for 35 days beginning on December 22, 2018, 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, on March 10, 2020 the FDA announced its intention to postpone most inspections of foreign manufacturing facilities, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, on July 10, 2020 the FDA announced its intention to resume certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to 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, the EMA 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 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, the EMA 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. For example, the results of the 2020 U.S. Presidential election may impact our business and industry. Namely, the Trump administration took several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict whether or how these orders will be implemented, or whether they will be rescinded and replaced under a Biden administration. The policies and priorities of an incoming presidential administration are unknown and could materially impact the regulations governing our product candidate. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

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, 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, 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 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 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 Innovation at the Centers for Medicare & 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 and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. The current presidential administration and Congress will likely continue to seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA. Further, on December 14, 2018, a U.S. District Court Judge in the Northern District of Texas ruled that the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the 2017 Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court's decision that the individual mandate was unconstitutional but remanded the case back to the District Court to determine whether the

remaining provisions of the ACA are invalid as well. The United States Supreme Court is currently reviewing this case, although it is unclear when a decision will be made. It is also unclear how other efforts to challenge, repeal or replace the ACA will impact the law.

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 of 2% per fiscal year, which, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2021, 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. 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. 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.

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;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and regulations implemented thereunder, which also imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by covered entities subject to the rule, such as health plans, healthcare clearinghouses and healthcare providers as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information;
- 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 health care professionals beginning in 2022, 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; 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 state laws governing the privacy and security of health-related and other personal information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. For example, California recently enacted the California Consumer Privacy Act, or CCPA, which went into effect on January 1, 2020. The CCPA, among other things, creates data privacy obligations for covered companies and provides expanded privacy rights to California residents, 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, including for "protected health

information" maintained by a covered entity or business associate, it may regulate or impact our processing of personal information depending on the context;

- in the European Union, 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 European Union. 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; and
- European and other foreign law equivalents of each of the laws, including reporting requirements detailing interactions with and payments to healthcare providers and laws governing the privacy and security of certain personal data, such as the European Union General Data Protection Regulation, or GDPR, which imposes obligations and restrictions on the collection and use of personal data relating to individuals located in the EEA (including health data). Relatedly, following the United Kingdom's withdrawal from the EEA and the EU, and the expiry of the transition period, companies have 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. The relationship between the United Kingdom and the EU in relation to certain aspects of data protection law remains unclear, for example around how data can lawfully be transferred between each jurisdiction, which exposes us to further compliance risk.

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.

We are subject to governmental regulation and other legal obligations in the EU and European Economic Area, or EEA, related to privacy, data protection and data security. Our actual or perceived failure to comply with such obligations could harm our business.

We are subject to diverse laws and regulations relating to data privacy and security in the EU and the EEA, including the 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. The law is also developing rapidly and, in July 2020, the Court of Justice of the EU limited how organizations could lawfully transfer personal data from the EEA to the U.S. In addition, EU and EEA member states may impose further obligations relating to the processing of genetic, biometric or health data, which could further add to our compliance costs and limit how we process this information. 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. Relatedly, following the United Kingdom's withdrawal from the EEA and the European Union, and the expiry of the transition period, companies have 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. The relationship between the United Kingdom and the European Union in relation to certain aspects of data protection

law remains unclear, for example around how data can lawfully be transferred between each jurisdiction, which exposes us to further compliance risk.

Pursuant to the EU-UK Trade and Cooperation Agreement of December 24, 2020, transfers of personal data from the European Union to the United Kingdom may continue to take place without a need for additional safeguards during a further transition period, to expire on (1) the date on which an adequacy decision with respect to the United Kingdom is adopted by the EU Commission; or (2) the expiry of four months, which shall be extended by a further two months unless either the European Union or the United Kingdom objects. It remains unclear whether the EU Commission will adopt an adequacy decision with respect to the United Kingdom. In the absence of such decision after the expiry of the additional transition period, companies may need to put in place additional safeguards for transfers of personal data from the European Union to the United Kingdom, such as standard contractual clauses approved by the EU Commission.

We are also subject to evolving European privacy laws on cookies, and if we commence any EU marketing campaigns, also on e-marketing. The EU is in the process of replacing the e-Privacy Directive (2002/58/EC) with a new set of rules taking the form of a regulation, which will be directly implemented in the laws of each European Member State. The draft e-Privacy Regulation imposes strict opt-in marketing rules with limited exceptions for business-to-business communications, alters rules on third-party cookies, web beacons and similar technology and significantly increases fining powers to the greater of €20 million or 4% of total global annual revenue. While the e-Privacy Regulation was originally intended to be adopted on May 25, 2018 (alongside the GDPR), it is still going through the European legislative process.

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.

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 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 be subject to fines 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.

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 United States 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 and CF, we expect to face intense competition if ensifentrine is approved for these indications. Companies including Boehringer Ingelheim, GlaxoSmithKline, AstraZeneca, Mylan, Novartis, Vertex, Mylan, Gilead, Genentech and Sunovion currently have treatments on the market for COPD, CF and asthma, and we anticipate that new companies will enter these markets in the future. If we successfully develop and commercialize ensifentrine, 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 and marketing; 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.

We may be unable to obtain orphan drug designation from the FDA or EU for ensifentrine for the treatment of CF, and even if we do obtain such designations, we may be unable to obtain or maintain the benefits associated with orphan drug designation, including the potential for orphan drug exclusivity.

Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, defined as one occurring in a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the EU, orphan drug designation may be granted to promote the development of products that are intended for the diagnosis, prevention or treatment that is life-threatening or chronically debilitating affecting not more than five in 10,000 persons in the EU and for which no satisfactory method of diagnosis, prevention or treatment of the condition concerned can be authorized, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition. Additionally, designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the drug or biological product or where there is no satisfactory method of diagnosis, prevention or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding toward clinical trial costs, tax credits for qualified clinical testing and application fee waivers. In addition, if a product receives the first FDA approval of that drug for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the rare disease or condition. Under the FDA's regulations, the FDA will deny orphan drug exclusivity to a designated drug upon approval if the FDA has already approved another drug with the same active ingredient for the same indication, unless the drug is demonstrated to be clinically superior to the previously approved drug. In the EU, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

We plan to seek orphan drug designation from the FDA and the EMA for ensifentrine for the treatment of CF. Even if we are able to obtain orphan designation for ensifentrine in the United States and/or the EU, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products, which could prevent us from marketing ensifentrine if another company is able to obtain orphan drug exclusivity before we do. In addition, exclusive marketing rights in the United States may be unavailable if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition following approval. Further, even if we obtain orphan drug exclusivity for ensifentrine, that exclusivity may not effectively protect ensifentrine from competition because different drugs with different active moieties can be approved for the same condition.

In addition, the FDA or the EMA can subsequently approve products with the same active moiety for the same condition if the FDA or the EMA concludes that the later drug is clinically superior on the basis of greater safety, greater effectiveness, or a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. In addition, while we intend to seek orphan drug designation for ensifentrine for the treatment of CF, we may never receive such designation.

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 anticipate that Medicare Part B will play an important role in the reimbursement of ensifentrine. Changes within how products are reimbursed through Medicare Part B are likely to occur and those changes may effect 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 European Union, 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, the EMA 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 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 currently have no marketing, sales or distribution infrastructure. If we are unable to develop sales, marketing and distribution capabilities on our own or through collaborations, we may not be successful in commercializing ensifentrine.

We have no marketing, sales or distribution capabilities and we have no experience with marketing, selling or distributing pharmaceutical products. If ensifentrine is approved, we intend either to establish a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize ensifentrine, or to outsource this function to a third party. Either of these options would be expensive and time consuming. Some or all of these costs may be 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 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, the Competent Authorities of the Member States of the EEA 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 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.

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 MDI 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;
- business combinations or significant changes in a collaborator's business strategy may adversely affect our willingness to complete our obligations under any arrangement; 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 have limited personnel with experience in manufacturing, and 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, or CMOs, for the supply of cGMP-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 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 of these supplies by any CMO or its third-party suppliers, or the quality or quantity of such supplies. Moreover, we currently do not have any agreements for the commercial production of these 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.

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, MDI, 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. Our ensifentrine development program relies on the patents and patent applications assigned and know-how licensed from Ligand. 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 with third parties, we could lose license 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. Any uncured, material breach under these license agreements could result in our loss of rights to practice the patent rights and other intellectual property licensed to us 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.

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 do not currently own any registered trademarks. We may not be able to obtain trademark protection 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 2036. 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.
- 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.

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 proprietary information, or that of our manufacturers, suppliers and other parties that we use to conduct our pre-clinical and clinical trials and any future collaborators, may be lost or we may suffer security breaches.

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, collect and store sensitive data, including intellectual property, clinical trial data, proprietary business information and personally identifiable 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 this information is critical to our operations. 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 the COVID-19 pandemic, 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, 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. Despite our security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or breached due to employee error, malfeasance or other disruptions. Although to our knowledge we have not experienced any such material security breach to date, any such breach could compromise our networks and the 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 including the GDPR, 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.

Our information technology systems, and that of our manufacturers, suppliers and other third parties that we use to conduct our pre-clinical and clinical trials, could experience serious disruptions that could distract our operations and cause delays in our research and development work.

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, 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.

Risks Related to Employee Matters and Managing Growth

Our future growth and ability to compete depends on the successful transition of our CEO and CFO roles, retaining our key personnel and recruiting 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. On February 3, 2020 we announced the appointment of David Zaccardelli as chief executive officer with effect from February 1, 2020, following the retirement of Jan-Anders Karlsson, PhD. We also announced the appointment of Mark Hahn as chief financial officer with effect from March 1, 2020, as successor to Piers Morgan. We anticipate that we will experience a transitional period until our new chief executive officer and chief financial officer are fully integrated into their new roles and the transition may not be successful. Moreover, we cannot provide any assurance that the transition in leadership will not result in a disruption that adversely impacts our business and employee morale, or that successful working relationships between our other key management individuals and the new chief executive officer and chief financial officer will be developed.

Our other key management individuals include our general counsel, Claire Poll, our chief medical officer, Kathleen Rickard, our senior vice president, chemistry manufacturing and controls, Peter Spargo, our vice president, regulatory affairs, Desiree Luthman, our vice president of commercial, Christopher Martin, and our vice president, R&D operations, Tara Rheault. The loss of key managers and senior scientists could delay our 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 and sales and marketing 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 drug development, regulatory affairs and sales and marketing. 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 own a majority of our ordinary shares (including ordinary shares represented by ADSs) and as a result, are be able to exercise significant control over us.

