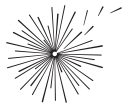
PROSPECTUS

47,399,001 Ordinary Shares

(including Ordinary Shares in the form of American Depositary Shares)



Verona Pharma

$13.50 per American Depositary Share

£1.32 per Ordinary Share

We are offering 47,399,001 of our ordinary shares in a global offering.

We are offering 5,768,000 American Depositary Shares, or ADSs, through the underwriters named in this prospectus, or the U.S. offering. Each ADS represents eight ordinary shares. This is our initial public offering of our ADSs, and no public market currently exists for our ADSs. Our ADSs have been approved for listing on The NASDAQ Global Market under the symbol "VRNA."

We are offering 1,225,001 ordinary shares through the underwriters named in this prospectus in Europe and countries outside of the United States and Canada in a concurrent private placement, or the European private placement.

The closing of each of the U.S. offering and the European private placement, together referred to as the global offering, will be conditioned upon the other.

Our ordinary shares trade on AIM, a market of the London Stock Exchange, under the symbol "VRP." On April 26, 2017, the last reported sale price of our ordinary shares on AIM was £1.33 per ordinary share.

Investing in our ordinary shares and ADSs involves risks. See "Risk Factors" beginning on page 11 of this prospectus.

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012 and, as such, will be eligible for reduced public company disclosure requirements. Please see "Prospectus Summary—Implications of Being an Emerging Growth Company and a Foreign Private Issuer" for additional information.

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

	PER SHARE	PER ADS	TOTAL
Public offering price	£ 1.32	$ 13.50	$79,985,633
Underwriting discounts and commissions[1]	£0.0924	$ 0.9450	$ 5,598,994
Proceeds to Verona Pharma plc, before expenses	£1.2276	$12.5550	$74,386,639

[1] See "Underwriting" for additional information regarding underwriting compensation.

Our existing institutional investors affiliated with certain of our directors have indicated an interest in purchasing securities offered in the global offering on the same terms as the other purchasers in the global offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no securities offered in the global offering to any of these investors, or any of these investors may determine to purchase more, less or no securities offered in the global offering. See "Prospectus Summary—The Global Offering."

In addition, our chairman of the board of directors and an existing shareholder have agreed to purchase an aggregate of approximately £335,400 (or the U.S. dollar equivalent) of our ordinary shares in a private placement separate from the global offering, or the shareholder private placement, contingent on and concurrent with the completion of the global offering at a price per share equal to the offering price per ordinary share in the European private placement. The underwriters will serve as placement agents for such shareholder private placement and receive a placement agent fee equal to a percentage of the total purchase price of the private placement shares, which percentage will be equal to the percentage discount the underwriters will receive on shares sold in this global offering. The closing of this global offering is not conditioned upon the closing of such shareholder private placement.

Delivery of our ADSs in the U.S. offering and our ordinary shares in the European private placement is expected to be made on or about May 2, 2017. We have granted the underwriters an option for a period of 30 days to purchase an additional 865,200 ADSs in the U.S. offering. If the underwriters exercise this option in full, the total underwriting discounts and commissions payable by us will be $6,416,608, and the total proceeds to us, before expenses, will be $85,249,225.

Jefferies **Stifel**

Wedbush PacGrow

SunTrust Robinson Humphrey

Prospectus dated April 26, 2017

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We are responsible for the information contained in this prospectus and any free-writing prospectus we prepare or authorize. We have not, and the underwriters have not, authorized anyone to provide you with different information, and we and the underwriters take no responsibility for any other information others may give you. We are not, and the underwriters are not, making an offer to sell our ADSs or ordinary shares in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in this prospectus is accurate as of any date other than the date on the front cover of this prospectus, regardless of the time of delivery of this prospectus or the sale of any ADSs or ordinary shares.

For investors outside the United States: Neither we nor the underwriters have done anything that would permit the global offering or possession or distribution of this prospectus in any jurisdiction, other than the United States, where action for that purpose is required. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the global offering of our ADSs and ordinary shares and the distribution of this prospectus outside the United States.

We are a public limited company incorporated under the laws of England and Wales and a majority of our outstanding securities are owned by non-U.S. residents. Under the rules of the U.S. Securities and Exchange Commission, or the SEC, we are currently eligible for treatment as a "foreign private issuer." As a foreign private issuer, we will not be required to file periodic reports and financial statements with the SEC as frequently or as promptly as domestic registrants whose securities are registered under the Securities Exchange Act of 1934, as amended.

ABOUT THIS PROSPECTUS

Unless otherwise indicated or the context otherwise requires, all references in this prospectus to the terms "Verona," the "Company," "we," "us" and "our" refer to Verona Pharma plc and our wholly owned subsidiaries Verona Pharma, Inc. and Rhinopharma Limited.

PRESENTATION OF FINANCIAL INFORMATION

This prospectus includes our audited consolidated financial statements as of and for the years ended December 31, 2015 and 2016 prepared in accordance with International Financial Reporting Standards, or IFRS, as issued by the International Accounting Standards Board, or IASB. We refer to these consolidated financial statements collectively as the "Annual Consolidated Financial Statements." None of our financial statements were prepared in accordance with U.S. GAAP.

Our financial information is presented in pounds sterling. For the convenience of the reader, in this prospectus, unless otherwise indicated, translations from pounds sterling into U.S. dollars were made at the rate of £1.00 to $1.2783, which was the noon buying rate of the Federal Reserve Bank of New York on April 21, 2017. However, where indicated, we have translated some of our historical financial information from pounds sterling into U.S. dollars at the rate of £1.00 to $1.2337, which was the noon buying rate of the Federal Reserve Bank of New York on December 30, 2016. Such U.S. dollar amounts are not necessarily indicative of the amounts of U.S. dollars that could actually have been purchased upon exchange of pounds sterling at the dates indicated. All references in this prospectus to "$" mean U.S. dollars and all references to "£" and "GBP" mean pounds sterling.

We have made rounding adjustments to some of the figures included in this prospectus. Accordingly, numerical figures shown as totals in some tables may not be an arithmetic aggregation of the figures that preceded them.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus. This summary may not contain all the information that may be important to you, and we urge you to read this entire prospectus carefully, including "Risk Factors," "Business," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements, including the notes thereto, before deciding to invest in our ADSs or ordinary shares.

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, RPL554, is a first-in-class, inhaled, dual inhibitor of the enzymes phosphodiesterase 3 and 4, or PDE3 and PDE4, that acts as both a bronchodilator and an anti-inflammatory agent in a single compound. We believe RPL554 has the potential to be the first novel class of bronchodilator in over 40 years. We have completed eight Phase 1 and 2a clinical trials for RPL554, with 282 subjects enrolled. In our clinical trials, treatment with RPL554 has been observed to result in statistically significant improvements in lung function as compared to placebo and has shown clinically meaningful and statistically significant improvements in lung function when added to two commonly used bronchodilators as compared to either bronchodilator administered as a single agent. Statistically significant means that there is a low statistical probability, typically less than 5%, that the observed results occurred by chance alone. RPL554 also has shown anti-inflammatory effects and been well tolerated in our clinical trials, and has not been observed to result in the gastrointestinal or other side effects commonly associated with roflumilast, the only PDE4 inhibitor currently on the market for the treatment of chronic obstructive pulmonary disease, or COPD.

We are developing RPL554 for the treatment of patients with COPD. We believe there is an urgent and unmet medical need for new and more effective treatments for COPD to reduce the number and burden of symptoms, reduce acute periods of worsening symptoms, or exacerbations, and establish a consistent and durable treatment response. We are also developing RPL554 for the treatment of cystic fibrosis, or CF, a fatal inherited disease where we believe the bronchodilatory and anti-inflammatory effects of RPL554 may be beneficial. We believe RPL554, if approved, has the potential to become an important and novel treatment and standard of care for COPD and CF patients. We may also explore, alone or with a collaborator, the development of RPL554 to treat asthma and other respiratory diseases.

We are developing RPL554 in a nebulized formulation for the maintenance treatment of COPD patients as a single agent and add-on therapy and for the treatment of CF. We also are developing RPL554 in a nebulized formulation as an add-on therapy to short-acting bronchodilators and other commonly used therapies for the treatment of hospitalized patients with acute exacerbations of COPD.

We plan to commence a four-week Phase 2b dose ranging clinical trial to evaluate RPL554 for the maintenance treatment of COPD in the second half of 2017. In this trial, we plan to compare the use of RPL554 in a nebulized formulation to placebo in approximately 400 patients. We expect to report top-line data from this trial in the second half of 2018. In February 2017, we commenced a Phase 2a clinical trial of RPL554 for the maintenance treatment of COPD in the United Kingdom. This trial is evaluating RPL554 as an add-on therapy to tiotropium, a commonly used long-acting bronchodilator, in approximately 30 patients. We expect to report top-line data from this trial in the fourth quarter of 2017. We also plan to commence a single-dose pharmacokinetic, or PK, trial of RPL554 in approximately 12 healthy volunteers in the United States in mid-2017. We expect to report top-line data from this trial in the fourth quarter of 2017. A PK trial involves the study of the process of bodily absorption, distribution, metabolism and excretion of a drug. In addition, we plan to commence a 12-week Phase 2b dose-ranging clinical trial of RPL554 for the maintenance treatment of COPD in the second half of 2018. In this trial, we plan to evaluate RPL554 as an add-on therapy to a long-acting bronchodilator in approximately 400 patients.

We plan to commence a Phase 2 trial of RPL554 for the treatment of acute exacerbations of COPD in hospitalized patients in the second half of 2018. In this trial, we plan to evaluate RPL554 in a nebulized formulation as an add-on therapy in approximately 150 patients.

In March 2017, we commenced a Phase 2a single-dose PK and pharmacodynamics, or PD, trial in the United Kingdom evaluating RPL554 in up to ten CF patients and expect to report top-line data from this trial in the first half of 2018. A PD trial involves the study of the biochemical and physiological effects of a drug and its mechanisms of action, including the correlation of the drug's actions and effects with its mechanism of action. The results of this clinical trial are expected to support dose selection for a proof-of-concept Phase 2b trial in approximately 100 patients with CF, which we plan to commence in 2018.

In addition to our nebulized formulation of RPL554, we are developing RPL554 in both dry powder inhaler, or DPI, and metered dose inhaler, or MDI, formulations for the maintenance treatment of COPD. We may explore the development of RPL554 in these formulations for the treatment of asthma and other respiratory diseases.

According to the World Health Organization, over one billion people suffer from chronic respiratory diseases. Among the most common of these afflictions is COPD, which is a progressive respiratory disease for which there is no cure. COPD damages the airways and the lungs and leads to shortness of breath, impacting a person's ability to perform daily activities. In some cases, patients experience acute exacerbations, which are estimated to cause approximately 1.5 million emergency department visits, 687,000 hospitalizations and 129,000 deaths per year in the United States alone. According to the World Health Organization, COPD is the third leading cause of death globally, with 210 million people worldwide suffering from the disease. Global sales of drugs currently indicated for COPD were $10.6 billion in 2016 and are expected to grow to $15.6 billion in 2019.

According to the Cystic Fibrosis Foundation, more than 30,000 people in the United States and more than 70,000 people worldwide are living with CF and approximately 1,000 new cases of CF are diagnosed each year. CF is the most common fatal inherited disease in the United States and Europe. CF causes impaired lung function and is commonly associated with repeat and persistent lung infections due to the inability to clear thickened phlegm, or mucus, from the lung. This condition often results in frequent exacerbations and hospitalizations. There is no cure for CF and the median age of death for CF patients is 37 years. CF is considered a rare, or orphan, disease by both the U.S. Food and Drug Administration, or FDA, and the European Medicines Agency, or EMA.

By inhibiting PDE3 and PDE4, RPL554 increases the levels of two critical intracellular messengers, resulting in bronchodilator and anti-inflammatory effects. RPL554 also stimulates the cystic fibrosis transmembrane conductance regulator, or 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. Dual inhibition of PDE3 and PDE4 has been observed to be more effective than inhibition of either PDE alone at relaxing airway smooth muscle cells and suppressing the activation and functions of pro-inflammatory cells residing in the lung, both of which are recognized to play a significant role in COPD and CF.

In our clinical trials, RPL554 has shown rapid onset and durable bronchodilation in healthy subjects and patients with COPD when inhaled from a nebulizer. In addition, RPL554 has been observed to be complementary and additive when administered as an add-on therapy to other currently marketed bronchodilators. Our most recent clinical trial of RPL554 was a Phase 2a clinical trial in 36 patients with COPD. Our primary objective in this clinical trial was to evaluate the improvement in lung function, as measured by the maximal volume of air a person can forcefully exhale in one second, or FEV_1, and the duration of action of RPL554. We evaluated RPL554 administered as a single agent as compared to placebo and two commonly used bronchodilators, albuterol, also known as salbutamol and marketed as

Ventolin, and ipratropium, marketed as Atrovent. We also evaluated RPL554 administered as an add-on therapy to either albuterol or ipratropium, in each case as compared to albuterol or ipratropium alone.

We have worldwide commercialization rights for RPL554. We have raised £74.6 million in gross proceeds from investors since our listing on AIM in 2006, of which £44.7 million was raised in our most recent private placement of equity securities in July 2016 with a number of European and U.S.-based healthcare specialist investment firms. Members of our management team and board of directors have extensive experience in large pharmaceutical and biotechnology companies in respiratory product development from drug discovery through commercialization and have played important roles in the development and commercialization of several approved respiratory treatments, including Symbicort, Daliresp/Daxas, Spiriva and Flutiform.

Product Candidate Pipeline

The following table depicts the potential indications for RPL554 and their current development status:

Indication	RPL554 Formulation	Pre-clinical	Phase 1	Phase 2	Phase 3	Anticipated Milestones
Maintenance treatment of COPD	Nebulizer					Commence 4-week Phase 2b clinical trial in the second half of 2017 and U.S. PK trial in mid-2017 Report Phase 2a top-line data in the fourth quarter of 2017
Treatment of acute COPD	Nebulizer					Commence Phase 2 clinical trial in the second half of 2018
CF	Nebulizer					Report Phase 2a top-line data in the first half of 2018
Maintenance treatment of COPD	DPI/MDI					Finalize formulation and commence pre-clinical studies in 2018
Treatment of asthma	DPI/MDI					Finalize formulation and commence pre-clinical studies in 2018

Our Strategy

We intend to become a leading biopharmaceutical company focused on the treatment of respiratory diseases with significant unmet medical needs. The key elements of our strategy to achieve this goal include:

- ***Rapidly advance the development of nebulized RPL554 for the maintenance treatment of COPD.*** We are developing RPL554 for the maintenance treatment of COPD. We plan to commence a four-week Phase 2b dose ranging clinical trial to evaluate RPL554 for the maintenance treatment of COPD in the second half of 2017. In this trial, we plan to compare the use of RPL554 in a nebulized formulation to placebo in approximately 400 patients. We expect to report top-line data from this trial in the second half of 2018. In February 2017, we commenced a Phase 2a clinical trial of RPL554 for the maintenance treatment of COPD in the United Kingdom. This trial is evaluating RPL554 as an add-on therapy to tiotropium in approximately 30 patients. We expect to report top-line data from this trial in the fourth quarter of 2017. We also plan to commence a PK trial of

RPL554 in approximately 12 healthy volunteers in the United States in mid-2017. We expect to report top-line data from this trial in the fourth quarter of 2017. In addition, we plan to commence a 12-week Phase 2b dose-ranging clinical trial of RPL554 for the maintenance treatment of COPD in the second half of 2018. In this trial, we plan to evaluate RPL554 as an add-on therapy to a long-acting bronchodilator in approximately 400 patients.