As of December 31, 2020, our senior management, board of directors and greater than 5% shareholders and their respective affiliates, in the aggregate, owned approximately 21% of our ordinary shares (including ordinary shares represented by ADSs) assuming no exercise of outstanding options or warrants, and approximately 33% of our ordinary shares, assuming exercise of all options available for exercise and outstanding warrants. 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 be 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.

As of January 1, 2021, we were no longer a foreign private issuer and we are required to comply with the provisions of the Exchange Act, and the rules of Nasdaq, applicable to U.S. domestic issuers, which will continue to require us to incur significant expenses and expend time and resources.

As of January 1, 2021, we were no longer a foreign private issuer, and we are required to comply with all of the provisions applicable to a U.S. domestic issuer under the Exchange Act, including filing an annual report on Form 10-K, quarterly periodic reports and current reports for certain events, complying with the sections of the Exchange Act regulating the solicitation of proxies, requiring insiders to file public reports of their share ownership and trading activities and insiders being liable for profit from trades made in a short period of time. We are also no longer exempt from the requirements of Regulation FD promulgated under the Exchange Act related to selective disclosures. We are also no longer permitted to follow our home country's rules in lieu of the corporate governance obligations imposed by Nasdaq, and are required to comply with the governance practices required by U.S. domestic issuers listed on Nasdaq. We are also required to comply with all other rules of Nasdaq applicable to U.S. domestic issuers, including that our articles of association specify a quorum of no less than one-third of our outstanding voting common shares for meetings of our common shareholders, the solicitation of proxies and the approval by our shareholders in connection with certain events such as the acquisition of stock or assets of another company, the establishment of or amendments to equity-based compensation plans for employees, a change of control and certain private placements. In addition, we are required to report our financial results under U.S. generally accepted accounting principles, including our historical financial results, which have previously been prepared in accordance with IFRS.The regulatory and compliance costs associated with the reporting and governance requirements applicable to U.S. domestic issuers may be significantly higher than the costs we previously incurred as a foreign private issuer.

The regulatory and compliance costs associated with the reporting and governance requirements applicable to U.S. domestic issuers may be significantly higher than the costs we previously incurred as a foreign private issuer. We expect to continue to incur significant legal, accounting, insurance and other expenses and to expend greater time and resources to comply with these requirements. In addition, we may need to develop our reporting and compliance infrastructure and may face challenges in complying with the new requirements applicable to us.

We are an "emerging growth company," and we cannot be certain if the reduced reporting requirements applicable to "emerging growth companies" will make our ADSs less attractive to investors.

For as long as we continue to be an EGC, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not EGCs, including not being required to comply with the auditor attestation requirements of Section 404, not being required to present selected financial data for any period prior to the earliest audited period presented in our first registration statement, and exemptions from the requirement of holding a shareholder nonbinding advisory vote on executive compensation and golden parachute payments and from having to disclose the ratio of compensation of our chief executive officer to the median compensation of our employee. We may take advantage of these exemptions until we are no longer an EGC. We could be an EGC for up to five years, although circumstances could cause us to lose that status earlier, including if the aggregate market value of our ADSs and ordinary shares held by non-affiliates exceeds $700 million as of any June 30 (the end of our second fiscal quarter), in which case we would no longer be an emerging growth company as of the following December 31 (our fiscal year-end). We cannot predict if investors will find our ADSs less attractive because we may rely on these exemptions. If some investors find our ADSs less attractive as a result, there may be a less active trading market for our ADSs and the price of our ADSs may be more volatile.

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.

Management will be required to assess the effectiveness of our internal controls annually. However, for as long as we are an EGC, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. An independent assessment of the effectiveness of our internal controls could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls could lead to financial statement restatements requiring us to incur the expense of remediation and could also result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

We may have inadvertently violated Section 13(k) of the Exchange Act (implementing Section 402 of the Sarbanes-Oxley Act of 2002) and may be subject to sanctions as a result.

Section 13(k) of the Exchange Act provides that it is unlawful for a company, such as ours, that has a class of securities registered under Section 12 of the Exchange Act to, directly or indirectly, including through any subsidiary, extend or maintain credit in the form of a personal loan to or for any director or executive officer of the company. In August 2018, a receivable arose with respect to taxes due upon the vesting of restricted share units held by one of our directors and two of our executive officers, which may have violated Section 13(k) of the Exchange Act. The receivable was repaid, with interest, in March 2019, as soon as management became aware of the possible violation. Issuers that are found to have violated Section 13(k) of the Exchange Act may be subject to civil sanctions, including injunctive remedies and monetary penalties, as well as criminal sanctions. The imposition of any of such sanctions on us could have a material adverse effect on our business, financial position, results of operations or cash flows.

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 carry out research and development activities including, but not limited to, developing ensifentrine for various indications and delivery methods, and as a result we 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 provides relief against U.K. Corporation Tax.

Broadly, SME R&D Relief comprises two elements, (a) allowing qualifying SMEs to deduct a total of 230% (an additional 130% deduction plus the usual 100% deduction) of their qualifying expenditure from their yearly profit for U.K. Corporation Tax purposes, 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 14.5% 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 year ended December 31, 2019, we recorded an SME R&D Tax Credit of $9.3 million which was subsequently received in cash in the year ended December 31, 2020. For the year ended December 31, 2020, we recorded an SME R&D Tax Credit of $8.3 million, which we expect to receive in the year ended December 31, 2021. We estimate that in the financial years 2021-2023 we could be eligible to receive $25 million – $35 million in cash from HMRC in SME R&D Tax Credits (including the 2020 tax credit).

Legislation has been proposed that will, if enacted, limit the amount of SME R&D Tax Credit a company can claim in a period to £20,000 plus 300% of such company's liability for Pay As You Earn ("PAYE") and national insurance contributions, from 1 April 2021. There can be no assurance that the U.K. Government will not amend the program further, impacting the timing or amount of credits, or discontinue it entirely.

We are currently reviewing recent clarifications to the proposed legislation to evaluate the effect on our financing strategy. It is possible that our tax credit for the 2021 financial year, payable in 2022, will be impacted by the cap. If the legislation is enacted as currently drafted, we estimate the cash receivable under this program could be approximately $15 million lower than currently anticipated for 2021 and $6 million lower for 2022.

Taxation

We believe we will likely be classified as a passive foreign investment company for U.S. federal income tax purposes for the taxable year ended December 31, 2020, which could result in adverse U.S. federal income tax consequences to U.S. investors in our ADSs.

Because we do not earn revenue from our business operations, and because our sole source of income currently is interest on bank accounts held by us, we believe we will likely be classified as a "passive foreign investment company," or PFIC, for the taxable year ended December 31, 2020. A non-U.S. company will be considered a PFIC for any taxable year if (i) at least 75% of its gross income is passive income (including interest income), or (ii) at least 50% of the value of its assets (based on an average of the quarterly values of the assets during a taxable year) is attributable to assets that produce or are held for the production of passive income. If we are classified as a PFIC in any year with respect to which a U.S. Holder (as defined below) 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 we are classified as a PFIC for any taxable year during which a U.S. Holder 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 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 with certain reporting requirements. 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 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; or an estate or trust the income of which is subject to U.S. federal income taxation regardless of its source.

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 controlled foreign corporation 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 CFCs, regardless of whether we 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 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.

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, and particularly after we no longer qualify as an emerging growth company, or EGC, 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. 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. However, while we remain an EGC, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To prepare for eventual compliance with Section 404, once we no longer qualify as an EGC, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt 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. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed time frame or at all, 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.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our corporate headquarters is in leased office space at 3 More London Riverside, London, U.K. The leases on the offices expire in the first quarter of 2022. We also have office space at 8045 Arco Corporate Drive, Suite 130, Raleigh, NC 27617, USA, that expires in the second quarter of 2024. We have vacated premises in New York after consolidating our U.S. operations in North Carolina but continue to hold the lease until the third quarter of 2021. 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 19, 2021, 94.5% of our ordinary shares are held in ADS form, between 73 holders. The 5.5% balance of our ordinary shares are held as unlisted ordinary shares between 436 holders.

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

On July 17, 2020, we issued securities in a private placement ("Private Placement") with new and existing institutional and accredited investors. The Private Placement comprised a placement, in reliance upon the exemption from securities registration afforded by the provisions of Section 4(a)(2) of Regulation D of the Securities Act, of 38,440,009 ADSs, each representing eight Ordinary Shares or non-voting Ordinary Shares of the Company, at a price of $4.50 per ADS, and 48,088,896 of the Company's Ordinary Shares at the equivalent price per Ordinary Share of $0.5625.

The net proceeds of the Private Placement were approximately $185.5 million after deducting fees paid to Jefferies LLC in its role as placement agent and associated expenses.

The securities were subsequently registered on a registration statement on Form F-1 filed with the SEC on August 17, 2020 (File No. 333-247928), as amended.

Use of Proceeds

In May 2017, we completed the initial public offering of our ADSs in the United States and a private placement of our ordinary shares in Europe, or the global offering. In the global offering we issued and sold 6,501,738 ADSs, including 733,738 ADSs issued and sold upon the partial exercises by the underwriters pursuant to their overallotment option to purchase additional ADSs, at a public offering price of $13.50 per ADS, and 1,225,001 ordinary shares at an offering price of £1.32 per share. We received aggregate gross proceeds from the global offering of approximately $89.9 million, and aggregate net proceeds of approximately $80.8 million after deducting underwriting discounts and commissions of approximately $6.3 million and offering expenses of approximately $3.2 million. No payments for such expenses were made directly or indirectly to (i) any of our officers, members of our board of directors, or their associates, (ii) any persons owning 10% or more of any class of our equity securities or (iii) any of our affiliates.

The offer and sale of the ADSs and ordinary shares in the global offering were registered under the Securities Act pursuant to a registration statement on Form F-1 (File No. 333-217124) to register ordinary shares, which was declared effective by the SEC on April 26, 2017, a registration statement on Form F-1 to register additional ordinary shares (File No. 333-217487), which was immediately effective upon filing on April 26, 2017, and a registration statement on Form F-6 (File No. 333-217353) to register the ADSs, which was declared effective by the SEC on April 26, 2017, or, collectively, the Registration Statements. Under the Registration Statements, we registered an aggregate offering price of approximately $91.7 million of ordinary shares and 100,000,000 ADSs for a registered aggregate offering price of $5.0 million.

There has been no material change in our planned use of the net proceeds from the global offering as described in our final prospectus filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on April 28, 2017. As of December 31, 2018, we had used all of the net proceeds from the global offering.

Item 6. Selected Financial Data

We are a smaller reporting company as defined in Rule 12b-2 of the Exchange Act and are not required to provide the information otherwise required under this Item 6.

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."

Overview

We are a clinical-stage biopharmaceutical company focused on developing and commercializing innovative therapeutics for the treatment of respiratory diseases with significant unmet medical need. Our product candidate, ensifentrine, is an investigational, potential first-in-class, inhaled, dual inhibitor of the enzymes phosphodiesterase 3 and 4, or PDE3 and PDE4, that is designed to act as both a bronchodilator and an anti-inflammatory agent. In the third quarter of 2020 we commenced our Phase 3 ENHANCE trials and, if approved, we intend to commercialize ensifentrine for the maintenance treatment of COPD for the nebulized formation in the U.S.

We have incurred recurring losses and negative cash flows from operations since inception, and have an accumulated deficit of $207.1 million as of December 31, 2020. 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 that our expenses will increase significantly in connection with our ongoing activities, as we:

- continue to invest in the clinical development of ensifentrine for the treatment of COPD;
- manufacture ensifentrine and engage in other Chemistry, Manufacturing and Control activities;
- maintain, expand and protect our intellectual property portfolio; and
- enhance our commercial insights and capabilities.

On July 17, 2020, we raised $200 million in a private placement (the "Private Placement"), with net proceeds after transaction related fees and expenses of $185.5 million.

In November 2020, we and Verona Pharma, Inc. ("Verona U.S.") entered into a term loan facility of up to $30.0 million (the "Term Loan"), consisting of term loan advances in an aggregate amount of $5.0 million funded at closing, a term loan advance available subject to certain terms and conditions in an aggregate amount of $10.0 million, and a term loan advance available subject to certain terms and conditions in an aggregate amount of $15.0 million with Silicon Valley Bank ("SVB"). See "Indebtedness" below.

We believe that our cash and cash equivalents as of December 31, 2020, together with funding expected to become available under the Term Loan and from cash receipts from U.K. tax credits, will enable us to fund our planned operating expenses and capital expenditure requirements into 2023.

COVID-19 impact and business continuity

To help protect the health and safety of the patients, caregivers and healthcare professionals involved in its ongoing clinical trials of ensifentrine, as well as our employees and independent contractors, we continue to follow guidance from the FDA and other health regulatory authorities regarding the conduct of clinical trials during the COVID-19 pandemic to ensure the safety of study participants, minimize risks to study integrity, and maintain compliance with good clinical practice. We continue to review this guidance and the effect of the COVID-19 pandemic on our operations and clinical trials and will provide an update if we become aware of any meaningful disruption caused by the pandemic to our clinical trials.

We are closely monitoring activities at our contract manufacturers associated with clinical supply for our ongoing clinical trials, and are satisfied that appropriate plans and procedures are in place to ensure uninterrupted future supply of ensifentrine to the clinical trial sites, subject to potential limitations on their operations and on the supply chain due to the COVID-19 pandemic. We continue to monitor this situation and will provide an update if we become aware of any meaningful disruption caused by the pandemic to the clinical supply of ensifentrine for our clinical trials.

Significant contracts

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 "Licensed Products") developed using Ligand Patents, Ligand know-how and the physical stock of certain compounds.

The contingent liability comprises a milestone payment on obtaining the first approval of any regulatory authority for the commercialization of a Licensed Product, low single digit royalties based on the future sales performance of all 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.

At time of the acquisition the contingent liability was not recognized as part of the acquisition accounting as it was immaterial. We will therefore record as an R&D expense the milestone payment or royalties when they are payable.

Warrants

On July 29, 2016, as part of a placement we issued warrants to investors. The warrant holders can subscribe for an ordinary share at a per share exercise price of £1.7238. They can also opt for a cashless exercise of their warrants whereby they can choose to exchange the warrants held for a reduced number of warrants exercisable at nil consideration.

If, after a transaction, should the warrants be exercisable for unlisted securities, the warrant holders may demand a cash payment instead of the delivery of the underlying securities. Accordingly, they are accounted for as a liability under ASC 480 "Distinguishing Liabilities from Equity" and recorded at fair value using the Black-Scholes valuation methodology, on recognition and at each reporting date. The warrants are currently exercisable and may be exercised by the holders until April 2022 when the warrant instruments may either be exercised, cashlessly exercised, or expire.

Loan and security agreement

In November, 2020, we entered into the Term Loan. See "Indebtedness" for additional information.

Critical accounting policies and significant judgments and estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America ("US 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 US 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 financial statements appearing elsewhere in this Annual Report, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

Stock-based compensation and warrants

We have share-based compensation plans under which various types of equity-based awards may be granted, including stock options and restricted stock units (RSUs). The fair value of share options and RSUs is recognized as compensation expense using the cliff vesting method; forfeitures are recognized as they occur. We use the fair-value based method to determine compensation for all arrangements under which employees receive shares, using the Black-Scholes methodology. The warrants are recorded at fair value, also using this methodology.

The Black-Scholes valuation methodology uses assumptions for expected volatility, expected dividends, expected term, and the risk-free interest rate.

Expected volatility for options is based on the historical volatility of our ordinary shares. For warrants, it is based on a basket of the Company's and similar entities' share or ADS prices.

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. For the warrants the expected term is assumed to be until expiry of the instruments.

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 began using U.S. government debt yields.

Research and development costs

Research and development ("R&D") costs are charged to the consolidated statements of operations and comprehensive loss, as incurred. As part of the process of preparing financial statements 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 its 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.

Components of results of operations

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

- conduct our ongoing Phase 3 clinical trials for ensifentrine for the maintenance treatment of COPD;
- continue the clinical development of our DPI and pMDI formulations of ensifentrine and research and develop other formulations of ensifentrine;
- initiate and conduct further clinical trials for ensifentrine for the treatment of 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;
- potentially establish a sales, marketing and distribution infrastructure and scale-up manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- maintain, expand and protect our intellectual property portfolio;
- 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.

Operating expenses

R&D costs

R&D 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.

We expect our research and development costs to significantly increase in the near future as we progress our ENHANCE program. Due to the nature of research and development, the expected costs are inherently uncertain and may vary significantly from our current expectations.

General and administrative costs

General and administrative costs consist of salary and personnel related costs, including share based expense, expenses relating to operating as a public company, including professional fees, insurance and commercial related costs.

We expect commercial costs to increase as we continue to develop our potential commercial operations and, in the event of successful regulatory approval, we expect to 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 foreign exchange movements on cash and cash equivalents, interest income and the U.K. tax credits.

We are entitled to participate in the U.K. Small and Medium Enterprises R&D 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 the Company. Credits recorded in the 2020 financial year are expected to be received in the 2021 financial year.

The U.K. tax authorities have reviewed legislation and have proposed to cap the amount payable in the program to a multiple of employment taxes a company pays in the year in question, from April 1, 2021. We are currently reviewing recent clarifications to these proposed changes to review the effect on our financing strategy. It is possible that our tax credit for the 2021 financial year, payable in 2022, will be impacted by the cap. If the legislation is enacted as currently drafted, we estimate the potential cash received under this program could be approximately $15 million and $6 million lower than currently anticipated in 2022 and 2023.

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, 2020 and 2019

In prior periods, we prepared our financial information in accordance with IFRS. As a consequence of becoming a U.S. domestic issuer as of January 1, 2021, we are required to present our financial information in accordance with US GAAP and expressed in U.S. dollars from that date. The below financial information has been prepared in accordance with US GAAP. The financial information should not be expected to correspond to figures we have previously presented under IFRS.

The following table shows our statements of operations for the years ended December 31, 2020 and 2019, (in thousands):

	Year ended December 31,		
	2020	2019	Variance
Operating expenses			
Research and development	$ 44,505	$ 42,417	$ 2,088
General and administrative	29,772	9,986	19,786
Total operating expenses	74,277	52,403	21,874
Operating loss	(74,277)	(52,403)	(21,874)
Other income / (expense)			
Benefit from R&D tax credit	8,267	9,283	(1,016)
Interest income	121	964	(843)
Interest expense	(35)	—	(35)
Fair value movement on warrants	(1,136)	2,066	(3,202)
Foreign exchange gain / (loss)	2,060	(399)	2,459
Total other income, net	9,277	11,914	(2,637)
Loss before income taxes	(65,000)	(40,489)	(24,511)
Income tax expense	(146)	(72)	(74)
Net loss	$ (65,146)	$ (40,561)	$ (24,585)

Research and development costs

Research and development costs were $44.5 million for the year ended December 31, 2020, compared to $42.4 million for the year ended December 31, 2020, an increase of $2.1 million. This increase was primarily due to a $7.7 million increase in share-based compensation charges and a $1.0 million increase in salary and related costs as we increased the development team in 2019 and 2020.

Offsetting this, clinical trial costs fell by $5.2 million from 2019 to 2020. There were seven clinical trials (ongoing, in preparation or closing down) in 2020 compared to five in 2019, but the costs related to the Phase 2b four-week clinical study with ensifentrine added on to tiotropium in 2019 were significantly higher than the start-up costs of the ENHANCE program in 2020. Additionally, travel, manufacturing and development related consulting expenses were $1.4 million lower in 2020 compared to 2019.

General and administrative costs

General and administrative costs were $29.8 million for the year ended 2020 compared to $10.0 million for the year ended 2019, an increase of $19.8 million. This increase was driven primarily by an $11.4 million increase in share-based compensation charges, $3.0 million related to severance and other executive change costs, a $2.5 million increase in Directors' and Officers' insurance, $1.9 million of expenses relating to the Private Placement and a $1.0 million increase in professional fees, office close down costs and foreign exchange movements, partially offset by lower travel and other expenses.

Other income / (expense)

The R&D tax credit for 2020 was $8.3 million compared to a credit of $9.3 million for the year ended December 31, 2019, a decrease of $1.0 million. This reduction is attributable to our lower qualifying expenditure on research and development in 2020 compared to 2019.