- ***Rapidly advance the development of nebulized RPL554 for the treatment of acute exacerbations of COPD.*** We also are developing RPL554 as an add-on therapy to short-acting bronchodilators and other commonly used therapies for the treatment of hospitalized patients with acute exacerbations of COPD. We plan to commence a Phase 2 clinical trial in the United States for RPL554 in this indication in approximately 150 patients in the second half of 2018.

- ***Develop RPL554 for the treatment of CF.*** In March 2017, we commenced a Phase 2a single-dose trial in the United Kingdom evaluating RPL554 in up to ten CF patients to evaluate the PK and PD profile and tolerability of RPL554, as well as examine the effect on lung function. We expect to report top-line data from this trial in the first half of 2018. The results of this clinical trial are expected to support dose selection for a proof-of-concept Phase 2b trial in approximately 100 patients with CF, which we plan to commence in 2018.

- ***Develop DPI and MDI formulations of RPL554.*** In addition to our nebulized formulation of RPL554, we are developing RPL554 in both DPI and MDI formulations for the maintenance treatment of COPD. We believe the development of DPI and MDI formulations has the potential to significantly increase the market opportunity for RPL554, if approved, for the maintenance treatment of COPD. In addition, we may explore the development of RPL554 in these formulations for the treatment of asthma. Following the completion of our DPI and MDI formulation process, we plan to commence pre-clinical studies for RPL554 in these formulations in 2018.

- ***Pursue development of RPL554 in other forms of respiratory disease.*** We believe that RPL554's properties as an inhaled, dual inhibitor of PDE3 and PDE4 give it broad potential applicability in the treatment of other respiratory diseases. We may explore development of RPL554 to treat other forms of respiratory disease following development of RPL554 for the treatment of COPD and CF.

- ***Seek strategic collaborative relationships.*** We may seek strategic collaborations with market-leading biopharmaceutical companies to develop and commercialize RPL554. We believe these collaborations could provide significant funding to advance the development of RPL554 while allowing us to benefit from the development or commercialization expertise of our collaborators.

- ***Acquire or in-license product candidates for the treatment of respiratory diseases.*** We plan to leverage our respiratory disease expertise to identify and in-license or acquire additional clinical-stage product candidates that we believe have the potential to become novel treatments for respiratory diseases with significant unmet medical needs.

Corporate Information

We were incorporated in February 2005 under the laws of England and Wales with the Registrar of Companies of England and Wales under the name Isis Resources plc. In September 2006, we acquired Rhinopharma Limited, or Rhinopharma, 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, and our telephone number is +(44) 203 283 4200. Since September 2006, our ordinary shares have traded on AIM, a market of the London Stock Exchange, under the symbol "VRP." Our website address is www.veronapharma.com. The information contained on, or that can be accessed from, our website does not form part of this prospectus. Our agent for service of process in the United States is National Corporate Research, Ltd.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. You should carefully consider all of the information set forth in this prospectus and, in particular, should evaluate the specific factors set forth under "Risk Factors" in deciding whether to invest in our ADSs or ordinary shares. Among these important risks are the following:

- We have a limited operating history, have never generated any product revenue, have incurred significant operating losses since our inception, expect to incur significant operating losses for the foreseeable future and may never achieve or maintain profitability.
- We will need additional funding to complete the development and commercialization of RPL554, if approved, and 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 depend heavily on the success of RPL554, our only product candidate, and we cannot give any assurance that RPL554 will receive regulatory approval for any indication, which is necessary before it can be commercialized.
- We may encounter regulatory changes that delay or impede our development and commercialization efforts.
- We rely, and expect to continue to rely, on third parties to conduct our clinical trials and to manufacture our product candidates for pre-clinical and clinical testing, and those third parties may not perform satisfactorily, which could delay our product development activities.
- If we are unable to adequately protect our technology, or to secure and maintain freedom to operate or issued patents protecting our product candidates, others could preclude us from commercializing our technology and products or compete against us more directly.
- We face significant competition from other biotechnology and pharmaceutical companies.
- Our future growth and ability to compete depends on retaining our key personnel and recruiting additional qualified personnel.
- If we are classified as a passive foreign investment company in any taxable year, it may result in adverse U.S. federal income tax consequences to U.S. holders of our ADSs or ordinary shares.
- As a foreign private issuer, we are exempt from a number of rules under the U.S. securities laws and NASDAQ Stock Market corporate governance rules and are permitted to file less information with the Securities and Exchange Commission, or the SEC, than U.S. companies, which may limit the information available to holders of our ADSs and ordinary shares.

Implications of Being an Emerging Growth Company and a Foreign Private Issuer

Emerging Growth Company

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As such, we may take advantage of certain exemptions from various reporting requirements that are applicable to other publicly traded entities that are not emerging growth companies. These exemptions include:

- the option to present only two years of audited financial statements and only two years of related Management's Discussion and Analysis of Financial Condition and Results of Operations in this prospectus;
- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board, or PCAOB, regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements (i.e., an auditor discussion and analysis);

- not being required to submit certain executive compensation matters to stockholder advisory votes, such as "say-on-pay," "say-on-frequency" and "say-on-golden parachutes;" and
- not being required to disclose certain executive compensation related items such as the correlation between executive compensation and performance and comparisons of the chief executive officer's compensation to median employee compensation.

As a result, we do not know if some investors will find our ADSs or ordinary shares less attractive. The result may be a less active trading market for our ADSs and ordinary shares, and the price of our ADSs and ordinary shares may become more volatile.

Section 107 of the JOBS Act also provides that an emerging growth company can take advantage of the extended transition period provided in Section 13(a) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, for complying with new or revised accounting standards. In other words, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We are choosing to irrevocably opt out of this extended transition period and as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies. Under federal securities laws, our decision to opt out of the extended transition period is irrevocable.

We will remain an emerging growth company until the earliest of: (i) the last day of the first fiscal year in which our annual gross revenues exceed $1.07 billion; (ii) the last day of the fiscal year following the fifth anniversary of the completion of the global offering; (iii) the date that we become a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our common equity held by non-affiliates exceeds $700 million as of the last business day of our most recently completed second fiscal quarter; or (iv) the date on which we have issued more than $1 billion in non-convertible debt securities during any three-year period.

Foreign Private Issuer

Upon the completion of the global offering, we will report under the Exchange Act as a non-U.S. company with foreign private issuer status. Even after we no longer qualify as an emerging growth company, as long as we qualify as a foreign private issuer under the Exchange Act we will be exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including:

- the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act;
- the sections of the Exchange Act requiring insiders to file public reports of their stock ownership and trading activities and liability for insiders who profit from trades made in a short period of time; and
- the rules under the Exchange Act requiring the filing with the SEC of quarterly reports on Form 10-Q containing unaudited financial and other specific information, or current reports on Form 8-K, upon the occurrence of specified significant events.

Both foreign private issuers and emerging growth companies also are exempt from certain more stringent executive compensation disclosure rules. Thus, even if we no longer qualify as an emerging growth company, but remain a foreign private issuer, we will continue to be exempt from the more stringent compensation disclosures required of companies that are neither an emerging growth company nor a foreign private issuer.

The Global Offering

Global offering	47,399,001 ordinary shares offered by us, consisting of ordinary shares in the form of ADSs offered in the U.S. offering and ordinary shares offered in the European private placement. The closing of each of the U.S. offering and the European private placement is conditioned upon the other.
U.S. offering	5,768,000 ADSs, each ADS representing eight ordinary shares
European private placement	1,255,001 ordinary shares
Ordinary shares to be outstanding immediately after the global offering and the shareholder private placement	99,014,164 ordinary shares (including 254,099 ordinary shares to be issued in the shareholder private placement)
Option to purchase additional ADSs in the U.S. offering	We have granted the underwriters an option to purchase up to an additional 865,200 ADSs from us within 30 days of the date of this prospectus.
Offering price	$13.50 per ADS in the U.S. offering and £1.32 per ordinary share in the European private placement. For a discussion of the factors considered in determining the initial public offering price of our ADSs and ordinary shares, see "Underwriting" in this prospectus.
American Depositary Shares	Each ADS represents eight ordinary shares, nominal value £0.05 per share. As an ADS holder you will not be treated as one of our shareholders and you will not have shareholder rights. You will have the rights of an ADS holder or beneficial owner (as applicable) as provided in the deposit agreement among us, the depositary and holders and beneficial owners of ADSs from time to time. To better understand the terms of our ADSs, see "Description of American Depositary Shares." We also encourage you to read the deposit agreement, the form of which is filed as an exhibit to the registration statement of which this prospectus forms a part.
Depositary	Citibank, N.A.
Use of proceeds	We estimate that the net proceeds to us from the global offering and shareholder private placement will be approximately $71.3 million (or approximately $82.1 million if the underwriters exercise in full their option to purchase an additional 865,200 ADSs), based on an initial public offering price of $13.50 per ADS in the U.S. offering and an offering price of £1.32 per ordinary share in the European private placement and shareholder private placement after deducting the underwriting discounts and commissions, placement agent fees and estimated offering expenses payable by us. We intend to use the net proceeds from the global offering and shareholder private placement, together with our cash and cash equivalents, to fund our planned clinical trials of RPL554 for the treatment of COPD and CF, current and future research and development activities and for working capital and other general corporate purposes. See "Use of Proceeds."

Risk factors	See "Risk Factors" and the other information included in this prospectus for a discussion of factors you should consider before deciding to invest in our ADSs or ordinary shares.
NASDAQ trading symbol for ADSs .	"VRNA"
AIM trading symbol	"VRP"

The number of our ordinary shares to be outstanding after the global offering and the shareholder private placement is based on 51,361,064 ordinary shares outstanding as of March 31, 2017 and excludes:

- 2,804,000 ordinary shares issuable upon the exercise of share options outstanding as of March 31, 2017 at a weighted average exercise price of £1.90 per share;
- 6,333,000 ordinary shares that may be issued under our 2017 Incentive Award Plan, or the New Incentive Plan, which became effective upon the pricing of the global offering, including ordinary shares underlying restricted share units and options that we have granted in connection with this global offering to each of our executive officers and a director, as more fully described in "Management—Equity Compensation Arrangements—2017 Incentive Award Plan—2017 Grants," as well as ordinary shares that may be issued pursuant to provisions in our New Incentive Plan that automatically increase the share reserve under our New Incentive Plan;
- 2,332,106 ordinary shares that may be issued under our existing equity incentive plans as of March 31, 2017; and
- 12,646,370 ordinary shares issuable upon the exercise of warrants outstanding as of March 31, 2017 at a weighted average exercise price of £1.7174 per share.

Unless otherwise indicated, all information contained in this prospectus assumes or gives effect to:

- a 50-for-one share consolidation in which we consolidated every 50 existing ordinary shares, nominal value £0.001 per share, in our issued share capital into one ordinary share, nominal value £0.05 per share, effected February 10, 2017;
- no exercise of the outstanding options or warrants described above after March 31, 2017; and
- no exercise by the underwriters of their option to purchase additional ADSs.

Participation in the Global Offering

Our existing institutional investors affiliated with certain of our directors have indicated an interest in purchasing up to an aggregate of approximately $23 million (or the pounds sterling equivalent) of the securities offered in the global offering on the same terms as the other purchasers in the global offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no securities offered in the global offering to any of these investors, or any of these investors may determine to purchase more, less or no securities offered in the global offering. The underwriters will receive the same underwriting discount on any securities purchased by these investors as they will on any other securities sold to the public in the global offering.

Shareholder Private Placement

Our chairman of the board of directors and an existing shareholder have agreed to purchase an aggregate of approximately £335,400 (or the U.S. dollar equivalent) of our ordinary shares in a private placement separate from the global offering, contingent on and concurrent with the completion of the global offering, at a price per share equal to the offering price per ordinary share in the European private placement. The underwriters will serve as placement agents for such shareholder private placement and receive a placement agent fee equal to a percentage of the total purchase price of the private placement shares, which percentage will be equal to the percentage discount the underwriters will receive on shares sold in this global offering. The closing of this global offering is not conditioned upon the closing of such shareholder private placement.

Summary Consolidated Financial Data

The following tables set forth our summary consolidated financial data for the periods indicated. We have derived the consolidated statement of comprehensive income data for the years ended December 31, 2015 and 2016 and the consolidated statement of financial position data as of December 31, 2016 from our Annual Consolidated Financial Statements included elsewhere in this prospectus.

Our historical results are not necessarily indicative of the results that should be expected for any future period. You should read the following summary consolidated financial data together with the Annual Consolidated Financial Statements included elsewhere in this prospectus and the sections titled "Exchange Rate Information" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

We maintain our books and records in pounds sterling, and we prepare our financial statements in accordance with IFRS as issued by the IASB. We report our financial results in pounds sterling. For the convenience of the reader, we have translated pound sterling amounts in the tables below as of December 31, 2016 and for the years ended December 31, 2015 and 2016 into U.S. dollars at the noon buying rate of the Federal Reserve Bank of New York on December 30, 2016, which was £1.00 to $1.2337. These translations should not be considered representations that any such amounts have been, could have been or could be converted into U.S. dollars at that or any other exchange rate as of that or any other date.

	Year Ended December 31,			
	2015		2016	
	(£)	($)	(£)	($)
	(in thousands, except per ordinary share data)			
Consolidated statement of comprehensive income data:				
Research and development costs	(7,269)	(8,968)	(4,522)	(5,579)
General and administrative costs	(1,706)	(2,105)	(2,498)	(3,082)
Operating loss	(8,975)	(11,072)	(7,020)	(8,661)
Finance income	45	55	1,841	2,272
Finance expense	(72)	(89)	(794)	(979)
Loss before taxation	(9,002)	(11,106)	(5,973)	(7,368)
Taxation — credit	1,509	1,862	954	1,177
Loss for the year	(7,493)	(9,244)	(5,018)	(6,191)
Other comprehensive income:				
Exchange differences on translating foreign operations	4	5	43	53
Total comprehensive loss attributable to owners of the company	(7,489)	(9,239)	(4,976)	(6,139)
Loss per ordinary share — basic and diluted	(0.37)	(0.46)	(0.15)	(0.19)

	As of December 31, 2016			
	Actual		As Adjusted[1]	
	(£)	($)	(£)	($)
	(in thousands)			
Consolidated statement of financial position data:				
Cash and cash equivalents	39,785	49,083	95,551	117,881
Total assets	46,143	56,926	101,909	125,725
Share premium	58,527	72,204	111,910	138,063
Total liabilities	11,674	14,402	11,674	14,402
Accumulated loss	(28,728)	(35,442)	(28,728)	(35,442)
Total equity	34,468	42,524	90,234	111,322

(1) The as adjusted statement of financial position data give effect to the sale by us of (i) 47,399,001 ordinary shares (including 46,144,000 ordinary shares in the form of ADSs) in the global offering at a public offering price of $13.50 per ADS in the U.S. offering and £1.32 per ordinary share in the European private placement after deducting the underwriting discounts and commissions and estimated offering expenses payable by us and (ii) £335,400 (or the U.S. dollar equivalent) of ordinary shares in the shareholder private placement, after deducting the placement agent fees.