Interest received on cash and short term investments decreased by $0.8 million due to lower overall interest rates and a change in our investment policy to use lower yielding government debt money market funds compared to term deposits previously utilized.

The foreign exchange gain of $2.1 million in 2020 and loss of $0.4 million in 2019 relate to the foreign exchange movements on the cash and short term investments the Company holds in pounds sterling.

Net loss

Net loss was $65.1 million for the year ended December 31, 2020, compared to $40.6 million for the year ended December 31, 2019. The increase in net loss was primarily the result of the increase in operating costs and the fall in other income, net, discussed above.

Cash flows

The following table summarizes our cash flows for the years ended December 31, 2020 and 2019 (in thousands):

	Year ended December 31,		
	2020	2019	Variance
Cash and cash equivalents at beginning of the year	$ 30,428	$ 25,243	$ 5,185
Net cash used in operating activities	(45,076)	(42,868)	(2,208)
Net cash provided by investing activities	9,710	47,314	(37,604)
Net cash provided by financing activities	192,343	—	192,343
Effect of exchange rate changes on cash and cash equivalents	581	739	(158)
Cash and cash equivalents at end of the year	$ 187,986	$ 30,428	$ 157,558

Operating activities

Net cash used in operating activities increased to $45.1 million 2020, from $42.9 million in 2019, an increase of $2.2 million. Operating expenses increased by $19.8 million, however $19.1 million of this was the non-cash share based compensation expense. The remaining variance of $1.5 million is due to the timing of supplier payments.

Investing activities

Net cash provided by investing activities decreased to $9.7 million for 2020, from $47.3 million in 2019 due to less movement of funds from short term investments to cash in 2020.

Financing activities

Net cash provided by financing activities was $192.3 million for 2020 driven by net proceeds from the Private Placement and the first advance received under the Term Loan. We received $185.5 million after costs in the Private Placement. Of the costs, $1.9 million were recorded in the statement of operations and comprehensive loss and therefore included in net cash used in operating activities. Financing activities also includes a net $4.9 million receipt from the term loan facility. There was no cash provided by financing activities during the year ended December 31, 2019.

Liquidity and capital resources

We do not currently have any approved products and have never generated any revenue from product sales or otherwise. To date, we have financed our operations primarily through the issuances of our equity securities, including warrants, and in 2020 from borrowings under the Term Loan.

We have incurred recurring losses since inception, including net losses of $65.1 million, and $40.6 million for the years ended December 31, 2020, and 2019, respectively. In addition, as of December 31, 2020, we had an accumulated deficit of $207.1 million. We expect to continue to generate operating losses for the foreseeable future.

In July 2020, we raised approximately $200 million in the Private Placement with new and existing institutional and accredited investors. The Private Placement comprised a placement of 38,440,009 ADSs, each representing eight Ordinary Shares or non-voting Ordinary Shares of the Company, at a price of $4.50 per ADS, and 48,088,896 of the Company's Ordinary Shares at the equivalent price per Ordinary Share of $0.5625.

The net proceeds of the Private Placement were approximately $185.5 million after deducting placement agent fees and associated expenses (including costs recorded to both equity and as expense in the consolidated statement of operations and comprehensive loss).

We have no ongoing material financing commitments, such as lines of credit or guarantees, that are expected to affect our liquidity over the next five years, other than leases and the Term Loan with Silicon Valley Bank.

Indebtedness

In November, 2020, we and Verona Pharma, Inc. (the "Borrowers") entered into the Term Loan facility of up to $30.0 million, consisting of term loan advances in an aggregate amount of $5.0 million funded at closing, a term loan advance available subject to certain terms and conditions in an aggregate amount of $10.0 million (the "Term B Loan") and a term loan advance available subject to certain terms and conditions in an aggregate amount of $15.0 million (the "Term C Loan"), with Silicon Valley Bank, a California corporation ("SVB"), the proceeds of which will be used for general corporate and working capital purposes.

The Term Loan is governed by a loan and security agreement, dated as of November 19, 2020, between the Borrowers and SVB (the "Loan Agreement"). The Term B Loan will be available, subject to and customary terms and conditions, during the period commencing upon the achievement of a specific clinical milestone relating to ensifentrine through and including June 30, 2022. The Term C Loan will be available, subject to customary terms and conditions, during the period commencing upon the achievement of an additional specific clinical milestone relating to ensifentrine through and including June 30, 2023.

The Term Loan will mature on November 1, 2024. Each advance under the Term Loan accrues interest at a floating per annum rate equal to the greater of (a) the sum of the prime rate reported in The Wall Street Journal plus 1.00% and (b) four and one-quarter of one percent (4.25%). The Term Loan provides for interest-only payments on a monthly basis until the payment date immediately preceding December 1, 2023. 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 Borrowers shall make a final payment to SVB in the amount of 10% of the aggregate Term Loans advanced (the "Final Payment"). The Borrowers may prepay the Term Loan in full but not in part provided that the Borrowers (i) provide ten days prior written notice to SVB, (ii) pays on the date of such prepayment (A) all outstanding principal plus accrued and unpaid interest, (B) a prepayment fee of $450,000 plus 3.0% of the Term C Loans advanced if paid on or before the first anniversary of the closing date; $300,000 plus 2.00% of the Term C Loans advanced if paid after the first anniversary of the closing date and on or before the second anniversary of the closing date; and $150,000 plus 1.00% of the Term C Loans advanced if paid thereafter and prior to maturity, (C) the Final Payment and (D) all other sums, if any, that shall become due and payable with respect to the Term Loan Advances, including interest at the Default Rate with respect to any past due amounts. Amounts outstanding during an event of default are payable upon SVB's demand and shall accrue interest at an additional rate of 3.0% per annum.

The Term Loan is secured by a lien on substantially all of the assets of the Borrowers, other than the equity interests of Verona U.S. and other than intellectual property, provided that such lien on substantially all assets includes any rights to payments and proceeds from the sale, licensing or disposition of intellectual property. The Borrowers have also granted SVB a negative pledge with respect to its intellectual property.

The Loan Agreement contains customary covenants and representations, including but not limited to financial reporting obligations and limitations on dividends, indebtedness, collateral, investments, distributions, transfers, mergers or acquisitions, taxes, corporate changes, deposit accounts, and subsidiaries. The Loan Agreement also contains other customary provisions, such as expense reimbursement, non-disclosure obligations as well as indemnification rights for the benefit of SVB. The Loan Agreement includes a minimum cash covenant triggered when Borrowers' consolidated cash and cash equivalents drop below $45.0 million at any time after the earliest to occur of any of the following: (i) the release of negative data from Enhance 2 and/or Enhance 1, which in the reasonable business discretion of Borrowers' senior management, would be considered insufficient to support submission of an NDA to the FDA, (ii) the FDA issues a complete response letter with respect to an NDA submitted for ensifentrine, or (iii) failure to achieve a specific regulatory milestone relating to ensifentrine by June 30, 2023 (extendable to March 31, 2024 upon the Borrowers receiving a specified amount of new cash proceeds after

September 8, 2020 from the sale of equity securities in one or more public financings or other bona fide equity financings, subordinated debt and/or upfront/milestone payments from one or more collaboration agreements not prohibited in the Loan Agreement). Upon such trigger, Borrowers must cash collateralize an amount equal to the outstanding obligations to SVB plus the amount of any prepayment penalty and Final Payment which would be due in the event the Loan Agreement were prepaid in full with respect to the Term Loans advanced as of such time.

The events of default under the Loan Agreement include, but are not limited to, the Borrowers' failure to make any payments of principal or interest under the Loan Agreement or other transaction documents, the Borrowers' breach or default in the performance of any covenant under the Loan Agreement or other transaction documents, the occurrence of a material adverse change, any Borrower making a false or misleading representation or warranty in any material respect under the Loan Agreement, any Borrower's insolvency or bankruptcy, any attachment or judgment on any Borrower's assets of at least $500,000, or the occurrence of any default under any agreement or obligation of any Borrower involving indebtedness in excess of $500,000. If an event of default occurs, SVB is entitled to take enforcement action, including acceleration of amounts due under the Loan Agreement.

Funding requirements

We initiated our Phase 3 ENHANCE program for the maintenance treatment of COPD in the third quarter of 2020 after raising funds in the Private Placement that we estimated to be the required funds to complete this program. We believe that our cash and cash equivalents as of December 31, 2020, together with funding expected to become available under the Term Loan and from cash receipts from U.K. tax credits, will enable us to fund our planned operating expenses and capital expenditure requirements into 2023.

We will require significant additional capital to further advance clinical and regulatory activities, to fund prelaunch and launch related costs and to create an effective sales and marketing organization to commercialize ensifentrine. We will 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 finance 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 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 revenues, 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 revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if ever. Accordingly, we will need to obtain substantial additional funds to achieve our business objective.

Off-balance sheet arrangements

We do not have any relationships with unconsolidated entities or financial partnerships, including entities sometimes referred to as structured finance or special purpose entities that were established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purposes. We do not engage in off-balance sheet financing arrangements. In addition, we do not engage in trading activities involving non-exchange traded contracts. We therefore believe that we are not materially exposed to any financing, liquidity, market or credit risk that could arise if we had engaged in these relationships.

Recent accounting pronouncements

For a discussion of pending and recently adopted accounting pronouncements, see Note 2 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K

Conversion from IFRS to US GAAP

As the Company no longer qualifies as a Foreign Private Issuer, its consolidated financial statements have been retroactively converted from IFRS to US GAAP.

The significant differences between IFRS and US GAAP as they relate to the Company are as follows:

(a) Rhinopharma acquisition

In connection with the Rhinopharma acquisition in 2006, an in-process R&D ("IP R&D") asset was recognized at fair value under both IFRS (IFRS 3 "Business Combinations") and US GAAP (FAS 141 "Business Combinations"). Under US GAAP the IP R&D asset was expensed immediately after its recognition in the business combination.

Also as part of the acquisition, and under both IFRS and US GAAP, an assumed contingent liability was identified but was not recognized as the fair value was immaterial. Under IFRS the assumed contingent liability was subsequently measured at amortized cost as the discounted expected value of the milestone payment and estimated royalty payments. It was re-measured for changes in these estimated cash flows or when the probability of achieving regulatory approval and commercial revenue changed. Re-measurements relating to changes in estimated cash flows and probabilities of success were recognized in the IP R&D asset. Under US GAAP, the contingent consideration will be recognized at the time each element of the contingency is resolved, and will be charged to R&D expense.