RISK FACTORS

You should carefully consider the risks and uncertainties described below and the other information in this prospectus before making an investment in our ADSs or ordinary shares. Our business, financial condition, results of operations, or prospects could be materially and adversely affected if any of these risks occurs, and as a result, the market price of our ADSs or ordinary shares could decline and you could lose all or part of your investment. This prospectus also contains forward-looking statements that involve risks and uncertainties. See "Cautionary Statement Regarding Forward-Looking Statements." Our actual results could differ materially and adversely from those anticipated in these forward-looking statements as a result of certain factors.

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 £7.5 million and £5.0 million for the years ended December 31, 2015 and 2016, respectively. As of December 31, 2016, we had an accumulated loss of £28.7 million. Our losses have resulted principally from expenses incurred in research and development of RPL554, 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 and seek to obtain regulatory approval and commercialization for RPL554. We anticipate that our expenses will increase substantially as we:

- conduct our ongoing Phase 2a clinical trial and initiate and conduct our planned Phase 2b and PK clinical trials and any other future clinical trials of RPL554 for the treatment of COPD;
- develop RPL554 as DPI and MDI formulations for maintenance treatment of COPD, asthma and other respiratory diseases;
- conduct our ongoing Phase 2a clinical trial and any future clinical trials of RPL554 for the treatment of CF;
- seek to discover and develop or in-license additional respiratory product candidates;
- seek regulatory approvals of RPL554;
- potentially establish a sales, marketing and distribution infrastructure and scale-up manufacturing capabilities to commercialize RPL554, 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 and the United Kingdom.

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 other regulatory challenges or an increase in the cost of manufacturing clinical and commercial supplies of RPL554 and related inhalation devices.

We have devoted substantially all of our financial resources and efforts to the research and development and pre-clinical studies and clinical trials of RPL554. We are in the early stages of development of RPL554, 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 RPL554, discovering and developing additional product candidates,

obtaining regulatory approval for RPL554 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 most 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 RPL554 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 ordinary shares 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 or ordinary shares also could cause you to lose all or a part of your investment.

We will need additional funding to complete development of RPL554 and any future product candidates, and to commercialize our products, 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 activities, particularly as we conduct our planned Phase 2 clinical trials and any other future clinical trials of RPL554 and develop RPL554 for other indications. In addition, if we obtain regulatory approval for RPL554 or any other product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Furthermore, upon the closing of the global offering, we expect to incur additional costs associated with operating as a public company in the United Kingdom and the United States and maintaining a listing on both AIM and 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.

We expect that our existing cash, cash equivalents and investments, together with anticipated net proceeds from the global offering and the shareholder private placement, will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months. We anticipate these funds will be sufficient for the completion of (i) our two planned Phase 2b clinical trials, our planned PK clinical trial and our ongoing Phase 2a clinical trial of RPL554 for the maintenance treatment of COPD, (ii) our planned Phase 2 clinical trial of RPL554 for the treatment of acute exacerbations of COPD and (iii) our ongoing Phase 2a clinical trial and our planned Phase 2b proof-of-concept trial of RPL554 for the treatment of CF. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect, or 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 cost, progress and results of our ongoing Phase 2a clinical trials, our planned Phase 2b and PK clinical trials and any other future clinical trials of RPL554 for the treatment of COPD and CF;
- the cost of manufacturing clinical and commercial supplies of RPL554 and related inhalation devices;

- the scope, progress, results and costs of pre-clinical development, laboratory testing and clinical trials for RPL554 in other indications and for the development of DPI and MDI formulations of RPL554 for maintenance treatment of COPD and potentially asthma and other respiratory diseases;
- the costs, timing and outcome of regulatory review of RPL554, including post-marketing studies that could be required by regulatory authorities;
- the costs, timing and outcome of potential future commercialization activities, including manufacturing, marketing, sales and distribution, for RPL554;
- 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 RPL554;
- the sales price and availability of adequate third-party coverage and reimbursement for RPL554;
- 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 RPL554, 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 RPL554. 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 RPL554 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 RPL554, our only product candidate under development. We cannot give any assurance that RPL554 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 RPL554, are unable to commercialize RPL554, 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 RPL554, 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 RPL554, if approved, which may never occur. RPL554 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 RPL554 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 RPL554 or any future product candidate. We have not submitted a New Drug Application, or NDA, to the FDA, a Marketing Authorization Application, or MAA, 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 RPL554 will depend on many factors, including the following:

- we may not be able to demonstrate that RPL554 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 of RPL554 for the treatment of COPD, including for inhalation devices used in the development of RPL554, which would increase our costs and prolong our development;
- the results of clinical trials of RPL554 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, or 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 RPL554 outweigh its safety risks;
- the applicable regulatory authorities may disagree with our interpretation of data from our pre-clinical studies and clinical trials or may require that we conduct additional studies;
- 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 its approval policies or adopt new regulations;
- if we license RPL554 to others, the efforts of those parties in completing clinical trials of, receiving regulatory approval for and commercializing, RPL554;
- through our clinical trials, we may discover factors that limit the commercial viability of RPL554 or make the commercialization of RPL554 unfeasible;
- if we retain rights under a collaboration agreement for RPL554, our efforts in completing pre-clinical studies and clinical trials of, receiving marketing approvals for, establishing commercial manufacturing capabilities for and commercializing, RPL554; and
- if approved, acceptance of RPL554 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.

If we or our collaborators, as applicable, do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize RPL554.

We cannot be certain that RPL554 or any future product candidates will be successful in clinical trials or receive regulatory approval. Further, RPL554 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 RPL554 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 RPL554 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 RPL554 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 RPL554, and we cannot predict success in these jurisdictions.

Our limited operating history may make it difficult for you 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 RPL554, 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 RPL554, 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 you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

Raising additional capital may cause dilution to our holders, including purchasers of our ADSs or ordinary shares in the global offering, 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, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a holder of our ADSs or ordinary shares. 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 shareholders, and may cause the market price of our ADSs or ordinary shares 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. Almost all 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 and changing 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 implications of the recent decision of the eligible members of the U.K. electorate for the United Kingdom to withdraw 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 geo-political actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

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 and ordinary shares.

Following the vote of a majority of the eligible members of the electorate in the United Kingdom to withdraw from the EU in a national referendum held on June 23, 2016, the U.K. government served notice under Article 50 of the Treaty of the European Union on March 29, 2017 to formally initiate a withdrawal process. The United Kingdom and the EU have a two-year period under Article 50 to negotiate the terms for withdrawal. Any extension of the negotiation period for withdrawal will require the consent of all of the remaining 27 member states.

The referendum and withdrawal have created significant uncertainty about the future relationship between the United Kingdom and the EU. Lack of clarity about future U.K. laws and regulations as the United Kingdom determines which EU-derived laws and regulations to replace or replicate as part of a withdrawal, including financial laws and regulations, tax and free trade agreements, intellectual property rights, supply chain logistics, environmental, health and safety laws and regulations, immigration laws and employment laws, could decrease foreign direct investment in the United Kingdom, increase costs, depress economic activity and restrict our access to capital. If the United Kingdom and the EU are unable to negotiate acceptable withdrawal terms or if other EU member states pursue withdrawal, barrier-free access between the United Kingdom and other EU member states or among the European economic area overall could be diminished or eliminated. 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.

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 and ordinary shares 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

Our only product candidate, RPL554, is in early-stage clinical development. Clinical drug development is a lengthy and expensive process with uncertain timelines and uncertain outcomes. If clinical trials of RPL554 are prolonged or delayed, or if RPL554 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 RPL554 on a timely basis, or at all.

To obtain the requisite regulatory approvals to market and sell RPL554, we or any collaborator for RPL554 must demonstrate through extensive pre-clinical studies and clinical trials that RPL554 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 RPL554 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 for a variety of reasons, including the following:

- delays in or failure to obtain regulatory approval 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, or IRB, 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;
- adding new clinical trial sites;
- unexpected technical issues during manufacture of RPL554 and the corresponding drug product;
- inability to manufacture sufficient quantities of RPL554 for use in clinical trials, including failure or delay in obtaining regulatory approval for excipients used in the drug product, or inhalation devices used in the development of RPL554;
- third-party actions claiming infringement by RPL554 in clinical trials inside or outside of the United States 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;
- our third-party research contractors failing to comply with regulatory requirements or to meet their contractual obligations to us in a timely manner, or at all;
- delays in establishing the appropriate dosage levels or frequency of dosing or treatment in clinical trials;

- difficulty in certain countries in identifying the sub-populations that we are trying to treat in a particular trial, which may delay enrollment and reduce the power of a clinical trial to detect statistically significant results;
- the quality or stability of RPL554 falling below acceptable standards for either safety or efficacy; and
- discoveries that may reduce the commercial viability of RPL554.

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 RPL554.

If we experience delays in the completion of any clinical trial of RPL554 or any clinical trial of RPL554 is terminated, the commercial prospects of RPL554 may be harmed, and our ability to generate product revenues from RPL554, 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 RPL554 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 RPL554 and could impair our ability to commercialize RPL554. 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 RPL554.

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 at the medical institutions where the clinical trials are conducted. In addition, clinical trials must be conducted with supplies of RPL554 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.

RPL554 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 RPL554 or following approval, if any, we may need to abandon our development of RPL554, 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 RPL554 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. We have completed eight Phase 1 and 2a clinical trials of RPL554. In these trials, some patients have experienced mild to moderate adverse reactions, including headache, dizziness, cough, heart palpitation, nausea, dry mouth, throat irritation, paresthesia (tingling) and rash. 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 RPL554 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 RPL554 receives marketing approval and we or others later identify undesirable or unacceptable side effects caused by RPL554, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such products and require us to take RPL554 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 RPL554 outweigh its risks;
- we may be required to change the way RPL554 is administered, conduct additional clinical trials or change the labeling of RPL554;
- we may be subject to limitations on how we may promote RPL554;
- sales of RPL554 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 RPL554 or could substantially increase commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenue from the sale of RPL554.

We depend on enrollment of patients in our clinical trials for RPL554. 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 RPL554 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. Patient enrollment depends on many factors, including the size and nature of the patient population, eligibility criteria for the trial, the proximity of patients to clinical sites, the design of the clinical protocol, 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. Delays in the completion of any clinical trial of RPL554 will increase our costs, slow down our development and approval of RPL554 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 RPL554.

We may become exposed to costly and damaging liability claims, either when testing RPL554 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 RPL554 by us and any collaborators in clinical trials, and the sale of RPL554, 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 RPL554. Any claims against us, regardless of their merit, could be difficult and costly to defend and could adversely affect the market for RPL554 or any prospects for commercialization of RPL554. In addition, regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for RPL554;
- 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 RPL554.

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 RPL554 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 RPL554.

Although we maintain product liability insurance for RPL554, 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 RPL554. 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 authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for RPL554, our business will be substantially harmed.

The time required to obtain approval by the FDA, the EMA and comparable foreign 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 RPL554 and it is possible that RPL554 or any product candidates we may develop in the future will never obtain regulatory approval.

RPL554 could fail to receive regulatory approval for many reasons, including the following:

- the FDA, the EMA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA, the EMA or comparable foreign regulatory authorities that RPL554 is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA, the EMA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that RPL554'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 data collected from clinical trials of RPL554 may 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 composition of the final drug product or the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;
- the FDA, the EMA or comparable foreign regulatory authorities may fail to approve RPL554 in the delivery device we choose to use for the development of RPL554; and
- 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.

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 RPL554. 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 RPL554. Even if we believe the data collected from clinical trials of RPL554 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 RPL554 for fewer or more limited indications than we request, may not approve the price we intend to charge for RPL554, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve RPL554 with a label that does not include the labeling claims necessary or desirable for the successful commercialization of RPL554. Any of the foregoing scenarios could materially harm the commercial prospects for RPL554.

Even if RPL554 obtains regulatory approval, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, RPL554, 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 RPL554.

If the FDA, the EMA or a comparable foreign regulatory authority approves RPL554, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for RPL554 will be subject to extensive and ongoing regulatory requirements. These requirements include 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 RPL554 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 RPL554. We and our contract manufacturers will also be subject to user fees and 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. In addition, any regulatory approvals that we receive for RPL554 may also be subject to limitations on the approved indicated uses for which RPL554 may be marketed or to the conditions of

approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of RPL554.

If there are changes in the application of legislation or regulatory policies, or if problems are discovered with a product or the manufacture of RPL554, or if we or one of our distributors, licensees or co-marketers fails to comply with regulatory requirements, the regulators could take various actions. These include imposing fines on us, imposing restrictions on RPL554 or its manufacture and requiring us to recall or remove RPL554 from the market. The regulators could also suspend or withdraw our marketing authorizations, or require us to conduct additional clinical trials, change our product labeling or submit additional applications for marketing authorization. If any of these events occurs, our ability to sell RPL554 may be impaired, and we may incur substantial additional expense to comply with regulatory requirements.

We may not be successful in our efforts to develop RPL554 for multiple indications, including CF or other respiratory diseases.

Part of our strategy is to continue to develop RPL554 in indications other than COPD such as CF. Although our research and development efforts to date have suggested that RPL554 has the potential to treat CF, we may not be able to develop RPL554 in CF or any other disease, or development may not be successful. In addition, the potential use of RPL554 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 RPL554 for multiple indications, we will face difficulty in obtaining product revenues in future periods, which could significantly harm our financial position.

Even if we obtain marketing approval of RPL554 for any indication in a major pharmaceutical market such as the United States or EU, we may never obtain approval or commercialize RPL554 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 countries or territories 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 RPL554 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 RPL554 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, EU rules and regulations and

other similar regulatory requirements, 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, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

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

From time to time, we may publish interim "top-line" or preliminary data from our clinical studies. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or "top-line" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

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 RPL554 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 United States 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 50% 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;
- new requirements to report certain financial arrangements with physicians and certain others, including reporting "transfers of value" made or distributed to prescribers and other healthcare providers and reporting investment interests held by physicians and their immediate family members;
- 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;
- creation of the Independent Payment Advisory Board, which, once empaneled, will have the authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs and those recommendations could have the effect of law unless overruled by a supermajority vote of Congress; 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 new Presidential Administration and U.S. Congress will likely continue to seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA. It is uncertain the extent to which any such changes may impact our business or financial condition.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2025 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 new laws 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. The U.S. Department of Health and Human Services, or HHS, has set a goal of moving 30% of Medicare payments to alternative payment models by 2016 and 50% of Medicare payments into these alternative payment models by the end of 2018. 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 RPL554 or additional pricing pressures.

Individual states in the United States have also become increasingly aggressive 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 RPL554 or put pressure on our product pricing.

In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize RPL554, 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 healthcare 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 RPL554, restrict or regulate post-approval activities and affect our ability to commercialize RPL554, 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, RPL554 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, health care 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 RPL554, 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, or HITECH, and its implementing regulations, 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 U.S. federal Food, Drug and Cosmetic Act, or 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) 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 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; and
- European and other foreign law equivalents of each of the laws, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve 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, 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 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 RPL554 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 RPL554.

Given the number of products already on the market to treat COPD and CF, we expect to face intense competition if RPL554 is approved for these indications. Boehringer Ingelheim, GlaxoSmithKline, AstraZeneca, Mylan, Novartis, Vertex and Sunovion currently have treatments on the market for COPD and CF, and we anticipate that new companies will enter these markets in the future. If we successfully develop and commercialize RPL554, 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 RPL554 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 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 and competing for other customers, for clinical trials, as well as in acquiring

technologies complementary to, or necessary for, our programs. In addition, our collaborators, if any, may decide to market and sell products that compete with RPL554. 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 RPL554. Our competitors may also obtain FDA or other regulatory approval for their products 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 for RPL554 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, the EMA's Committee for Orphan Medicinal Products, or COMP, grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU. 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 towards clinical trial costs, tax credits for qualified clinical testing and user-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 RPL554 for the treatment of CF. Even if we are able to obtain orphan designation for RPL554 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 RPL554 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 RPL554, that exclusivity may not effectively protect RPL554 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 safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a 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 RPL554 for the treatment of CF, we may never receive such designations.

There have been legal challenges to aspects of the FDA's regulations and policies concerning the exclusivity provisions of the Orphan Drug Act, and future challenges could lead to changes that affect the protections afforded our products in ways that are difficult to predict. In 2014, a U.S. district court invalidated the FDA's denial of orphan exclusivity to an orphan designated drug, which the FDA had based on its determination that the drug was not proven to be clinically superior to a previously approved "same drug." In response to the decision, the FDA released a policy statement stating that the court's decision is limited just to the facts of that particular case and that the FDA will continue to deny orphan drug exclusivity to a designated drug upon approval if the drug is the "same" as a previously approved drug, unless the drug is demonstrated to be clinically superior to that previously approved drug. In April 2016, another similar legal challenge was initiated against the FDA for its denial of orphan drug exclusivity to another designated drug. In the future, there is the potential for additional legal challenges to the FDA's orphan drug regulations and policies, and it is uncertain how ongoing and future challenges might affect our business.

The successful commercialization of RPL554 will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage, reimbursement levels and pricing policies. Failure to obtain or maintain adequate coverage and reimbursement for RPL554, if approved, could limit our ability to market those products 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 RPL554, assuming approval. Our ability to achieve acceptable levels of coverage and reimbursement for products by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize RPL554. Assuming we obtain coverage for RPL554 by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the United States, the EU or elsewhere will be available for RPL554 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 RPL554 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 RPL554, pricing of existing drugs may limit the amount we will be able to charge for RPL554. 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 RPL554. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize RPL554, and may not be able to obtain a satisfactory financial return on RPL554.

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 health care 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 RPL554.

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 RPL554 to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases at short notice, and we believe that changes in these rules and regulations are likely.

Outside the 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 RPL554. 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 RPL554. Accordingly, in markets outside the United States, the reimbursement for RPL554 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 RPL554. We expect to experience pricing pressures in connection with the sale of RPL554 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.

RPL554 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 RPL554, whether developed on our own or with a collaborator, physicians, healthcare providers, patients or the medical community may not accept or use RPL554. If RPL554 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 RPL554 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 RPL554 is approved;
- our ability to provide acceptable evidence of safety and efficacy;
- the prevalence and severity of any side effects;
- relative convenience and ease of administration;
- the availability of inhalation devices, such as nebulizers, used to administer RPL554;
- 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 RPL554 fails to gain market acceptance, this will adversely impact on our ability to generate revenues. Even if RPL554 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 RPL554.

We have no marketing, sales or distribution capabilities and we have no experience with marketing, selling or distributing pharmaceutical products. If RPL554 is approved, we intend either to establish a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize RPL554, 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 RPL554. 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 RPL554.

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 RPL554, 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 RPL554. If we are not successful in commercializing RPL554, 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 RPL554 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 third-party 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 European Economic Area, or 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 assure you 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 RPL554 and clinical trials. If independent investigators or CROs fail to devote sufficient resources to the development of RPL554, or if their performance is substandard, it may delay or compromise the prospects for approval and commercialization of RPL554. 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. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced 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 successfully commercialize RPL554. As a result, our results of operations and the commercial prospects for RPL554 would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Switching or adding additional CROs involves additional cost and requires management 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.

If we fail to enter into new strategic relationships for RPL554, our business, research and development and commercialization prospects could be adversely affected.

Our development program for RPL554 and the potential commercialization of RPL554 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 RPL554. For example, we may seek a collaborator for development of a DPI or MDI formulation of RPL554 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 RPL554, 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 RPL554 to market and generate product revenue. If we do enter into a collaboration agreement, we could be subject to the following risks, among others:

- we may not be able to control the amount and timing of resources that the collaborator devotes to the development of RPL554;
- 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 obligations under our agreement with Vernalis Development Limited, or Vernalis.

We currently rely on third-party manufacturers and suppliers for the production, storage and distribution of RPL554. Our dependence on these third parties may impair the advancement of our research and development programs and the development of RPL554. Moreover, we intend to rely on third parties to produce commercial supplies of RPL554, if approved, and commercialization could be stopped, delayed or made less profitable if those third parties fail to obtain approval of the FDA or comparable regulatory authorities, fail to provide us with sufficient quantities of product 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 RPL554. Instead, we rely on and expect to continue to rely on third-party contract manufacturing organizations, or CMOs, for the supply, storage and distribution of cGMP-grade clinical trial materials and commercial quantities of RPL554, if approved. While we may contract with other CMOs in the future, we currently contract with only one pharmaceuticals CMO for the manufacture of RPL554 drug substance. For RPL554 drug product in our new nebulized suspension formulation, we currently have two CMOs. Reliance on third-party suppliers for RPL554 may expose us to more risk than if we were to manufacture RPL554 ourselves. The facilities used to manufacture RPL554 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 control the manufacturing process of, and are or will be essentially dependent on, our CMOs for compliance with cGMP requirements for the manufacture of RPL554. 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 its manufacturing facilities. In addition, we have very little 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 RPL554 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 RPL554, 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 manufacturing of RPL554 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 RPL554 means that we are subject to the risk that RPL554 may have manufacturing defects that we have limited ability to prevent or control. Any natural or other disasters, acts of war or terrorism, shipping embargoes, labor unrest or political instability or similar events at our third-party manufacturers' facilities that causes a loss of manufacturing capacity could also heighten the risks we face.

We rely on and will continue to rely on CMOs to purchase from third-party suppliers the materials necessary to produce RPL554 for our clinical trials. There are a limited number of suppliers for raw materials that we may use to manufacture RPL554 and there may be a need to assess alternate suppliers to prevent a

possible disruption of the manufacture of the materials necessary to produce RPL554 for our clinical trials, and if approved, ultimately for commercial sale. Any disruption in our relationship with our current CMOs could have a material impact on our ability to continue our clinical development of RPL554. We do not and will not have any control over the process or timing of the acquisition of these raw materials by any CMO. Moreover, we currently do not have any agreements for the commercial production of these raw materials. Supplies of raw material 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 at all. 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 RPL554 to complete the clinical trial, any significant delay in the supply of RPL554, or the raw material components needed to produce RPL554, for an ongoing clinical trial due to the need to replace our CMO or a third-party supplier could considerably delay completion of our clinical trials, product testing and potential regulatory approval of RPL554. If our CMO or we are unable to purchase these raw materials after regulatory approval has been obtained for RPL554, the commercial launch of RPL554 would be delayed or there would be a shortage in supply, which would impair our ability to generate revenues from the sale of RPL554. In addition, growth in the costs and expenses of raw materials may impair our ability to cost-effectively manufacture RPL554.

We rely and will 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 fail to acquire the proper licenses or otherwise infringe 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 RPL554, if approved.

Risks Related to Intellectual Property and Information Technology

We rely on patents and other intellectual property rights to protect RPL554, 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 RPL554, formulations of RPL554, polymorphs, salts and analogs of RPL554, methods used to manufacture RPL554, 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 RPL554 alone or in combination with other available products, or on in-licensing such rights. Our RPL554 development program relies on the patents and patent applications assigned and know-how licensed from Vernalis Development Limited, or Vernalis. 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 RPL554.

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 assure you 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 our RPL554, 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 RPL554. 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 RPL554.

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 RPL554 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 RPL554 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 RPL554 or the use of RPL554. 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 RPL554. We may incorrectly determine that RPL554 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 RPL554. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market RPL554.

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 RPL554. We might, if possible, also be forced to redesign RPL554 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 RPL554, 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 RPL554, 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 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 RPL554. 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 or investors perceive these results to be negative, it could have an adverse effect on the price of our ADSs and ordinary shares.

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 U.S. Patent and Trademark Office, or 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 product candidates. 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 RPL554 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 our current and 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 RPL554 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 RPL554 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 RPL554. 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, we could have a substantial adverse effect on the price of our ordinary shares or 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 Vernalis, 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 any current or future product candidates. Under our agreement with Vernalis, we may not abandon any of the assigned patents or allow any of the assigned patents to lapse without consent from Vernalis, 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 Vernalis 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 Vernalis does not provide consent and such patent rights lapse, we may lose all intellectual property rights covering RPL554 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 necessary rights to RPL554 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 RPL554, 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, RPL554 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 from third parties that we identify as necessary for RPL554. 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 RPL554 or a development program on acceptable terms, we may have to abandon development of RPL554 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 RPL554 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 RPL554 expire in 2020, and our other issued patents will expire in 2031, 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 RPL554 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 FDA marketing approval of RPL554, 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 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 twelve months after the priority filing. Based on the PCT filing, national and regional patent applications may be filed in additional jurisdictions where we believe RPL554 may be marketed or manufactured. We have so far not filed for patent protection in all national and regional jurisdictions where such protection may be available. Filing, prosecuting and defending patents covering RPL554 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 and 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 and our licensors or collaborators have patent protection, but enforcement is not as strong as that in the United States. These products may compete with RPL554, 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 RPL554. 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 RPL554 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 RPL554 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 RPL554.
- 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 strategic 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 products 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 RPL554 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 in 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 United States Patent and Trademark Office, or 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 will require us to be cognizant going forward 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 the U.S. 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 advisers 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 RPL554, our competitors might be able to enter the market, which would hurt our competitive position and could impair our ability to successfully commercialize RPL554 in any indication for which it is approved.

Our proprietary information, or that of our suppliers and any future collaborators, may be lost or we may suffer security breaches.

In the ordinary course of our business, we 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 data centers and on our networks. The secure processing, maintenance and transmission of this information is critical to our operations. 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 information, 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 our clinical development of RPL554.

Our information technology systems 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, face the risk of systemic failure that could disrupt our operations. A significant disruption in the availability of our 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 retaining our key personnel and recruiting additional qualified personnel.

Our success depends upon the continued contributions of our key management, scientific and technical personnel, many of whom have been instrumental for us and have substantial experience with RPL554 and related technologies. These key management individuals include our chief executive officer, Jan-Anders Karlsson, our chief medical officer, Kenneth Newman, our chief financial officer, Piers Morgan, our legal counsel, Claire Poll, and our senior vice president, chemistry manufacturing and controls, Peter Spargo.

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 the Global Offering and Our ADSs and Ordinary Shares

The price of our ADSs and ordinary shares 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 and ordinary shares may fluctuate significantly due to a variety of factors, including:

- positive or negative results from, or delays in, testing and clinical trials by us, collaborators or competitors;
- delays in entering into collaborations and strategic relationships with respect to development or commercialization of RPL554 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 RPL554;
- financing or other corporate transactions;
- publication of research reports or comments by securities or industry analysts;
- 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 or ordinary shares by us, our senior management and board members, holders of our ADSs or our shareholders in the future; 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 and ordinary shares to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from readily selling their ADSs or ordinary shares and may otherwise negatively affect the liquidity of our ADSs and ordinary shares. 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 or ordinary shares 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.

We will incur increased costs as a result of operating as a public company in the United States, and our senior management will be 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, we will incur significant legal, accounting and other expenses that we did not incur previously. 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 will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified senior management personnel or members for our board of directors.

However, 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 will be required to furnish a report by our senior management on our internal control over financial reporting. However, while we remain an emerging growth company, or 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 timeframe 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.

There has been no public market for our ADSs prior to the U.S. offering, and an active market may not develop in which investors can resell our ADSs.

Prior to the U.S. offering, there has been no public market for our ADSs, although our ordinary shares have traded on AIM. We cannot predict the extent to which an active market for our ADSs will develop or be sustained after the U.S. offering, or how the development of such a market might affect the market price for our ADSs. The initial public offering price of our ADSs in the U.S. offering has been agreed upon between us and the underwriters based on a number of factors, including market conditions in effect at the time of the offering, which may not be indicative of the price at which our ADSs will trade following completion of the offering. Investors may not be able to sell their ADSs at or above the initial public offering price.

The dual listing of our ordinary shares and our ADSs following the U.S. offering may adversely affect the liquidity and value of our ordinary shares and ADSs.

Following the U.S. offering and after our ADSs begin trading on NASDAQ, our ordinary shares will continue to be admitted to trading on AIM. We cannot predict the effect of this dual listing on the value of our ADSs and ordinary shares. However, the dual listing of our ADSs and ordinary shares may dilute the liquidity of these securities in one or both markets and may adversely affect the development of an active trading market for our ADSs in the United States. The price of our ADSs could also be adversely affected by trading in our ordinary shares on AIM. Although our ordinary shares are currently admitted to trading on AIM, following the global offering, we may decide to cancel the admission of our ordinary shares to trading on AIM. Cancellation of the admission of our ordinary shares to trading on AIM would require the requisite consent of shareholders in a general meeting prescribed by AIM Rules for Companies, unless the London Stock Exchange agrees otherwise. We cannot predict the effect such cancellation would have on the market price of our ADSs or ordinary shares.

Certain of our existing shareholders, members of our board of directors, and senior management will maintain the ability to exercise significant control over us. Your interests may conflict with the interests of these existing shareholders.

As of March 31, 2017, after giving effect to the closing of the global offering and the shareholder private placement, our senior management, board of directors and greater than 5% shareholders and their respective affiliates, in the aggregate, will own 38.3% of our ordinary shares (including ordinary shares in the form of ADSs) assuming no exercise of outstanding options or warrants, and 51.6% of our ordinary shares, assuming exercise of all outstanding warrants, which become exercisable upon the completion of the global offering. Based on the public offering price of $13.50 per ADS in the U.S. offering and the offering

price £1.32 per share in the European private placement and the shareholder private placement, if our existing institutional investors that are affiliated with certain of our directors purchase all of the securities they have indicated an interest in purchasing in the global offering and all of the securities for which there are indications of interest are sold in the shareholder private placement, and assuming exercise of all outstanding warrants, the number of ordinary shares beneficially owned by our senior management, board of directors and greater than 5% shareholders and their respective affiliates, in the aggregate, will be 61.2% of our ordinary shares (including ordinary shares in the form of ADSs). 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, the approval of certain significant corporate transactions and amendments to our Articles of Association. 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.

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 and ordinary shares.