(b) Patents

Under IFRS the Company recognized the cost of patent applications and associated legal costs as intangible fixed assets. Under US GAAP, in the absence of regulatory approval, these costs are expensed as incurred.

(c) Social security costs on share based compensation

Under IFRS the Company accrued the cost of the Company's social security contributions on share-based compensation. Under US GAAP this cost is recognized when RSUs vest or options are exercised.

The significant differences in the Consolidated Statements of Operations and Comprehensive Loss were as follows (in thousands):

	December 31, 2019
Net loss - IFRS	$ (40,511)
Reversal of accounting for contingent consideration	135
Reversal of patent amortization and current period patent costs, net	(185)
Net loss - US GAAP	$ (40,561)

(d) Research and development tax credit - reclassification

The U.K R&D tax credit receivable is an estimate of the amount expected to be received in cash from the U.K. government in the following fiscal year relating to the Small and Medium Enterprise Program (the "R&D Tax Credit"). It relates to the estimated research and development tax credit receivable on qualifying expenditure incurred in the year.

Under IFRS the Company recorded the R&D Tax Credit in income taxes. Under US GAAP the credit is considered to be akin to a government grant and is recorded as other income.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We are a smaller reporting company as defined in Rule 12b-2 of the Exchange Act and are not required to provide the information otherwise required under this Item 7A.

Item 8. Financial Statements and Supplementary Data

The information required by this Item is set forth in the consolidated financial statements and notes thereto in Item 15 of Part IV of this Annual Report.

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

None

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.

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, 2020, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

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

Our management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth 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, 2020, our internal control over financial reporting was effective.

Attestation Report of the Registered Public Accounting Firm

This Annual Report does not include an attestation report of our registered public accounting firm due to an exemption established by the JOBS Act for "emerging growth companies."

Changes in Internal Control over Financial Reporting

Our consolidated financial statements for the year ended December 31, 2020, were prepared in compliance with generally accepted accounting principles in the U.S. which represents a change in accounting principles previously applied in financial statements prepared by us for prior periods that were prepared in accordance with International Financial Reporting Standards. We have added to or updated the functioning of our existing internal controls over financial reporting to accommodate the necessary changes to continue to provide reasonable assurance to prevent or detect misstatements in the preparation and presentation of our financial statements. Except as described herein, there was no change in our internal control over financial reporting (as defined in Rules 13a-15(f) under the Exchange Act) that occurred during the fourth quarter of fiscal year ended December 31, 2020, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None

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 amendment to, or waiver 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 2021 Annual General Meeting of Stockholders 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 2021 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 2021 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 2021 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 2021 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

As part of this Annual Report on Form 10-K, the consolidated financial statements are listed in the accompanying index to financial statements on page F-1.

(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 on Form 10-K.

		Incorporated by Reference to Filings Indicated				
Exhibit Number	Exhibit Description	Form	File No.	Exhibit No.	Filing date	Filed / Furnished Herewith
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					*
10.1	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	16, 2020, by and among Verona Pharma plc and the investors set forth therein	6-K	001-38067	2	7/22/2020	
10.3†	Limited, as predecessor to Verona Pharma plc, dated February 7, 2005	F-1	333-217124	10.2	4/3/2017	
10.4	Management (UK) Limited dated October 19, 2017	20-F	001-38067	4.3	3/19/2019	
10.4.1	Management (UK) Limited dated November 8, 2017	20-F	001-38067	4.3.1	3/19/2019	
10.4.2	Management (UK) Limited dated April 3, 2018	20-F	001-38067	4.3.2	3/19/2019	
10.4.3	Management (UK) Limited dated September 16, 2017#1	20-F	001-38067	4.3.3	2/27/2020	
10.4.4	Management (UK) Limited dated September 16, 2017#2	20-F	001-38067	4.3.4	2/27/2020	
10.4.5	Management (UK) Limited dated September 16, 2017#3	20-F	001-38067	4.3.5	2/27/2020	
10.4.6	between the Verona Pharma Inc. and Regus Management Group LLC dated July 16, 2019	20-F	001-38067	4.3.6	2/27/2020	
10.5#	EMI Option Scheme	F-1	333-217124	10.4	4/3/2017	
10.6#	Unapproved Share Option Scheme, as amended	F-1	333-217124	10.5	4/3/2017	

10.7#	2017 Incentive Award Plan and forms of award agreements thereunder	20-F	001-38067	4.6	2/27/2018	
10.8#	Employment Agreement, dated January 20, 2020, between Verona Pharma Inc. and David Zaccardelli, Pharm. D.	20-F	001-38067	4.7	2/27/2020	
10.9#	Employment Agreement, dated October 21, 2019, between Verona Pharma plc and Kathleen Rickard	20-F	001-38067	4.8	3/19/2019	
10.11#	Employment Agreement, dated October 31, 2016, between Verona Pharma plc and Claire Poll	F-1	333-217124	10.9	4/3/2017	
10.12#	Employment Agreement, dated January 20, 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	Relationship Agreement relating to Verona Pharma plc, dated July 29, 2016, by and among the 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	10.12	4/3/2017	
10.16	Relationship Agreement relating to Verona Pharma plc, dated July 29, 2016, by and among the 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	10.13	4/3/2017	
10.17	Relationship Agreement relating to Verona Pharma plc, dated July 29, 2016, by and among the 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	
10.18	Relationship Agreement relating to Verona Pharma plc, dated July 29, 2016, by and among the 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	
10.19.1	Loan and Security Agreement, dated as of November 19, 2020, by and among Silicon Valley Bank, Verona Pharma plc and Verona Pharma, Inc.	6-K	001-38067	1.1	11/24/2020	
10.19.2	First Amendment to Loan and Security Agreement, dated as of November 19, 2020, by and among Silicon Valley Bank, Verona Pharma plc and Verona Pharma, Inc.					*
10.20#	Form of Non-Executive Director letter of appointment					*
21.1	List of Subsidiaries of Verona Pharma plc	F-1	333-217124	21.1	4/3/2017	
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					**
101.INS	XBRL Instance Document					*
101.SCH	XBRL Taxonomy Extension Schema Document					*
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document					*
101.LAB	XBRL Taxonomy Extension Label Linkbase Document					*
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document					*
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document					*

* Filed herewith.

** Furnished herewith.

# Indicates management contract or compensatory plan.

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 25, 2021

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 25, 2021
/s/ Mark W. Hahn **Mark W. Hahn**	Chief Financial Officer *(principal financial and accounting officer)*	February 25, 2021
/s/ David Ebsworth, Ph.D. **David Ebsworth, Ph.D.**	Chairperson of the Board of Directors	February 25, 2021
/s/ Ken Cunningham, M.D. **Ken Cunningham, M.D.**	Director	February 25, 2021
/s/ Martin Edwards, M.D. **Martin Edwards, M.D.**	Director	February 25, 2021
/s/ Rishi Gupta **Rishi Gupta**	Director	February 25, 2021
/s/ Mahendra Shah, Ph.D. **Mahendra Shah, Ph.D.**	Director	February 25, 2021
/s/ Andrew Sinclair, Ph.D. **Andrew Sinclair, Ph.D.**	Director	February 25, 2021
/s/ Vikas Sinha **Vikas Sinha**	Director	February 25, 2021
/s/ Anders Ullman, M.D., Ph.D. **Anders Ullman, M.D., Ph.D.**	Director	February 25, 2021

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Shareholders of Verona Pharma Plc

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Verona Pharma Plc and its subsidiaries (the "Company") as of December 31, 2020 and 2019, 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"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2020 and 2019, 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.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the 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. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP
Reading, United Kingdom
February 25, 2021

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

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

	December 31, 2020	December 31, 2019
ASSETS		
Current assets:		
Cash and cash equivalents	$ 187,986	$ 30,428
Short-term investments	—	10,380
Prepaid expenses	4,538	1,655
Tax and tax incentive receivables	8,260	9,814
Other current assets	1,720	2,021
Total current assets:	202,504	54,298
Non-current assets:		
Furniture and equipment, net	107	63
Goodwill	545	585
Right-of-use assets	1,050	1,288
Total non-current assets:	1,702	1,936
Total assets	$ 204,206	$ 56,234
LIABILITIES AND SHAREHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 178	$ 1,931
Accrued expenses	10,863	8,971
Operating lease liability	798	611
Warrants	2,246	1,188
Other current liabilities	118	140
Total current liabilities	14,203	12,841
Non-current liabilities:		
Term loan	4,635	—
Operating lease liability	514	652
Total non-current liabilities	5,149	652
Total liabilities	19,352	13,493
Commitments and contingencies		
Shareholders' equity		
Ordinary £0.05 par value shares; 488,304,446 and 105,326,638 issued, and 463,304,446 and 105,326,638 outstanding, at December 31, 2020 and 2019, respectively	31,794	7,265
Additional paid-in capital	366,411	179,535
Ordinary shares held in treasury	(1,700)	—
Accumulated other comprehensive loss	(4,601)	(2,280)
Accumulated deficit	(207,050)	(141,779)
Total shareholders' equity	184,854	42,741
Total liabilities and shareholders' equity	$ 204,206	$ 56,234

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 per share amounts)

	Year ended December 31,	
	2020	**2019**
Operating expenses		
Research and development	$ 44,505	$ 42,417
General and administrative	29,772	9,986
Total operating expenses	74,277	52,403
Operating loss	(74,277)	(52,403)
Other income / (expense)		
Benefit from R&D tax credit	8,267	9,283
Interest income	121	964
Interest expense	(35)	—
Fair value movement on warrants	(1,136)	2,066
Foreign exchange gain / (loss)	2,060	(399)
Total other income, net	9,277	11,914
Loss before income taxes	(65,000)	(40,489)
Income tax expense	(146)	(72)
Net loss	$ (65,146)	$ (40,561)
Other comprehensive (loss) / income:		
Foreign currency translation adjustments	(2,321)	1,348
Total comprehensive loss attributable to shareholders of the Company	$ (67,467)	$ (39,213)
Loss per ordinary share — basic and diluted	$ (0.25)	$ (0.39)