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 and ordinary shares. Based upon the number of shares outstanding as of March 31, 2017, after giving effect to the closing of the global offering and the shareholder private placement, we will have 99,014,164 ordinary shares outstanding, assuming no exercise of outstanding options or warrants. ADSs and ordinary shares issued and sold in the global offering may be resold in the public market immediately without restriction, unless purchased by our affiliates. A significant portion of these ordinary shares and ADSs will be subject to the lock-up agreements described in the "Ordinary Shares and ADSs Eligible for Future Sale" and "Underwriting." If, after the end of such lock-up agreements, 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 or ordinary shares and our ability to raise capital through an issue of equity securities in the future could be adversely affected. We have also entered into a registration rights agreement pursuant to which we agreed under certain circumstances to file a registration statement to register the resale of the ordinary shares held by certain of our existing shareholders, as well as to cooperate in certain public offerings of such shares.

If you purchase ordinary shares or ADSs in the global offering, you will suffer immediate dilution of your investment.

We expect the initial public offering price of our ADSs in the U.S. offering and the offering price of our ordinary shares in the European private placement to be substantially higher than the net tangible book value per ADS and per ordinary share prior to the global offering. Therefore, if you purchase ADSs or ordinary shares in the global offering, you will pay a price per ADSs and per ordinary share that substantially exceeds our net tangible book value per ADS and per ordinary share after the global offering. To the extent outstanding options or warrants are exercised for ordinary shares, you may experience further dilution. Based on the initial public offering price of $13.50 per ADS in the U.S. offering and the offering price of £1.32 per ordinary share in the European private placement, you will experience immediate dilution of $4.60 per ADS and £0.45 per ordinary share, representing the difference between our net tangible book value per ADS and per ordinary share after giving effect to the global offering. See "Dilution."

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 your sole source of gains and you may never receive a return on your investment.

Under current U.K. 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 your sole source of gains for the foreseeable future, and you will suffer a loss on your investment if you are unable to sell your ADSs or ordinary shares at or above the offering price. Investors seeking cash dividends should not purchase our ADSs or ordinary shares in the global offering.

We have broad discretion in the use of the net proceeds from the global offering and the shareholder private placement and may not use them effectively.

Our senior management will have broad discretion in the application of the net proceeds from the global offering and the shareholder private placement and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our ordinary shares or ADSs. The failure by our senior management to apply these funds effectively could result in financial losses, cause the price of our ADSs or ordinary shares to decline and delay the development of RPL554. Pending their use, we may invest the net proceeds from the global offering and the shareholder private placement in a manner that does not produce income or that loses value.

Securities traded on AIM may carry a higher risk than securities traded on other exchanges, which may impact the value of your investment.

Our ordinary shares are currently traded on AIM. Investment in equities traded on AIM is sometimes perceived to carry a higher risk than an investment in equities quoted on exchanges with more stringent listing requirements, such as the main market of the London Stock Exchange, New York Stock Exchange or NASDAQ. This is because AIM imposes less stringent corporate governance and ongoing reporting requirements than those other exchanges. In addition, AIM requires only half-yearly, rather than quarterly, financial reporting. You should be aware that the value of our ordinary shares may be influenced by many factors, some of which may be specific to us and some of which may affect AIM-quoted companies generally, including the depth and liquidity of the market, our performance, a large or small volume of trading in our ordinary shares, legislative changes and general economic, political or regulatory conditions, and that the prices may be volatile and subject to extensive fluctuations. Therefore, the market price of our ordinary shares, our ADSs, or of the ordinary shares underlying our ADSs, may not reflect the underlying value of our company.

Purchasers of ADSs in the U.S. offering 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.

Except as described in this prospectus, holders of our ADSs will not be able to exercise voting rights attaching to the ordinary shares evidenced by our ADSs on an individual basis. Holders of our ADSs will appoint the depositary or its nominee as their representative to exercise the voting rights attaching to the ordinary shares in the form of ADSs. Purchasers of ADSs in the U.S. offering 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, purchasers of ADSs in the U.S. offering may not be able to exercise voting rights and may lack recourse if their ADSs are not voted as requested. In addition, in their capacity as ADS holders, purchasers of ADSs in the U.S. offering will not be able to call a shareholders' meeting.

Purchasers of ADSs in the U.S. offering may not receive distributions on our ordinary shares in the form of ADSs or any value for them if it is illegal or impractical to make them available to holders of ADSs.

The depositary for our ADSs has agreed to pay to purchasers of ADSs in the U.S. offering 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. Purchasers 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, it may be unlawful or impractical to make a distribution available to holders of 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 purchasers of ADSs in the U.S. offering may not receive the distributions we make on our ordinary shares or any value from them if it is unlawful or impractical to make them available to them. These restrictions may have a material adverse effect on the value of a purchaser's ADSs.

Purchasers of ADSs in the U.S. offering 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.

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 respects from the rights of shareholders in typical U.S. corporations. See "Description of Share Capital and Articles of Association — Differences in Corporate Law" in this prospectus for a description of the principal differences between the provisions of the Companies Act 2006 applicable to us and, for example, the Delaware General Corporation Law relating to shareholders' rights and protections.

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.

We qualify as a foreign private issuer and, as a result, we will not be subject to U.S. proxy rules and will be subject to Exchange Act reporting obligations that, to some extent, are more lenient and less frequent than those of a U.S. domestic public company.

Upon the closing of the U.S. offering, we will report under the Securities Exchange Act of 1934, as amended, or the Exchange Act, as a non-U.S. company with foreign private issuer status. Because we qualify as a foreign private issuer under the Exchange Act, we are exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including (i) the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act; (ii) the sections of the Exchange Act requiring insiders to file public reports of their stock ownership and trading activities and liability for insiders who profit from trades made in a short period of time; and (iii) the rules under the Exchange Act requiring the filing with the SEC of quarterly reports on Form 10-Q containing unaudited financial and other specified information, or current reports on Form 8-K, upon the occurrence of specified significant events. Although it is not required because we are a foreign private issuer, we intend to furnish quarterly unaudited financial information to the SEC on Form 6-K. In addition, foreign private issuers are not required to file their annual report on Form 20-F until 120 days after the end of each fiscal year, while U.S. domestic issuers that are accelerated filers are required to file their annual report on Form 10-K within 75 days after the end of each fiscal year. Foreign private issuers also are exempt from Regulation Fair Disclosure, aimed at preventing issuers from making selective disclosures of material information. As a result of the above, you may not have the same protections afforded to shareholders of companies that are not foreign private issuers.

As a foreign private issuer, we are permitted to adopt certain home country practices in relation to corporate governance matters that differ significantly from NASDAQ corporate governance listing standards. These practices may afford less protection to shareholders than they would enjoy if we complied fully with NASDAQ corporate governance listing standards.

As a foreign private issuer listed on NASDAQ, we will be subject to corporate governance listing standards. However, NASDAQ rules permit a foreign private issuer like us to follow the corporate governance practices of its home country in lieu of certain NASDAQ corporate governance listing standards. Certain corporate governance practices in the United Kingdom, which is our home country, may differ significantly from NASDAQ corporate governance listing standards. For example, neither the corporate laws of the United Kingdom nor our Articles of Association require a majority of our directors to be independent; we could include non-independent directors as members of our nomination and remuneration committee; and our independent directors would not necessarily hold regularly scheduled meetings at which only independent directors are present. Therefore, our shareholders may be afforded less protection than they otherwise would have under NASDAQ corporate governance listing standards applicable to U.S. domestic issuers. See "Management—Foreign Private Issuer Exemption."

We may lose our foreign private issuer status, which would then require us to comply with the Exchange Act's domestic reporting regime and cause us to incur significant legal, accounting and other expenses.

As a foreign private issuer, we are not required to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act applicable to U.S. domestic issuers. We may no longer be a foreign private issuer as of June 30, 2018 (the end of our second fiscal quarter in the fiscal year after the global offering), which would require us to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act applicable to U.S. domestic issuers as of January 1, 2019. In order to maintain our current status as a foreign private issuer, either (a) a majority of our ADSs must be either directly or indirectly owned of record by non-residents of the United States or (b)(i) a majority of our executive officers or directors cannot be U.S. citizens or residents, (ii) more than 50 percent of our assets must be located outside the United States and (iii) our business must be administered principally outside the United States. If we lose our status as a foreign private issuer, we would be required to comply with the Exchange Act reporting and other requirements applicable to U.S. domestic issuers, which are more detailed and extensive than the requirements for foreign private issuers. We may also be required to make

changes in our corporate governance practices in accordance with various SEC and NASDAQ rules. The regulatory and compliance costs to us under U.S. securities laws if we are required to comply with the reporting requirements applicable to a U.S. domestic issuer may be significantly higher than the cost we would incur as a foreign private issuer. As a result, we expect that a loss of foreign private issuer status would increase our legal and financial compliance costs and would make some activities highly time consuming and costly. We also expect that if we were required to comply with the rules and regulations applicable to U.S. domestic issuers, it would make it more difficult and expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These rules and regulations could also make it more difficult for us to attract and retain qualified members of our board of directors.

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 or ordinary shares less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404, exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. As an emerging growth company, we are required to report only two years of financial results and selected financial data compared to three and five years, respectively, for comparable data reported by other public companies. We may take advantage of these exemptions until we are no longer an emerging growth company. We could be an emerging growth company 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) before that time, 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 or ordinary shares less attractive because we may rely on these exemptions. If some investors find our ADSs or ordinary shares less attractive as a result, there may be a less active trading market for our ADSs or ordinary shares and the price of our ADSs or ordinary shares 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 or ordinary shares.

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 or ordinary shares.

In connection with the preparation for this initial public offering, we reassessed our critical accounting policies to ensure compliance with IFRS. As part of this reassessment, we identified errors relating to the recognition of assumed liabilities and goodwill in connection with the acquisition of Rhinopharma in September 2006. We concluded that a lack of adequate controls surrounding our historic accounting for business combinations constituted a material weakness in our internal control over financial reporting, as

defined in the standards established by the U.S. Public Accounting Oversight Board, or PCAOB. The PCAOB defines a material weakness as a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of the company's annual or interim financial statements will not be prevented or detected in a timely basis. We are currently in the process of remediating this material weakness and have taken steps that we believe will address the underlying causes of the material weakness by the hiring of our new chief financial officer and enhancing our financial reporting team's technical accounting knowledge associated with the accounting rules for business combinations. However, we cannot be certain that these efforts will be sufficient to remediate this material weakness or prevent future material weaknesses or significant deficiencies from occurring.

Management will be required to assess the effectiveness of our internal controls annually. However, for as long as we are an "emerging growth company" under the JOBS Act, 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.

If securities or industry analysts do not publish research, or 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 will depend in part on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts do not currently, and may never, publish research on us. If no or too few securities or industry analysts commence coverage on us, the trading price for our ADSs and ordinary shares would likely be negatively affected. In the event securities or industry analysts initiate coverage, if one or more of the analysts who cover us downgrade our ADSs or ordinary shares or publish inaccurate or unfavorable research 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 or ordinary shares could decrease, which might cause the price of our ADSs and ordinary shares and trading volume to decline.

We believe we will likely be classified as a passive foreign investment company for U.S. federal income tax purposes for the current year, which could result in adverse U.S. federal income tax consequences to U.S. investors in our ordinary shares or ADSs.

Because we do not expect to earn revenue from our business operations during the current taxable year, 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 current taxable year. 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 under "Material Tax Considerations — Material U.S. Federal Income Tax Considerations for U.S. Holders") owns the 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 the 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. See "Material Tax Considerations — Material U.S. Federal Income Tax Considerations for U.S. Holders — Passive Foreign Investment Company Rules."

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains statements that constitute forward-looking statements. Many of the forward-looking statements contained in this prospectus can be identified by the use of forward-looking words such as "anticipate," "believe," "could," "estimate," "expect," "intend," "plan," "potential" and "should," among others.

Forward-looking statements appear in a number of places in this prospectus and include, but are not limited to, statements regarding our intent, belief or current expectations. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. Such statements are subject to substantial risks and uncertainties, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various important factors, including, but not limited to, those identified under "Risk Factors." In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a guarantee by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all.

Forward-looking statements include, but are not limited to, statements about:

- the development of RPL554, including statements regarding the expected initiation, timing, progress and availability of data from our clinical trials;
- the potential attributes and benefit of RPL554 and its competitive position;
- our ability to successfully commercialize RPL554, if approved;
- our expectations regarding the use of proceeds from the global offering and the shareholder private placement;
- our estimates regarding expenses, future revenues, capital requirements and our need for additional financing;
- our ability to acquire or in-license new product candidates;
- potential collaborations; and
- the duration of our patent portfolio.

Forward-looking statements speak only as of the date they are made, and we do not undertake any obligation to update them in light of new information or future developments or to release publicly any revisions to these statements in order to reflect later events or circumstances or to reflect the occurrence of unanticipated events.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

MARKET AND INDUSTRY DATA

Certain industry data and market data included in this prospectus were obtained from independent third-party surveys, market research, publicly available information, reports of governmental agencies and industry publications and surveys. All of the market data used in this prospectus involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. We believe that the information from these industry publications and surveys included in this prospectus is reliable. The industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of factors, including those described in "Risk Factors." These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

TRADEMARKS, SERVICE MARKS AND TRADENAMES

Solely for convenience, the trademarks, service marks, logos and trade names referred to in this prospectus are without the ® and ™ symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensors to these trademarks, service marks and trade names. This prospectus contains additional trademarks, service marks and trade names of others, which are the property of their respective owners. All trademarks, service marks and trade names appearing in this prospectus are, to our knowledge, the property of their respective owners. We do not intend our use or display of other companies' trademarks, service marks, copyrights or trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

EXCHANGE RATE INFORMATION

Our business is primarily conducted in the United Kingdom, and we maintain our books and records in pounds sterling. In this prospectus, unless otherwise indicated, translations from pounds sterling into U.S. dollars were made at the rate of £1.00 to $1.2783, which was the noon buying rate of the Federal Reserve Bank of New York on April 21, 2017. Such U.S. dollar amounts are not necessarily indicative of the amounts of U.S. dollars that could actually have been purchased upon exchange of pounds sterling at the dates indicated.

The following table presents information on the exchange rates between the pound sterling and the U.S. dollar for the periods indicated:

	Period-end[1]	Average for period[2]	Low	High
	(U.S. dollars per pound sterling)			
Year Ended December 31:				
2012	1.6262	1.5853	1.5301	1.6275
2013	1.6574	1.5641	1.4837	1.6574
2014	1.5578	1.6484	1.5517	1.7165
2015	1.4746	1.5284	1.4648	1.5882
2016	1.2337	1.3555	1.2155	1.4800
2017 (through April 21)	1.2783	1.2432	1.2118	1.2830

(1) In the event that the period end fell on a day for which data are not available, the exchange rate on the prior most recent business day is given.

(2) The average of the noon buying rate for pounds sterling on the last day of each full month during the relevant year or each business day during the relevant month indicated.

	Low	High
	(U.S. dollars per pound sterling)	
Month Ended:		
October 31, 2016	1.2155	1.2840
November 30, 2016	1.2218	1.2546
December 31, 2016	1.2222	1.2708
January 31, 2017	1.2118	1.2620
February 28, 2017	1.2427	1.2643
March 31, 2017	1.2152	1.2583
April 2017 (through April 21)	1.2398	1.2830

PRICE RANGE OF OUR ORDINARY SHARES

Our ordinary shares have been trading on AIM under the symbol "VRP" since September 19, 2006.