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, 2019	105,326,638	$ 7,265	$176,416	$ —	$ (3,628)	$ (101,192)	$ 78,861
Cumulative effect adjustment for ASU 2016-02 adoption	—	—	—	—	—	(26)	(26)
Adjusted balance at January 1, 2019	105,326,638	$ 7,265	$176,416	$ —	$ (3,628)	$ (101,218)	$ 78,835
Net loss	—	—	—	—	—	(40,561)	(40,561)
Effect of foreign currency translation adjustments	—	—	—	—	1,348	—	1,348
Share-based compensation	—	—	3,119	—	—	—	3,119
Balance at December 31, 2019	105,326,638	$ 7,265	$179,535	$ —	$ (2,280)	$ (141,779)	$ 42,741
Net loss	—	—	—	—	—	(65,146)	(65,146)
Effect of foreign currency translation adjustments	—	—	—	—	(2,321)	—	(2,321)
Issuance of ordinary shares, net of issuance costs	355,831,184	22,700	164,660	—	—	—	187,360
Issuance of ordinary shares to treasury	25,000,000	1,700	—	(1,700)	—	—	—
Issuance of ordinary shares from restricted share units and share options	2,146,624	129	39	—	—	(125)	43
Share-based compensation	—	—	22,177	—	—	—	22,177
Balance at December 31, 2020	488,304,446	$ 31,794	$366,411	$ (1,700)	$ (4,601)	$ (207,050)	$ 184,854

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,	
	2020	**2019**
Operating activities:		
Net loss:	$ (65,146)	$ (40,561)
Adjustments to reconcile net income to net cash used in operating activities:		
Foreign exchange (gain) / loss	(2,060)	399
Amortization of debt issue costs	10	—
Accretion of redemption premium on debt	8	—
Fair value movement on warrants	1,136	(2,066)
Impairment of right-of-use asset	289	—
Share-based compensation	22,177	3,119
Depreciation and amortization	623	510
Changes in operating assets and liabilities:		
Prepaid expenses	(3,065)	(158)
Tax and tax incentive receivables	768	(3,929)
Other current assets	187	(289)
Non-current assets	(703)	(1,325)
Accounts payable	(1,398)	(1,734)
Accrued expenses	1,940	2,454
Lease liabilities	110	849
Other liabilities	48	(137)
Net cash used in operating activities	(45,076)	(42,868)
Cash flows from investing activities		
Purchases of furniture and equipment	(82)	(53)
Purchases of short-term investments	—	(9,777)
Sale of short-term investments	9,792	57,144
Net cash provided by investing activities	9,710	47,314
Cash flows from financing activities		
Proceeds from issuance of ordinary shares	200,156	—
Payment of offering costs in connection with the issuance of ordinary shares	(12,748)	—
Proceeds from the issuance of term loan	5,000	—
Term loan issuance costs	(108)	—
Proceeds from exercise of share options	43	—
Net cash provided by financing activities	192,343	—
Effect of exchange rate changes on cash and cash equivalents	581	739
Net increase in cash and cash equivalents	157,558	5,185
Cash and cash equivalents at beginning of the year	30,428	25,243
Cash and cash equivalents at end of the year	$ 187,986	$ 30,428
Supplemental disclosure of cash flow information:		
Income taxes paid	$ 8	$ —
Interest paid	$ 7	$ —

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

Note 1 - Organization and description of business operations

Verona Pharma plc (the "Company") is incorporated and domiciled in the United Kingdom. Verona Pharma plc has two wholly-owned subsidiaries, Verona Pharma, Inc., a Delaware corporation and Rhinopharma Limited ("Rhinopharma"), a Canadian 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 listed its American Depositary Shares ("ADSs") on Nasdaq in April, 2017, which trade under the symbol “VRNA". The Company’s ordinary shares were also listed on the Alternative Investment Market of the London Stock Exchange (“AIM”) until October 30, 2020, when the shares were delisted from AIM in an effort to enhance liquidity of trading by combining all transactions on Nasdaq and to reduce costs through removing duplicative listing and compliance fees.

Liquidity

The Company has incurred recurring losses and negative cashflows from operations since inception, and has an accumulated deficit of $207.1 million as of December 31, 2020. 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.

In July, 2020, the Company raised $200 million in a private placement (the "Private Placement"), with net proceeds after transaction related fees and expenses of $185.5 million. Additionally, in November, 2020, the Company entered into a term loan facility with Silicon Valley Bank for up to $30 million (the “Term Loan”). As of December 31, 2020, $5 million had been drawn down. The Company expects that its cash and cash equivalents as of December 31, 2020, will be sufficient to fund its operating expenses and capital expenditure requirements for at least the next 12 months from the date of issuance.

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 subsidiaries Verona Pharma, Inc. and Rhinopharma. 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 U.S. ("US GAAP") and the following accounting policies have been consistently applied.

Previously, the Company prepared its consolidated financial statements in accordance with International Financial Reporting Standards as issued by the International Accounting Standards Board ("IFRS").

At the end of the second quarter of 2020, the Company determined that it no longer qualified as a Foreign Private Issuer under SEC rules. As a result, beginning January 1, 2020, the Company is required to report with the SEC on domestic forms and comply with domestic company rules in the United States. The transition to US GAAP was made retrospectively for all periods from the Company’s inception.

Use of estimates

The preparation of consolidated financial statements in conformity with US 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 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, the fair value of share-based compensation and the fair value of warrants. 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, term deposits with maturities of less than three months at inception, and in money market funds investing in U.S. and U.K. government debt and liquid securities from highly rated institutions.

Short-term investments

Short-term investments include fixed term deposits held at banks with original maturities between three months and a year. They are classified as loans and receivables and are measured at amortized cost using the effective interest method.

Furniture and equipment, net

Furniture and equipment comprise office furniture and computer equipment and are stated at cost less accumulated depreciation, which is calculated on a straight-line basis over the expected useful economic lives, generally two to five years.

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. The Company initially compares the market capitalization of the Company to the book value of its assets. If the value of the market capitalization does not support the valuation of the assets, the Company reviews estimates of the cash flows over the remaining lives of its other intangible assets, or related group of assets where applicable, in measuring whether the assets to be held and used will be realizable. In the event of impairment, the Company would discount the future cash flows using its then estimated incremental borrowing rate to estimate the amount of the impairment.

Leases

Effective January 1, 2019, the Company adopted ASC 842, Leases (“ASC842”) using the modified retrospective transition approach and did not restate comparative periods. The Company determines if an arrangement is a lease at inception. Leases are classified as operating or finance leases in accordance with the recognition criteria in ASC 842-20-25. The Company’s lease portfolio consists entirely of operating leases as of December 31, 2020. The Company’s leases do not contain any material residual value guarantees or material restrictive covenants.

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 "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 on obtaining the first approval of any regulatory authority for the commercialization of a Licensed Product, low single digit royalties based on the future sales performance of all 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 and will classify it within R&D expenses.

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 contracts with clinical research organizations and contract manufacturers. As part of the process of preparing financial statements the Company is required to estimate its expenses resulting from its obligation 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 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 measured by patient progression and the timing of various aspects of the trial. 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 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 and restricted stock units (RSUs). The fair value of share options and RSUs, which are subject to service conditions with graded vesting, are recognized as compensation expense using the cliff vesting method; forfeitures are recognized as they occur.

The Company uses the fair-value based method to determine compensation for all arrangements under which employees receive shares. The fair value of each option and RSU 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 began using U.S. government debt yields.

Details of the assumptions used are set out in note 11 to the consolidated financial statements.

Other income - United Kingdom R&D tax credits

Other operating income relates to R&D tax credits receivable in the UK. As a company that carries out extensive research and development activities, Verona is subject to the UK 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"). This Topic 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 income represents all changes in stockholders' equity during the period except those resulting from investments by, or distributions to, stockholders.

Segment Reporting

The Company has one operating and reportable segment, pharmaceutical development. The Company's long-lived assets are held in the United Kingdom.

Foreign Currencies

Reporting currency

The Company's reporting currency is U.S. dollars. Prior to July 1, 2020, Verona Pharma plc's functional currency was pounds sterling and its financial statements were translated to U.S. dollars. The statement of comprehensive income was translated at average rates for the period, assets and liabilities at the balance sheet date exchange rate and equity balances at historical rates. Translation differences were recorded in accumulated other comprehensive income / (loss).

Functional currency

The Company's consolidated financial statements are measured using the currency of the primary economic environment in which the entity operates, which was pounds sterling for Verona Pharma plc until June 30, 2020.

In the six months to June 30, 2020, management changes resulted in lower people costs being paid in pounds sterling. Following the Private Placement the Company entered into contracts to commence Phase 3 trials for ensifentrine and the majority of the costs are incurred in U.S. dollars. Management reviewed budgeted activities over the next five years and identified that the majority of costs from the second half of 2020 onwards will be incurred in U.S. dollars. Furthermore, the Private Placement in July, 2020, raised funds in U.S. dollars and having delisted from AIM any future fundraises will be in U.S. dollars. Also, the commercial focus of Company is the U.S. market.

As a consequence, management determined the Company's functional currency changed from pounds sterling to U.S. dollars and this has been accounted for prospectively from July 1, 2020. To convert Verona Pharma plc's books and records into U.S. dollars income and expenses were translated at average rates, assets and liabilities at the June 30, 2020, exchange rate and equity balances at historical rates. Translation differences were recorded in accumulated other comprehensive income / (loss).

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. The Company issued 25 million ordinary shares (equivalent to 3.125 million ADSs) 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 Sheet as treasury shares.

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, short-term investments, 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 these 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 and 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.

Recently adopted accounting pronouncements

In February 2016, the FASB issued ASU No. 2016-02, "Leases" (Topic 842) ("ASC 842"). The standard requires lessees to recognize almost all leases on the balance sheet as right-of-use ("ROU") assets and lease liabilities, and requires leases to be classified as either an operating or a finance type lease. The standard excludes leases of intangible assets or inventory. The standard became effective for the Company beginning January 1, 2019. The Company adopted ASC 842 using the modified retrospective approach, by applying the new standard to all leases existing at the date of initial application. Results and disclosure requirements for reporting periods beginning after January 1, 2019, are presented under ASC 842, while prior period amounts have not been adjusted and continue to be reported in accordance with our historical accounting under ASC 840 "Leases". The Company elected the package of practical expedients permitted under ASC 842, which also allowed the Company to carry forward historical lease classifications. The Company also elected the practical expedient related to treating lease and non-lease components as a single lease component for all equipment leases as well as electing a policy exclusion permitting leases with an original lease term of less than one year to be excluded from the ROU assets and lease liabilities.

As a result of the adoption of ASC 842 on January 1, 2019, the Company recorded an operating lease ROU asset of $415 thousand and an operating lease liability of $441 thousand. The adoption increased opening accumulated losses by $26 thousand but did not impact the Company's prior year financial statements.

Under ASC 842, 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 remaining lease payments over the lease term. 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 determined the incremental borrowing rate in determining 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 operating lease ROU assets and current and non-current operating lease liabilities, on the Company's consolidated balance sheets.

The FASB issued ASU 2020-04 to provide optional expedients and exceptions for applying US GAAP to contract modifications, hedging relationships, and other transactions affected by the anticipated transition away from LIBOR. There is no material impact of the adoption of ASU 2020-04 on our consolidated financial statements.

Recently issued accounting pronouncements, not yet adopted

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 the new guidance, 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. In November 2019, the FASB issued ASU No. 2019-10, Financial Instruments - Credit Losses (Topic 326), Derivatives and Hedging (Topic 815), and Leases (Topic 842): Effective Dates ("ASU 2019-10"). The purpose of this amendment is to create a two tier rollout of major updates, staggering the effective dates between larger public companies and all other entities. This granted certain classes of companies, including Smaller Reporting Companies ("SRCs"), additional time to implement major FASB standards, including ASU 2016-13. Larger public companies will have an effective date for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. All other entities are permitted to defer adoption of ASU 2016-13, and its related amendments, until the earlier of fiscal periods beginning after December 15, 2022. Under the current SEC definitions, we meet the definition of an SRC as of the ASU 2019-10 issuance date and are deferring adoption for ASU 2016-13. 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. We are currently evaluating the impact of the adoption of ASU 2016-13 on our consolidated financial statements, but do not believe the adoption of this standard will have a material impact on our consolidated financial statements.

Note 3 - Prepaid expenses

Prepaid expenses consisted of the following (in thousands):

	Year ended December 31,	
	2020	2019
Clinical trial and other development costs	$ 2,551	$ 874
Insurance	1,701	534
Other	286	247
Total prepaid expenses and other current assets	$ 4,538	$ 1,655

Note 4 - Tax and tax incentive receivables

Taxes receivable consisted of the following (in thousands):

	Year ended December 31,	
	2020	2019
R&D tax credit receivable - U.K.	$ 8,202	$ 9,618
Tax receivable - U.S.	58	196
Total tax receivable	$ 8,260	$ 9,814

Note 5 - Property leases

The right-of-use assets ("ROU") relate to rented office space in London and North Carolina, with leases ending in 2022 and 2024, respectively.

In the year ended December 31, 2019, the Company determined that it was reasonably likely to extend its existing London lease. As a consequence it modified its accounting for the lease and recorded an additional $0.7 million ROU and associated liability. The Company has the option to further extend this lease but is not reasonably certain to do so and therefore has not recognized this extension as an asset and liability.

In the year ended December 31, 2019, the Company entered into a lease arrangement in New York for serviced offices and recognized a right of use asset and corresponding lease liability of $0.4 million. In the year ended December 31, 2020, the Company's New York office was closed and the related ROU asset of $290 thousand was subsequently expensed in the consolidated statements of operations and comprehensive loss. The Company retains a liability of $195 thousand relating to this lease arrangement.

In the year ended December 31, 2020, the Company entered into a lease arrangement in North Carolina for office space and recognized an ROU asset and corresponding lease liability of $0.7 million.

To calculate lease liabilities the Company used a weighted average discount rate of 8%. The weighted average remaining lease term is 2.2 years.

Minimum annual payments over the remaining lease periods as of December 31, 2020 are as follows (in thousands):

2021	$ 862
2022	281
2023	201
2024	44
Total minimum future lease payments	$ 1,388
Less: imputed interest	(76)
Total operating lease liabilities	$ 1,312

The total operating lease expense included in general and administrative costs was $692,000.

Under the prior lease accounting guidance minimum rental commitments under non-cancelable leases, for each of the five years and total thereafter as of December 31, 2019, were as follows:

	2020	2021	2022	2023	2024
Minimum lease payments	$ 680	$ 862	$ 281	$ 201	$ 44

Note 6 - Accrued expenses

Accrued expenses consisted of the following (in thousands):

	Year ended December 31,	
	2020	2019
Clinical trial and other development costs	$ 8,607	$ 6,394
Professional fees, listing and general corporate costs	2,149	2,191
People related costs	107	386
Total accrued expenses	$ 10,863	$ 8,971

Other expenses include people costs, professional fees and other accrued costs.

Note 7 - Warrants

In 2016, the Company issued 31,115,926 units to new and existing investors at the placing price of £1.4365 per unit. Each unit comprised one ordinary share and one warrant. The warrant holders can subscribe for 0.4 of an ordinary share at a per share exercise price of £1.7238 until May 2, 2022. The warrant holders can opt for a cashless exercise of their warrants, whereby the warrant holders can choose to exchange the warrants held for a reduced number of warrants exercisable at nil consideration. The reduced number of warrants is calculated based on a formula considering the share price and the exercise price of the warrants.

At December 31, 2020, 31,003,155 warrants remain outstanding and entitle the investors to subscribe for, in aggregate, a maximum of 12,401,262 ordinary shares.

If, after a transaction, should the warrants be exercisable for unlisted securities, the warrant holders may demand a cash payment instead of the delivery of the underlying securities. Accordingly, the warrants are accounted for as a liability under ASC 480 “Distinguishing Liabilities from Equity”.The warrants are measured at fair value, Level 3 in the fair value hierarchy, with movements recorded in finance income / (expense) in the consolidated statements of operations and comprehensive loss.

In the years ended December 31, 2020, and 2019, no warrants were exercised or forfeited.

The warrants had no intrinsic value as at December 31, 2020.

There have been no changes in valuation techniques or transfers between fair value measurement levels during the years ended December 31, 2020 and 2019. The warrants are valued using the Black-Scholes model and the table below presents the assumptions used:

	Year ended December 31,	
	2020	2019
Shares potentially issued under warrants	12,401,262	12,401,262
Exercise price in pounds sterling	£ 1.7238	£ 1.7238
Equivalent price of ordinary share (ADS price divided by eight)	$ 0.64	$ 0.62
Risk-free interest rate	— %	0.54 %
Expected term to exercise	1.33	2.34
Annualized volatility	105.4 %	65.6 %
Dividend rate	— %	— %
Calculated value of the warrants, in thousands of U.S. dollars	$ 2,246	$ 1,188

The following table shows the movement of the value of the warrants (in thousands):

	Year ended December 31,	
	2020	2019
At January 1	$ 1,188	$ 3,180
Fair value adjustment	1,114	(2,066)
Foreign exchange differences recognized in loss for the period	22	—
Translation differences recognized in other comprehensive loss	(78)	74
At December 31	$ 2,246	$ 1,188

For the amount recognized at December 31, 2020, the effect when the following parameter deviates up or down is presented in the below table (in thousands):

10% volatility increase	$ 2,734
Base case, reported fair value	**2,246**
10% volatility decrease	$ 1,772

Note 8 - Term loan

In November 2020, the Company and its wholly owned subsidiary, Verona Pharma, Inc. (the "Borrowers") entered into a term loan facility of up to $30.0 million (the "Term Loan"), consisting of term loan advances in an aggregate amount of $5.0 million funded at closing, a term loan advance available subject to certain terms and conditions in an aggregate amount of $10.0 million (the "Term B Loan") and a term loan advance available subject to certain terms and conditions in an aggregate amount of $15.0 million (the "Term C Loan"), with Silicon Valley Bank, a California corporation ("SVB"), the proceeds of which will be used for general corporate and working capital purposes.

The Term Loan is governed by a loan and security agreement, dated as of November 19, 2020, between the Borrowers and SVB (the "Loan Agreement"). The Term B Loan will be available, subject to and customary terms and conditions, only during the period commencing upon the achievement of a specific clinical milestone relating to ensifentrine through and including June 30, 2022. The Term C Loan will be available, subject to customary terms and conditions, only during the period commencing upon the achievement of an additional specific clinical milestone relating to ensifentrine through and including June 30, 2023.

The Term Loan will mature on November 1, 2024. Each advance under the Term Loan accrues interest at a floating per annum rate equal to the greater of (a) the sum of the prime rate reported in The Wall Street Journal plus 1.00% and (b) four and one-quarter of one percent (4.25%). The Term Loan provides for interest-only payments on a monthly basis until the payment date immediately preceding December 1, 2023. 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 Borrowers shall make a final payment to SVB in the amount of 10% of the aggregate Term Loans advanced (the "Final Payment"). The Borrowers may prepay the Term Loan in full but not in part provided that the Borrowers (i) provide ten days' prior written notice to SVB, (ii) pays on the date of such prepayment (A) all outstanding principal plus accrued and unpaid interest, (B) a prepayment fee of $450,000 plus 3.0% of the Term C Loans advanced if paid on or before the first anniversary of the closing date; $300,000 plus 2.00% of the Term C Loans advanced if paid after the first anniversary of the closing date and on or before the second anniversary of the closing date; and $150,000 plus 1.00% of the Term C Loans advanced if paid thereafter and prior to maturity, (C) the Final Payment and (D) all other sums, if any, that shall become due and payable with respect to the Term Loan Advances, including interest at the Default Rate with respect to any past due amounts. Amounts outstanding during an event of default are payable upon SVB's demand and shall accrue interest at an additional rate of 3.0% per annum.

The Term Loan is secured by a lien on substantially all of the assets of the Borrowers, other than the equity interests of Verona U.S. and other than intellectual property, provided that such lien on substantially all assets includes any rights to payments and proceeds from the sale, licensing or disposition of intellectual property. The Borrowers have also granted SVB a negative pledge with respect to its intellectual property.