The following table presents, for the periods indicated, the reported high and low sale prices of our ordinary shares on AIM in pounds sterling and U.S. dollars. The price information below has been adjusted to reflect the 50-for-one share consolidation effected February 10, 2017. Price per ordinary share in U.S. dollars amounts below have been translated into U.S. dollars at the noon buying rate of the Federal Reserve Bank of New York on April 21, 2017 of £1.00 to $1.2783.

	Price Per Ordinary Share £		Price Per Ordinary Share $	
	High	Low	High	Low
Year Ended December 31:				
2012	2.8550	1.2500	3.5396	1.5498
2013	2.8750	0.8350	3.5644	1.0352
2014	2.2500	0.5000	2.7896	0.6199
2015	3.3530	0.5750	4.1570	0.7129
2016	2.1700	1.1500	2.6904	1.4258
2017 (through April 26)	1.7055	1.2400	2.1801	1.5851
Quarterly:				
First Quarter 2014	2.2500	1.0750	2.7896	1.3328
Second Quarter 2014	1.1900	0.5950	1.4754	0.7377
Third Quarter 2014	0.6950	0.5000	0.8617	0.6199
Fourth Quarter 2014	0.8600	0.5000	1.0662	0.6199
First Quarter 2015	1.4700	0.5750	1.8225	0.7129
Second Quarter 2015	3.3530	1.2380	4.1570	1.5349
Third Quarter 2015	2.6750	2.0000	3.3165	2.4796
Fourth Quarter 2015	2.2950	1.3000	2.8453	1.6117
First Quarter 2016	2.1700	1.1500	2.6904	1.4258
Second Quarter 2016	1.8885	1.3938	2.3414	1.7280
Third Quarter 2016	1.7000	1.4665	2.1077	1.8182
Fourth Quarter 2016	2.0450	1.5250	2.5354	1.8907
First Quarter 2017	1.7055	1.2400	2.1145	1.5374
Second Quarter 2017 (through April 26)	1.4400	1.3021	1.8408	1.6645
Most Recent Six Months:				
October 2016	2.0450	1.5800	2.5354	1.9589
November 2016	2.0000	1.7500	2.4796	2.1697
December 2016	1.7245	1.5250	2.1380	1.8907
January 2017	1.7055	1.5000	2.1145	1.8597
February 2017	1.5000	1.2400	1.8597	1.5374
March 2017	1.5080	1.3820	1.8696	1.7134
April 2017 (through April 26)	1.4400	1.3021	1.8408	1.6645

On April 26, 2017, the last reported sale price of our ordinary shares on AIM was £1.33 per ordinary share ($1.70 per ordinary share based on the exchange rate set forth above).

USE OF PROCEEDS

We estimate that the net proceeds to us from the global offering will be approximately $70.9 million (or approximately $81.7 million if the underwriters exercise in full their option to purchase an additional 865,200 ADSs), based on initial public offering price of $13.50 per ADS in the U.S. offering and an offering price of £1.32 per ordinary share in the European private placement, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. In addition, we expect to receive net proceeds of approximately $398,700 from the sale by us of ordinary shares in the shareholder private placement, after deducting placement agent fees.

We intend to use the net proceeds from the global offering and the shareholder private placement, together with our existing cash and cash equivalents, as follows:

- approximately $49.0 million to advance clinical development of RPL554 for the maintenance treatment of COPD;
- approximately $13.0 million to advance clinical development of RPL554 for the treatment of acute exacerbations of COPD;
- approximately $14.0 million to advance clinical development of RPL554 for the treatment of CF; and
- the remainder to fund our other current and future research and development activities and for working capital and other general corporate purposes.

This expected use of the net proceeds from the global offering and the shareholder private placement represents our intentions based upon our current plans and business conditions. We may also use a portion of the net proceeds to in-license, acquire or invest in additional businesses, technologies, products or assets, although currently we have no specific agreements, commitments or understandings in this regard. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the closing of the global offering and the shareholder private placement or the amounts that we will actually spend on the uses set forth above. Predicting the costs necessary to develop RPL554 and other product candidates can be difficult. The amounts and timing of our actual expenditures and the extent of clinical development may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from pre-clinical studies and any ongoing clinical trials or clinical trials we may commence in the future, as well as any collaborations that we may enter into with third parties for RPL554 or other product candidates and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from the global offering and the shareholder private placement.

Based on our planned use of the net proceeds of the global offering, the shareholder private placement and our current cash and cash equivalents, we estimate that such funds will be sufficient to enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months. We anticipate these funds will be sufficient for the completion of (i) our two planned Phase 2b clinical trials, our planned PK clinical trial and our ongoing Phase 2a clinical trial of RPL554 for the maintenance treatment of COPD, (ii) our planned Phase 2 clinical trial of RPL554 for the treatment of acute exacerbations of COPD and (iii) our ongoing Phase 2a clinical trial and our planned Phase 2b proof-of-concept trial of RPL554 for the treatment of CF. 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.

Pending their use, we plan to invest the net proceeds from the global offering and the shareholder private placement in short- and intermediate-term interest-bearing obligations and certificates of deposit.

DIVIDEND POLICY

We have never paid or declared any cash dividends on our ordinary shares, and we do not anticipate paying any cash dividends on our ordinary shares in the foreseeable future. We intend to retain all available funds and any future earnings to fund the development and expansion of our business. Under English law, among other things, we may only pay dividends if we have sufficient distributable reserves (on a non-consolidated basis), which are our accumulated realized profits that have not been previously distributed or capitalized less our accumulated realized losses, so far as such losses have not been previously written off in a reduction or reorganization of capital.

CAPITALIZATION

The table below sets forth our cash and cash equivalents and capitalization as of December 31, 2016 derived from our Annual Consolidated Financial Statements included elsewhere in this prospectus:

- on an actual basis; and
- on an as adjusted basis to give effect to our sale of (i) 47,399,001 ordinary shares (including 46,144,000 ordinary shares in the form of ADSs) in the global offering at the public offering price of $13.50 per ADS in the U.S. offering and £1.32 per ordinary share in the European private placement, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us and (ii) £335,400 (or the U.S. dollar equivalent) of ordinary shares at a price per share equal to the offering price in the European private placement, after deducting the placement agent fees.

You should read this table in conjunction with our Annual Consolidated Financial Statements included elsewhere in this prospectus and "Exchange Rate Information," "Use of Proceeds," "Selected Consolidated Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." For the convenience of the reader, we have translated pound sterling amounts in the table below as of December 31, 2016 into U.S. dollars at the noon buying rate of the Federal Reserve Bank of New York on December 30, 2016, which was £1.00 to $1.2337. These translations should not be considered representations that any such amounts have been, could have been or could be converted into U.S. dollars at that or any other exchange rate as of that or any other date.

	As of December 31, 2016			
	Actual		As Adjusted	
	(in thousands)			
Cash and cash equivalents	£ 39,785	$ 49,083	£ 95,551	$117,881
Derivative financial instrument	£ 7,923	$ 9,774	£ 7,923	$ 9,774
Equity:				
Share capital	2,568	3,168	4,951	6,108
Share premium	58,527	72,204	11,910	138,063
Share-based payments reserve	2,102	2,593	2,102	2,593
Accumulated loss	(28,728)	(35,442)	(28,728)	(35,442)
Total equity	34,468	42,524	90,234	111,322
Total capitalization	£ 42,391	$ 52,298	£ 98,157	$121,096

The table above excludes:

- 2,837,333 ordinary shares issuable upon the exercise of share options outstanding as of December 31, 2016 at a weighted average exercise price of £1.87 per share;
- 6,333,000 ordinary that may be issued under the New Incentive Plan, which became effective upon the pricing of the global offering, including ordinary shares underlying restricted share units and options that we intend to grant in connection with this global offering to each of our executive officers and a director, as more fully described in "Management—Equity Compensation Arrangements—2017 Incentive Award Plan—2017 Grants," as well as ordinary shares that may be issued pursuant to provisions in our New Incentive Plan that automatically increase the share reserve under our New Incentive Plan;
- 2,298,773 ordinary shares that may be issued under our existing equity incentive plans as of December 31, 2016; and
- 12,646,370 ordinary shares issuable upon the exercise of warrants outstanding as of December 31, 2016 at a weighted average exercise price of £1.7174 per share.

DILUTION

If you invest in our ADSs or ordinary shares, your interest will be diluted to the extent of the difference between the offering price per ADS or ordinary share paid by purchasers in the global offering and our as adjusted net tangible book value per ADS or ordinary share after completion of the global offering.

At December 31, 2016, we had a historical net tangible book value of £32.2 million ($41.1 million), corresponding to a net tangible book value of £0.63 per ordinary share (equivalent to $6.40 per ADS). Net tangible book value per ordinary share represents the amount of our total assets less our total liabilities, excluding goodwill and other intangible assets, divided by the total number of our ordinary shares outstanding as of December 31, 2016.

After giving effect to the sale by us of (i) 47,399,001 ordinary shares (including 46,144,000 ordinary shares in the form of ADSs) in the global offering at the public offering price of $13.50 per ADS in the U.S. offering and £1.32 per ordinary share in the European private placement after deducting the underwriting discounts and commissions and estimated expenses payable by us and (ii) £335,400 (or the U.S. dollar equivalent) of ordinary shares at a price per share equal to the offering price in the European private placement, after deducting the placement agent fees and estimated expenses payable by us, our as adjusted net tangible book value as of December 31, 2016 would have been £81.8 million ($104.5 million), representing an as adjusted net tangible book value of £0.87 per ordinary share and $8.90 per ADS. This represents an immediate increase in net tangible book value of £0.24 per ordinary share ($2.50 per ADS) to existing shareholders and an immediate dilution of £0.45 per ordinary share and $4.60 per ADS, to new investors purchasing ordinary shares or ADSs in the global offering or the shareholder private placement. Dilution per ADS or ordinary share to new investors is determined by subtracting the as adjusted net tangible book value per ADS or ordinary share after the global offering and the shareholder private placement from the initial public offering price per ADS or the offering price per ordinary share, as applicable, paid by new investors.

The following table illustrates this dilution to new investors purchasing ADSs or ordinary shares in the global offering and the shareholder private placement.

	As of December 31, 2016			
	Ordinary Shares		ADSs	
Offering price		£1.32		$13.50
Net tangible book value per ordinary share or ADS	£0.63		$6.40	
Increase in net tangible book value per ordinary share or ADS attributable to the global offering and the shareholder private placement	0.24		2.50	
As adjusted net tangible book value per ordinary share or ADS after the global offering and the shareholder private placement		0.87		8.90
Dilution per ADS or ordinary share to new investors in the global offering and the shareholder private placement		£0.45		$ 4.60

If the underwriters exercise in full their option to purchase an additional 865,200 ADSs, our as adjusted net tangible book value after the global offering and the shareholder private placement would be £0.85 per ordinary share ($8.74 per ADS), representing an immediate increase in as adjusted net tangible book value of £0.23 per ordinary share ($2.33 per ADS), to existing shareholders and immediate dilution of £0.47 per ordinary share and $4.76 per ADS to new investors participating in the global offering or shareholder private placement, based

on the initial public offering price of $13.50 per ADS in the U.S. offering and the offering price of £1.32 per ordinary share in the European private placement and shareholder private placement.

The following table summarizes, as of December 31, 2016, on the as adjusted basis described above, the number of ordinary shares purchased from us (including ordinary shares in the form of ADSs) the total consideration paid to us and the average price per ordinary share and per ADS paid by existing shareholders and by new investors purchasing ADSs or ordinary shares in the global offering and shareholder private placement. The table below is based on the initial public offering price of $13.50 per ADS in the U.S. offering and the offering price of £1.32 per ordinary share in the European private placement and shareholder private placement before deducting the underwriting discounts and commissions, placement agent fees and estimated offering expenses payable by us:

	Ordinary Shares Purchased[1]		Total Consideration		Average Price per Ordinary Share	Average Price per ADS
	Number	Percent	Amount	Percent		
Existing shareholders	51,361,063	51.9%	$ 95,190,863	54.2%	$ 1.85	$ 14.83
New investors	47,653,100	48.1	80,414,389	45.8	1.69	13.50
Total	99,014,163	100.0%	$175,605,252	100.0%		

[1] Including ordinary shares in the form of ADSs.

If the underwriters exercise in full their option to purchase an additional 865,200 ADSs, the following will occur:

- the percentage of our ordinary shares held by existing shareholders will decrease to 48.5% of the total number of our ordinary shares outstanding after the global offering and shareholder private placement; and
- the percentage of our ordinary shares held by new investors will increase to approximately 51.5% of the total number of our ordinary shares outstanding after the global offering.

The tables above are based on 51,361,063 ordinary shares outstanding as of December 31, 2016. The tables above exclude:

- 2,837,333 ordinary shares issuable upon the exercise of share options outstanding as of December 31, 2016 at a weighted average exercise price of £1.87 per share;
- 6,330,000 ordinary shares that may be issued under the New Incentive Plan, which became effective upon the pricing of the global offering, including ordinary shares underlying restricted share units and options that we intend to grant in connection with this global offering to each of our executive officers and a director, as more fully described in "Management—Equity Compensation Arrangements—2017 Incentive Award Plan—2017 Grants," as well as ordinary shares that may be issued pursuant to provisions in our New Incentive Plan that automatically increase the share reserve under our New Incentive Plan;
- 2,298,773 ordinary shares that may be issued under our existing equity incentive plans as of December 31, 2016; and
- 12,646,370 ordinary shares issuable upon the exercise of warrants outstanding as of December 31, 2016 at a weighted average exercise price of £1.7174 per share.

Our existing institutional investors affiliated with certain of our directors have indicated an interest in purchasing up to an aggregate of approximately $23 million (or the pounds sterling equivalent) in the global offering on the same terms as the other purchasers in the global offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell

more, less or no securities offered in the global offering to any of these investors or any of these investors may determine to purchase more, less or no securities offered in the global offering. The underwriters will receive the same underwriting discount on any securities purchased by these investors as they will on any other securities sold to the public in the global offering.

To the extent that stock options or warrants are exercised or we issue additional ADSs or ordinary shares in the future, there will be further dilution to investors participating in the global offering. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

SELECTED CONSOLIDATED FINANCIAL DATA

You should read the following selected consolidated financial data together with the Annual Consolidated Financial Statements and the sections titled "Exchange Rate Information" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." We have derived the consolidated statement of comprehensive income data for the years ended December 31, 2015 and 2016 and the consolidated statement of financial position as of December 31, 2015 and 2016 from our Annual Consolidated Financial Statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that should be expected in any future period.

We maintain our books and records in pounds sterling, and we prepare our financial statements in accordance with IFRS as issued by the IASB. We report our financial results in pounds sterling. For the convenience of the reader, we have translated pound sterling amounts as of and for the years ended December 31, 2015 and 2016 into U.S. dollars at the noon buying rate of the Federal Reserve Bank of New York on December 30, 2016, which was £1.00 to $1.2337. These translations should not be considered representations that any such amounts have been, could have been or could be converted into U.S. dollars at that or any other exchange rate as of that or any other date.

	Year Ended December 31,			
	2015		2016	
	(£)	($)	(£)	($)
	(in thousands, except per ordinary share data)			
Consolidated statement of comprehensive income data:				
Research and development costs	(7,269)	(8,968)	(4,522)	(5,579)
General and administrative costs	(1,706)	(2,105)	(2,498)	(3,082)
Operating loss	(8,975)	(11,072)	(7,020)	(8,661)
Finance income	45	55	1,841	2,272
Finance expense	(72)	(89)	(794)	(979)
Loss before taxation	(9,002)	(11,106)	(5,973)	(7,368)
Taxation — credit	1,509	1,862	954	1,177
Loss for the year	(7,493)	(9,244)	(5,018)	(6,191)
Other comprehensive income:				
Exchange differences on translating foreign operations	4	5	43	53
Total comprehensive loss attributable to owners of the company	(7,489)	(9,239)	(4,976)	(6,139)
Loss per ordinary share — basic and diluted	(0.37)	(0.46)	(0.15)	(0.19)

	Year Ended December 31,			
	2015		2016	
	(£)	($)	(£)	($)
	(in thousands)			
Consolidated statement of financial position data:				
Cash and cash equivalents	3,524	4,348	39,785	49,083
Total assets	7,840	9,673	46,143	56,926
Share premium	26,650	32,878	58,527	72,204
Total liabilities	2,407	2,969	11,674	14,402
Accumulated loss	(23,752)	(29,303)	(28,728)	(35,442)
Total equity	5,434	6,704	34,468	42,524

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 together with the information in "Selected Consolidated Financial Data" and our Annual Consolidated Financial Statements, including the notes thereto. The following discussion is based on our financial information prepared in accordance with IFRS as issued by the IASB, which may differ in material respects from generally accepted accounting principles in other jurisdictions, including generally accepted accounting principles in the United States, or U.S. GAAP. The following discussion includes forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of many factors, including but not limited to those described under "Risk Factors" and elsewhere in this prospectus.

For the convenience of the reader, we have translated some pound sterling amounts as of and for the years ended December 31, 2015 and 2016 and into U.S. dollars at the noon buying rate of the Federal Reserve Bank of New York on December 30, 2016, which was £1.00 to $1.2337. These translations should not be considered representations that any such amounts have been, could have been or could be converted into U.S. dollars at that or any other exchange rate as of that or any other date.

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, RPL554, is a first-in-class, inhaled, dual inhibitor of PDE3 and PDE4, that acts as both a bronchodilator and an anti-inflammatory agent in a single compound. We are not aware of any therapy in a single compound approved by the FDA or the EMA for the treatment of respiratory diseases that acts as both a bronchodilator and anti-inflammatory agent. We believe RPL554 has the potential to be the first novel class of bronchodilator in over 40 years. We have completed eight Phase 1 and 2a clinical trials for RPL554, with 282 subjects enrolled. In our clinical trials, treatment with RPL554 has been observed to result in statistically significant improvements in lung function as compared to placebo. Our clinical trials also have shown clinically meaningful and statistically significant improvements in lung function when RPL554 is added to two commonly used bronchodilators as compared to either bronchodilator administered as a single agent. RPL554 also has shown anti-inflammatory effects and has been well tolerated in our clinical trials, and has not been observed to result in the gastrointestinal or other side effects commonly associated with roflumilast, the only PDE4 inhibitor currently on the market for the treatment of COPD. We are developing RPL554 for the treatment of patients with COPD and for the treatment of patients with CF. We believe RPL554, if approved, has the potential to become an important and novel treatment and standard of care for COPD and CF patients. We may also explore, alone or with a collaborator, development of RPL554 to treat asthma and other respiratory diseases.

We plan to commence a four-week Phase 2b dose ranging clinical trial to evaluate RPL554 for the maintenance treatment of COPD in the second half of 2017. In this trial, we plan to compare the use of RPL554 in a nebulized formulation to placebo in approximately 400 patients. We expect to report top-line data from this trial in the second half of 2018. In February 2017, we commenced a Phase 2a clinical trial of RPL554 for the maintenance treatment of COPD in the United Kingdom. This trial is evaluating RPL554 as an add-on therapy to tiotropium in approximately 30 patients. We expect to report top-line data from this trial in the fourth quarter of 2017. We also plan to commence a single-dose PK trial of RPL554 in approximately 12 healthy volunteers in the United States in mid-2017. We expect to report top-line data from this trial in the fourth quarter of 2017. In addition, we plan to commence a 12-week Phase 2b dose-ranging clinical trial of RPL554 for the maintenance treatment of COPD in the second half of 2018. In this trial, we plan to evaluate RPL554 as an add-on therapy to a long-acting bronchodilator in approximately 400 patients.

We plan to commence a Phase 2 trial of RPL554 for the treatment of acute exacerbations of COPD in hospitalized patients in the second half of 2018. In this trial, we plan to evaluate RPL554 in a nebulized formulation as an add-on therapy in approximately 150 patients.

In March 2017, we commenced a Phase 2a single-dose PK and PD trial in the United Kingdom evaluating RPL554 in up to ten CF patients and expect to report top-line data from this trial in the first half of 2018. The results of this clinical trial are expected to support dose selection for a proof-of-concept Phase 2b trial in approximately 100 patients with CF, which we plan to commence in 2018.

We do not have any approved products and, as a result, have not generated any revenue from product sales or otherwise. RPL554 is our only current product candidate and our ability to generate revenue sufficient to achieve profitability will depend on our successful development and eventual commercialization of RPL554, if approved, for one or more of its targeted indications. Since our inception, we have incurred significant operating losses. For the years ended December 31, 2015 and 2016 we incurred net losses of £7.5 million and £5.0 million, respectively. As of December 31, 2016, we had an accumulated loss of £28.7 million.

We expect to incur significant expenses and operating losses for the foreseeable future as we advance the clinical development of RPL554, and seek regulatory approval and pursue commercialization of RPL554, if approved. In addition, if we obtain regulatory approval for RPL554, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. In addition, we may incur expenses in connection with the in-license or acquisition of additional product candidates and the potential clinical development of any such product candidates. Furthermore, upon the closing of the global offering, we expect to incur additional costs associated with operating as a U.S. public company listed on the NASDAQ in addition to operating as a U.K. public company listed on AIM, including significant legal, accounting, investor relations and other expenses that we did not previously incur.

As a result of these anticipated expenditures, we will need additional financing to support our continuing operations. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of public or private equity or debt financings or other sources, which may include collaborations with third parties. Adequate additional financing may not be available to us on acceptable terms, or at all. Our inability to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. We will need to generate significant revenue to achieve profitability, and we may never do so.

We were incorporated in 2005 and are headquartered in the United Kingdom. Since 2006, our ordinary shares have traded on AIM, a market of the London Stock Exchange, under the symbol "VRP". We have raised £74.6 million in gross proceeds from investors since such listing, of which £44.7 million was raised in our most recent private placement of equity securities in July 2016 with a number of European and U.S.-based healthcare specialist investment firms.

License Agreement with Vernalis

In February 2005, Rhinopharma entered into an assignment and license agreement with Vernalis, which we refer to as the Vernalis Agreement. In 2006, we acquired Rhinopharma and all of its rights and obligations under the Vernalis Agreement. Pursuant to the Vernalis Agreement, Vernalis assigned to us all of its rights to certain patents and patent applications relating to RPL554 and related compounds, or the Vernalis Patents. Vernalis also granted to us an exclusive, worldwide, royalty-bearing license to certain Vernalis know-how to develop, manufacture and commercialize products, or the Licensed Products, based on PDE inhibitors developed using Vernalis Patents, Vernalis know-how and the physical stock of certain compounds, including RPL554, in the treatment of human or animal allergic or inflammatory disorders.

Under the Vernalis Agreement, we are obligated to pay Vernalis 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 Vernalis Patents or Vernalis know-how, excluding royalties. We must also pay Vernalis, on a Licensed Product-by-Product and country-by-country basis, a low to mid-single digit percentage royalty based on net sales of each Licensed Product. See "Business — Vernalis Agreement" for further information regarding this agreement.

We have recorded a liability in our statement of financial position reflecting the contingent obligation we assumed from Rhinopharma to make payments to Vernalis under the Vernalis Agreement. Any change in the carrying value of this assumed contingent obligation in any reporting period is recorded as finance expense or finance income in our statement of comprehensive income. See "— Financial Operations Overview — Finance Income and Expense" and Note 2.13 of our Annual Consolidated Financial Statements.

Financial Operations Overview

Revenue

We do not have any approved products. Accordingly, we have not generated any revenue, and we do not expect to generate any revenue from the sale of any products unless or until we obtain regulatory approvals of and commercialize RPL554 or any other product candidate we may develop in the future, which may never occur.

Research and Development Costs

Research and development costs include:

- employee-related expenses, such as salaries, share-based compensation, benefits and travel expense, for our research and development personnel;
- costs for production of drug substance by CMOs;
- fees and other costs paid to CROs and consultants to conduct our clinical trials and pre-clinical and non-clinical studies;
- costs of related facilities, materials and equipment;
- costs associated with obtaining and maintaining patents and other intellectual property; and
- amortization and depreciation of intangible and tangible fixed assets used to develop RPL554.

Research and development activities will continue to be central to our business model. Product candidates in later stages of clinical development, such as RPL554 for the treatment of COPD, generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect our research and development costs to be significant over the next several years as we hire additional research and development personnel and increase compensation costs, advance the clinical development of RPL554, develop new formulations of RPL554 for the treatment of COPD, commence the clinical development of RPL554 for the treatment of CF and potentially pursue the development of RPL554 for other forms of respiratory disease, including asthma.

The successful development and commercialization of RPL554 is highly uncertain. At this time, we cannot reasonably estimate the nature, timing and estimated costs of the efforts that will be necessary to complete the development of, or the period, if any, in which material net cash inflows may commence from, RPL554 or any future product candidates. This is due to numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- the scope, rate of progress and expense of our research and development activities;
- the progress and results of clinical trials and pre-clinical and non-clinical studies;
- the terms and timing of regulatory approvals;
- the expense of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights; and
- the ability to market, commercialize and achieve market acceptance for RPL554 or any other future product candidate, if approved.

Any of these variables with respect to the development of RPL554 or any other future candidate that we may develop could result in a significant change in the costs and timing associated with the development of RPL554 or such future product candidate. For example, if the FDA, the EMA or other regulatory authority were to require us to conduct pre-clinical studies and clinical trials beyond those we currently anticipate will be required for the completion of clinical development or if we experience significant delays in enrollment in any clinical trials, we could be required to expend significant additional financial resources and time on the completion of our clinical development programs.

General and Administrative Costs

Our general and administrative costs principally consist of salaries and related benefits, including share-based compensation, for personnel in our executive, finance and other administrative functions. Other general and administrative costs include facility-related costs and professional services fees for auditing, tax and general legal services, as well as expenses associated with the requirements of being a listed public company on AIM. We expect that our general and administrative costs will increase in the future as our business expands and we increase our headcount to support the expected growth in our operating activities. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, lawyers and accountants, among other expenses. Additionally, we anticipate increased costs associated with being a U.S. public company, including expenses related to services associated with maintaining compliance with NASDAQ rules and SEC requirements, director compensation, insurance and investor relation costs. If RPL554 obtains regulatory approval for marketing, we expect that we will incur expenses associated with building a sales and marketing team. In addition, we expect to continue to grant share-based compensation awards to key management personnel and other employees.

Finance Income and Expense

Finance income consists of interest earned on our cash and cash equivalents and any decrease in the carrying value resulting from the remeasurement of the assumed contingent obligation under the Vernalis Agreement and any decrease in the fair value of the derivative financial liability related to the 31,115,926 units issued by us to new and existing institutional and other investors in July 2016, or the July Placement.

Finance expense consists of any increase in the carrying value resulting from the remeasurement of the assumed contingent obligation under the Vernalis Agreement and any increase in the fair value of the derivative financial liability related to the July Placement. See "— License Agreement with Vernalis" and "Business — Vernalis Agreement" for further information regarding the Vernalis Agreement and see "Related Party Transactions — Ordinary Share and Warrant Placement" for further information regarding the July Placement.

Taxation

As a U.K. resident trading entity, we are subject to U.K. corporate taxation. Due to the nature of our business, we have generated losses since inception. As a company that carries out extensive research and development activities, we benefit from the U.K. research and development tax credit regime and are able to surrender some of our trading losses that arise from our research and development activities for a cash rebate of up to 33.35% of eligible research and development expenditure. Qualifying expenditures largely comprise employment costs for research staff, consumables and certain internal overhead costs incurred as part of research projects. In the event we generate revenues in the future, we may benefit from the new "patent box" initiative that allows profits attributable to revenues from patents or patented products to be taxed at a lower rate than other revenue. This relief applies to profits earned from April 1, 2013 and following the transitional arrangements that will phase in the relief, the rate of tax for relevant streams of revenue for companies receiving this relief will be 10%.

Results of Operations

The following table sets forth our results of operations for the periods indicated.

	Year Ended December 31,			
	2015		2016	
	(in thousands)			
Research and development costs	£(7,269)	$ (8,968)	£(4,522)	$(5,579)
General and administrative costs	(1,706)	(2,105)	(2,498)	(3,082)
Operating loss	(8,975)	(11,072)	(7,020)	(8,661)
Finance income	45	55	1,841	2,272
Finance expense	(72)	(89)	(794)	(979)
Loss before taxation	(9,002)	(11,106)	(5,973)	(7,368)
Taxation — credit	1,509	1,862	954	1,177
Loss for the year	(7,493)	(9,244)	(5,018)	(6,191)
Other comprehensive income:				
Exchange differences on translating foreign operations	4	5	43	53
Total comprehensive loss attributable to owners of the company	£(7,489)	$ (9,239)	£(4,976)	$(6,139)

Comparison of Operations for the Years ended December 31, 2015 and 2016

Research and Development Costs

Research and development costs were £4.5 million for the year ended December 31, 2016 as compared to £7.3 million for the year ended December 31, 2015, a decrease of £2.8 million. The decrease was attributable to a £3.6 million decrease in clinical trial expenses related to the completion of our Phase 2a clinical trials of RPL554 in late 2015 and early 2016, which were partially offset by a £0.7 million increase in research and development personnel costs and a £0.1 million increase in pre-clinical research, contract manufacturing, patent and other costs.

General and Administrative Costs

General and administrative costs were £2.5 million for the year ended December 31, 2016 as compared to £1.7 million for the year ended December 31, 2015, an increase of £0.8 million. The increase was attributable to a £0.2 million increase in personnel costs, a £0.3 million increase in professional service fees and expenses, and a £0.2 million increase in other facility and office related costs.

Finance Income and Expense

Finance income was £1.8 million for the year ended December 31, 2016 and £45 thousand for the year ended December 31, 2015. The increase in finance income was primarily due to a decrease in the fair value of the warrant liability of £1.1 million caused by changes in the underlying assumptions for measuring the liability of the warrants issued in the July Placement, including the price and volatility of our ordinary shares and the unwinding of the expected life of the warrants.

Finance expense was £0.8 million for the year ended December 31, 2016 as compared to £0.1 million for the year ended December 31, 2015. The increase was primarily due to the inclusion of the proportion of expenses incurred in connection with the July Placement which related to the issue of warrants, and which were recorded as a finance expense (the remainder of the July Placement expenses related to the equity issued and were recorded as a charge against share premium), as well as an increase in the calculated value of the assumed contingent obligation resulting from the Vernalis Agreement.

Taxation

Taxation for the year ended December 31, 2016 amounted to a credit of £1.0 million as compared to a credit of £1.5 million for the year ended December 31, 2015, a decrease in the credit amount of £0.5 million. The credits are obtained at a rate of 14.5% of 230% of our qualifying research and development expenditure, and the decrease in the credit amount was primarily attributable to our decreased expenditure on research and development.