The Loan Agreement contains customary covenants and representations, including but not limited to financial reporting obligations and limitations on dividends, indebtedness, collateral, investments, distributions, transfers, mergers or acquisitions, taxes, corporate changes, deposit accounts, and subsidiaries. The Loan Agreement also contains other customary provisions, such as expense reimbursement, non-disclosure obligations as well as indemnification rights for the benefit of SVB. The Loan Agreement includes a minimum cash covenant triggered when Borrowers' consolidated cash and cash equivalents drop below $45.0 million at any time after the earliest to occur of any of the following: (i) the release of negative data from Enhance 2 and/or Enhance 1, which in the reasonable business discretion Borrowers' senior management, would be considered insufficient to support submission of an NDA to the FDA, (ii) the FDA issues a complete response letter with respect to an NDA submitted for ensifentrine, or (iii) failure to achieve a specific regulatory milestone relating to ensifentrine by June 30, 2023 (extendable to March 31, 2024 upon the Borrowers receiving a specified amount of new cash proceeds after September 8, 2020 from the sale of equity securities in one or more public financings or other bona fide equity financings, subordinated debt and/or upfront/milestone payments from one or more collaboration agreements not prohibited in the Loan Agreement). Upon such trigger, Borrowers must cash collateralize an amount equal to the outstanding obligations to SVB plus the amount of any prepayment penalty and Final Payment which would be due in the event the Loan Agreement were prepaid in full with respect to the Term Loans advanced as of such time.

The events of default under the Loan Agreement include, but are not limited to, the Borrowers' failure to make any payments of principal or interest under the Loan Agreement or other transaction documents, the Borrowers' breach or default in the performance of any covenant under the Loan Agreement or other transaction documents, the occurrence of a material adverse change, any Borrower making a false or misleading representation or warranty in any material respect under the Loan Agreement, any Borrower's insolvency or bankruptcy, any attachment or judgment on any Borrower's assets of at least $500,000, or the occurrence of any default under any agreement or

obligation of any Borrower involving indebtedness in excess of $500,000. If an event of default occurs, SVB is entitled to take enforcement action, including acceleration of amounts due under the Loan Agreement.

In connection with the Term Loan the Company incurred debt issuance costs totaling approximately $400 thousand which were deducted from the carrying amount of the debt and are being amortized over the estimated term of the debt using the effective interest method.

As of December 31, 2020, the carrying value of the Term Loan was approximately $4.6 million, of which all was due in greater than 12 months. The debt balance has been categorized within Level 3 of the fair value hierarchy. The carrying amount of the debt approximates its fair value based on prevailing interest rates as of the balance sheet date.

Note 9 - 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 director. The assets of the plans are held separately from those of the Company in independently administered funds.

The retirement plan cost charge represents the contributions payable by the Company to the plans during the year. Defined contribution costs during the years ended December 31, 2020 and 2019 amounted to $315 thousand and $203 thousand, respectively.

Note 10 - 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. U.K. corporation tax is charged at 19% and the U.S. Federal Income tax rate is 21%.

The components of loss before income taxes are as follows (in thousands):

	Year ended December 31,	
	2020	2019
United States	$ (3,191)	$ 198
United Kingdom	68,191	40,291
Total	$ 65,000	$ 40,489

The components of income tax expense are as follows (in thousands):

	Year ended December 31,	
	2020	2019
United States	$ 146	$ 72
United Kingdom	—	—
Total current tax expense	$ 146	$ 72
United States	—	—
United Kingdom	—	—
Total deferred tax expense	—	—
Total income tax expense	$ 146	$ 72

A reconciliation of the U.K. statutory income tax rate to our effective income tax rate is as follows (in percentages):

	Year ended December 31,	
	2020	2019
U.K. tax rate	19.0 %	19.0 %
Non-deductible expenses	(8.9)%	(0.7)%
Research and development incentive	(4.8)%	(8.6)%
Share options exercised	0.4 %	— %
Change in deferred tax valuation allowance	(5.9)%	(9.9)%
Difference in overseas statutory tax rates	— %	(0.1)%
Effective income tax rate	(0.2)%	(0.3)%

Significant components of the Company's deferred tax assets and liabilities were as follows (in thousands):

	Year ended December 31,	
	2020	2019
Deferred tax liabilities:		
Contingent liability [(1)]	$ (5,860)	$ (95)
Total deferred tax liabilities	(5,860)	(95)
Deferred tax assets:		
Net operating losses	19,855	12,835
IPR&D asset [(1)]	5,631	310
Future exercisable shares	10,480	273
Other	215	181
Total deferred tax assets	36,181	13,599
Less: valuation allowance	(30,321)	(13,504)
Deferred tax assets, net of valuation allowance	$ —	$ —
Movements in the deferred tax valuation allowance		
Valuation allowance at January 1	$ 13,504	$ 9,322
Change in tax rates	1,632	—
Increase in valuation allowance	14,815	3,802
Foreign currency translation adjustments	370	380
Valuation allowance at December 31	$ 30,321	$ 13,504

[(1)] These relate to the difference in the tax base of the IP R&D asset and assumed contingent liability and the accounting base, which is nil under US 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, 2020 and December 31, 2019, the Company had U.K. net operating losses ("NOLs") of $95.7 million and $75.5 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, 2019, and there are no ongoing tax examinations in any jurisdiction. No interest or penalties were recognized in the consolidated statements of operations or consolidated balance sheets. As of December 31, 2020, the Company has no uncertain tax positions.

Note 11 - 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 R&D and 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 market price on the day of 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 R&D and general and administrative costs (in thousands):

	Year ended December 31,	
	2020	2019
Research and development	$ 9,319	$ 1,692
General and administrative	12,858	1,427
Total	$ 22,177	$ 3,119

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, or 114,000 ordinary shares, or 14,250 ADSs, for the EMI Option Plan and 1,860,000 ordinary shares, or 232,500 ADSs, for the Pre-IPO Option Plan.

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

2017 Incentive Plan

The 2017 Incentive 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.

In the year ended December 31, 2019, the Company modified the terms of all RSUs issued prior to January 1, 2019 to include a market based condition, which was also included in the terms of RSUs issued during 2019. The Company's stock price must be maintained above the equivalent of £2 per ordinary share for thirty days for the RSUs to vest, in addition to the existing service condition. The RSUs vest five years after the date of grant irrespective of whether the £2 market condition was met. This modification did not result in an increase in the fair value of the RSUs.

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 outstanding	Weighted average exercise price [(1)]	Weighted average remaining contractual term (years)	Aggregate intrinsic value
Outstanding at January 1, 2019	8,752,114	$ 2.02		
Granted	5,569,050	0.72		
Forfeited	(121,970)	1.09		
Expired	(19,998)	2.65		
Outstanding at December 31, 2019	14,179,196	$ 1.53	7.7	$ 933
Granted	2,096,285	0.73		
Forfeited	(2,506,017)	1.53		
Expired	(589,128)	1.93		
Exercised	(54,664)	$ 0.75		
Outstanding at December 31, 2020	13,125,672	$ 1.41	7.3	$ 914
Exercisable at December 31, 2020	7,749,296	$ 1.75	6.5	$ 220

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

Determining the fair value of share options and RSUs

The total fair values of the options and RSUs were estimated using the Black-Scholes option-pricing model for equity-settled compensation, amounted to $62.1 million for instruments granted in the year ended December 31, 2020 (2019: $3.1 million). The cost is amortized over the vesting period of the options and RSUs on a straight-line basis using the cliff-vesting method.The following assumptions were used for the Black-Scholes valuation of share options granted in 2020 and 2019.

Expected volatility

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

Fair value of ordinary shares.

The fair value of ordinary shares has been based on the share price of the Company's shares on AIM on the evening before the date of grant, as the Company's primary listing was previously on this market.

Risk-free interest rate

The risk-free interest rate has been based on the U.K. Government debt yield for the relevant term at the time of grant, as the Company's primary listing was previously on AIM. Effective from the delisting from AIM the Company will use appropriate U.S Government debt yields.

Expected term.

The expected term is determined using the simplified method.

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:

	Year ended December 31,	
	2020	2019
Risk-free interest rate	0% - 0.21%	0.39% - 0.82%
Expected lives (years)	5.05 - 7	5.5 - 7
Expected volatility	65.83% - 75.40%	67.98% - 68.71%
Expected dividend yield	— %	— %
Grant date fair value (per share)	$0.40 - $0.62	$0.31 - $0.49

Restricted stock units activity

The following table shows RSU activity:

	Number of RSUs outstanding	Weighted average remaining contractual term (years)
Outstanding at January 1, 2019	862,473	
Granted	740,496	
Outstanding at December 31, 2019	1,602,969	3.4
Granted	62,566,271	
Forfeited	(84,920)	
Vested	(2,091,960)	
Outstanding at December 31, 2020	61,992,360	1.5

	Number of RSUs outstanding	Weighted average remaining vesting Period	Period in which the target must be achieved
RSUs subject to time based vesting	61,416,336	1.5	n/a
RSUs subject to milestone based vesting	576,024	2.5	2022 - 2024

The intrinsic and fair value of RSUs that vested in the year ended December 31, 2020, was $1.5 million (2019: $nil).

As of December 31, 2020, total compensation cost related to share options and RSUs granted but not yet recognized was $41.8 million. This cost will be amortized to expense over a weighted average remaining period of 1.5 years and will be adjusted for subsequent forfeitures.

Note 12 - 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 2020 and 2019 (net loss in thousands, loss per share in cents):

	Year ended December 31,	
	2020	2019
Numerator:		
Net loss	$ 65,146	$ 40,561
Net loss available to ordinary shareholders - basic and diluted	$ 65,146	$ 40,561
Denominator:		
Weighted-average shares outstanding - basic and diluted	262,932,653	105,326,638
Net loss per share - basic and diluted	$ (0.25)	$ (0.39)

During the years ended December 31, 2020 and 2019, outstanding share options, RSUs and warrants of 87,519,294 and 28,183,427, respectively, were not included in the computation of diluted earnings per ordinary share, because to do so would be antidilutive.

Note 13 - Related party transactions and other shareholder matters

In the year ended December 31, 2019, Anders Ullman, a director of the Company, provided consultancy services to the Company for which the Company paid him $33 thousand.

In the year ended December 31, 2020, certain directors and officers participated in the Private Placement, summarized below (in thousands, except for number of shares acquired):

Participation in Private Placement	**Ordinary Shares**	**Consideration**	
Dr. Ebsworth	222,216	£	100,000
Dr. Zaccardelli	444,440	$	249,998
Mr. Sinha (through connected persons)	533,328	$	299,997
Dr. Ullman	266,664	$	149,983
Dr. Edwards	53,328	$	29,997
Mr. Hahn	177,784	$	100,004