Liquidity and Capital Resources

Overview

Since our inception, we have incurred significant operating losses. We anticipate that we will continue to incur losses for at least the next several years. We expect that our research and development and general and administrative costs will increase in connection with conducting clinical trials for RPL554 and seeking marketing approval for RPL554 in the United States and Europe as well as other jurisdictions. As a result, we will need additional capital to fund our operations, which we may obtain from additional financings, research funding, collaborations, contract and grant revenue or other sources.

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. Since our inception, we raised gross proceeds of £74.6 million from private placements of equity securities. As of December 31, 2016, we had cash and cash equivalents of £39.8 million.

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.

Cash Flows

The table below summaries our cash flows for each of the periods presented.

	Year Ended December 31,			
	2015		2016	
	(in thousands)			
Net cash used in operating activities	£(6,357)	$(7,842)	£ (5,588)	$ (6,894)
Net cash used in investing activities	(92)	(114)	(41)	(51)
Net cash from financing activities	—	—	41,203	50,833
Net (decrease) increase in cash and cash equivalents	£(6,449)	$(7,956)	£35,574	$43,888

The decrease in net cash used in operating activities to £5.6 million for the year ended December 31, 2016 from £6.4 million for the year ended December 31, 2015 was primarily due to a decrease in loss before taxation driven by lower research and development costs.

The decrease in net cash used in investing activities to £41 thousand for the year ended December 31, 2016 from £92 thousand for the year ended December 31, 2015 was primarily due to an increase in interest income received on the company cash balances during 2016.

The increase in net cash from financing activities to £41.2 million for the year ended December 31, 2016 from £nil for the year ended December 31, 2015 was due to the cash received from the sale of our equity securities and warrants in connection with the July Placement.

Operating and Capital Expenditure Requirements

As of December 31, 2016, we had an accumulated loss of £28.7 million. We expect to continue to incur significant operating losses for the foreseeable future as we continue our research and development efforts and seek to obtain regulatory approval and commercialization of RPL554 and any future product candidate we develop.

We expect our expenses to increase substantially in connection with our ongoing development activities related to RPL554 and any future product candidates. In addition, upon the closing of the global offering, we expect to incur additional costs associated with operating as a U.S. public company listed on NASDAQ in addition to operating as a U.K. public company listed on AIM. We anticipate that our expenses will increase substantially if and as we:

- initiate and conduct our planned clinical trials for RPL554 for the maintenance treatment of COPD and as a treatment for acute COPD;
- initiate and conduct our planned clinical trials for RPL554 for the treatment of CF;
- continue the research and development of other formulations of RPL554, including developing our DPI and MDI formulations of RPL554;
- initiate and progress pre-clinical studies relating to other potential indications of RPL554;
- seek to discover and develop additional product candidates;
- seek regulatory approvals for any of our product candidates that successfully completes 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 operations as a U.S. public company listed on the NASDAQ; 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.

We expect that our existing cash and cash equivalents, together with anticipated net proceeds from the global offering and shareholder private placement, will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months. We anticipate these funds will be sufficient for the completion of (i) our two planned Phase 2b clinical trials, our planned PK clinical trial and our ongoing Phase 2a clinical trial of RPL554 for the maintenance treatment of COPD, (ii) our planned Phase 2 clinical trial of RPL554 for the treatment of acute exacerbations of COPD and (iii) our ongoing Phase 2a clinical trial and our planned Phase 2b proof-of-concept trial of RPL554 for the treatment of CF. We have based this estimate on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development of RPL554 and any future product candidates and because the extent to which we may enter into collaborations with third parties for development of RPL554 is unknown, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the research and development of RPL554. Our future capital requirements for RPL554 or any future product candidates will depend on many factors, including:

- the progress, timing and completion of pre-clinical testing and clinical trials for RPL554 or any future product candidates and the potential that we may be required to conduct additional clinical trials for RPL554;
- 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 RPL554 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 RPL554 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 RPL554 any future product candidates;
- any licensing or milestone fees we might have to pay during future development of RPL554 or any future product candidates;
- selling and marketing activities undertaken in connection with the anticipated commercialization of RPL554 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 RPL554 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.

Adequate additional funds may not be available to us on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a shareholder. 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 your ownership interests.

If we raised 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.

Contractual Obligations and Commitments

The table below summarizes our contractual obligations at December 31, 2016.

	Payments Due by Period				
	Total	Less than 1 year	1 - 3 years	3 - 5 years	More than 5 years
	(in thousands)				
Operating lease obligations	£270	£270	£—	£—	£—
Total	£270	£270	£—	£—	£—

The table above does not include assumed contingent obligation payments we may be required to make under the Vernalis Agreement because the amount, timing and likelihood of payment are not known. Such additional payment obligations may be material. See sections titled "— License Agreement with Vernalis" and "Business — Vernalis Agreement."

In addition, we enter into contracts in the ordinary course of business with CROs to assist in the performance of our research and development activities and other services and products for operating

purposes. These contracts generally provide for termination on notice, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments.

Internal Control Over Financial Reporting

In connection with the preparation for this initial public offering, we reassessed our critical accounting policies to ensure compliance with IFRS. As part of this reassessment, we identified errors relating to the recognition of assumed liabilities and goodwill in connection with the acquisition of Rhinopharma in September 2006. These errors are discussed further in the notes to our Annual Consolidated Financial Statements included elsewhere in this prospectus. The correction of these errors is reflected within our consolidated financial statements included elsewhere in this prospectus and is reflected in our financial statements prepared for U.K. reporting requirements for the year ended December 31, 2016.

We concluded that a lack of adequate controls surrounding our historic accounting for business combinations constituted a material weakness in our internal control over financial reporting, as defined in the standards established by the U.S. Public Accounting Oversight Board, or the PCAOB. The PCAOB defines a material weakness as a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of the company's annual or interim financial statements will not be prevented or detected in a timely basis. We are currently in the process of remediating this material weakness and are taking steps that we believe will address the underlying causes of the material weakness by the hiring of our new chief financial officer and enhancing our financial reporting team's technical accounting knowledge associated with the accounting rules for business combinations. However, we cannot be certain that these efforts will be sufficient to remediate this material weakness or prevent future material weaknesses or significant deficiencies from occurring.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Quantitative and Qualitative Disclosures About Market Risk

We are exposed to a variety of financial risks. Our overall risk management program seeks to minimize potential adverse effects of these financial risks on our financial performance.

Credit Risk

We consider all of our material counterparties to be creditworthy. We consider the credit risk for each of our counterparties to be low and do not have a significant concentration of credit risk at any of our counterparties.

Liquidity Risk

We manage our liquidity risk by maintaining adequate cash reserves at banking facilities, and by continuously monitoring our cash forecasts, our actual cash flows and by matching the maturity profiles of financial assets and liabilities.

Market Risk

Foreign currency risk reflects the risk that the value of a financial commitment or recognized asset or liability will fluctuate due to changes in foreign currency rates. Our financial position, as expressed in pounds sterling, are exposed to movements in foreign exchange rates against the U.S. dollar and the euro. Our main trading currencies are pounds sterling, the U.S. dollar and the euro. We are exposed to foreign currency risk as a result of operating transactions and the translation for foreign bank accounts. We monitor our exposure to foreign exchange risk. We have not entered into foreign exchange contracts to hedge against gains or losses from foreign exchange fluctuations.

Interest rate risk reflects the risk that the value of a financial instrument will fluctuate as a result of change in market interest rates on classes of financial assets and financial liabilities. We do not hold any derivative instruments to manage interest rate risk.

Critical Accounting Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with IFRS as issued by the IASB. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenues and expenses during the reporting periods. Actual results may differ from these estimates under different assumptions or conditions. There have been no material adjustments to prior period estimates for any of the periods included in this prospectus.

Our significant accounting policies are more fully described in the notes to our financial statements appearing elsewhere in this prospectus. We believe that the following accounting policies are the most critical to aid you in fully understanding and evaluating our financial condition and results of operations.

Assumed Contingent Obligation

A significant management estimate relates to the probability, amount and timing of any payment relating to the assumed contingent obligation under the Vernalis Agreement, a provision for which is recorded in our statement of financial position. See "— License Agreement with Vernalis," "Business — Vernalis Agreement" and Note 21 to our Annual Consolidated Financial Statements included elsewhere in this prospectus. A change in the probability and timing of any payment relating to the assumed contingent obligation could result in a significant fluctuation in our financial results in future periods.

Share-Based Compensation

We measure share options at fair value at their grant date in accordance with IFRS 2, "Share-based Payment." We calculate the fair value of the share options using either the Black-Scholes model, or for options with performance conditions, a simulation model. We charge the fair value to the statement of comprehensive income over the expected vesting period.

Impairment of Intangible Assets

Determining whether an intangible asset is impaired requires an estimation of whether there are any indications that its carrying value is not recoverable.

At each reporting date, we review the carrying value of our tangible and intangible assets to determine whether there is any indication that those assets have been impaired. If such an indication exists, the recoverable amount of the asset, being the higher of the asset's fair value less costs to sell and value in use, is compared to the asset's carrying value. Any excess of the asset's carrying value over its recoverable amount is expensed to the income statement.

Valuation of Derivative Financial Liability

In connection with the July Placement, we issued 31,115,926 warrants to new and existing institutional and other investors. Each warrant is entitled to purchase 0.4 of an ordinary share at a price of £1.7238. Each warrant is exercisable beginning upon the closing of the global offering and will expire on the fifth anniversary of the closing of the global offering.

We classify these warrants as a derivative financial liability to be presented on our consolidated statement of financial position. The fair value of these warrants is determined by applying the Black-Scholes model. Assumptions are made on inputs such as time to maturity, the share price, volatility and risk free rate, in order to determine the fair value per warrant. For valuation purposes at recognition of the liability, we used the closing share price of our ordinary shares as reported on AIM on July 29, 2016, the date of issuance of the warrants.

At the date of issuance of the warrants we calculated a fair value and recorded a derivative financial liability, which on initial recognition was offset against the share premium in relation to the funds received in connection with the July Placement. Subsequent updates to the fair value of the derivative financial liability will not result in changes to share premium, but will result in an adjusting entry in the consolidated derivative financial liability statement of comprehensive income. We will continue to adjust the derivative financial liability until the earlier of the exercise of the warrants or expiration of the warrants occurs.

Recent Accounting Pronouncements

We refer to Note 2 to our Annual Consolidated Financial Statements for the year ended December 31, 2016 included elsewhere in this prospectus for a discussion of new standards and interpretations not yet adopted by us.

JOBS Act

In April 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107(b) of the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period, and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

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, RPL554, is a first-in-class, inhaled, dual inhibitor of the enzymes phosphodiesterase 3 and 4, or PDE3 and PDE4, that acts as both a bronchodilator and an anti-inflammatory agent in a single compound. We are not aware of any therapy in a single compound in clinical development or approved by the U.S. Food and Drug Administration, or FDA, or the European Medicines Agency, or EMA, for the treatment of respiratory diseases that acts as both a bronchodilator and anti-inflammatory agent. We believe RPL554 has the potential to be the first novel class of bronchodilator in over 40 years. We have completed eight Phase 1 and 2a clinical trials for RPL554, with 282 subjects enrolled. In our clinical trials, treatment with RPL554 has been observed to result in statistically significant improvements in lung function as compared to placebo. Statistically significant means that there is a low statistical probability, typically less than 5%, that the observed results occurred by chance alone. Our clinical trials also have shown clinically meaningful and statistically significant improvements in lung function when RPL554 is added to two commonly used bronchodilators as compared to either bronchodilator administered as a single agent. RPL554 also has shown anti-inflammatory effects and been well tolerated in our clinical trials, and has not been observed to result in the gastrointestinal or other side effects commonly associated with roflumilast, the only PDE4 inhibitor currently on the market for the treatment of COPD. We are developing RPL554 for the treatment of patients with chronic obstructive pulmonary disease, or COPD, and for the treatment of patients with cystic fibrosis, or CF. We believe RPL554, if approved, has the potential to become an important and novel treatment and standard of care for these patients. We may also explore, alone or with a collaborator, the development of RPL554 to treat asthma and other respiratory diseases.

We are developing RPL554 in a nebulized formulation for the maintenance treatment of COPD patients. We also are developing RPL554 in a nebulized formulation as an add-on therapy to short-acting bronchodilators and other commonly used therapies for the treatment of hospitalized patients with acute exacerbations of COPD. Patients with more severe COPD, who tend to suffer more frequent exacerbations, generally prefer treatment with a nebulizer as they view its perceived benefits, including greater confidence in effective drug administration and a reduced need to visit health care providers, as outweighing its perceived disadvantages, which include length of treatment administration and required cleaning. In addition, use of a nebulizer is generally preferred when administering larger doses in the hospital setting. We also are developing our nebulized formulation of RPL554 for CF, which is a disease commonly treated with a nebulizer.

We plan to commence a four-week Phase 2b dose ranging clinical trial to evaluate RPL554 for the maintenance treatment of COPD in the second half of 2017. In this trial, we plan to compare the use of RPL554 in a nebulized formulation to placebo in approximately 400 patients. We expect to report top-line data from this trial in the second half of 2018. In February 2017, we commenced a Phase 2a clinical trial of RPL554 for the maintenance treatment of COPD in the United Kingdom. This trial is evaluating RPL554 as an add-on therapy to tiotropium, a commonly used long-acting bronchodilator, in approximately 30 patients. We expect to report top-line data from this trial in the fourth quarter of 2017. We also plan to commence a single-dose pharmacokinetic, or PK, trial of RPL554 in approximately 12 healthy volunteers in the United States in mid-2017. We expect to report top-line data from this trial in the fourth quarter of 2017. A PK trial involves the study of the process of bodily absorption, distribution, metabolism and excretion of a drug. In addition, we plan to commence a 12-week Phase 2b dose-ranging clinical trial of RPL554 for the maintenance treatment of COPD in the second half of 2018. In this trial, we plan to evaluate RPL554 as an add-on therapy to a long-acting bronchodilator in approximately 400 patients. Our planned clinical trials for RPL554 for the maintenance treatment of COPD will be designed to evaluate the effect on lung function, as measured by the maximal volume of air a person can forcefully exhale in one second, or $FEV_{1,}$ and duration of action of the product candidate. These clinical endpoints are commonly

used in clinical trials for respiratory diseases and have been used by other companies in obtaining FDA approval of drugs addressing respiratory diseases.

We plan to commence a Phase 2 trial of RPL554 for the treatment of acute exacerbations of COPD in hospitalized patients in the second half of 2018. In this trial, we plan to evaluate RPL554 in a nebulized formulation as an add-on therapy in approximately 150 patients.

In March 2017, we commenced a Phase 2a single-dose PK and pharmacodynamics, or PD, trial in the United Kingdom evaluating RPL554 in up to ten CF patients and expect to report top-line data from this trial in the first half of 2018. A PD trial involves the study of the biochemical and physiological effects of a drug and its mechanisms of action, including the correlation of the drug's actions and effects with its mechanism of action. The results of this clinical trial are expected to support dose selection for a proof-of-concept Phase 2b trial in approximately 100 patients with CF, which we plan to commence in 2018.

We also are developing RPL554 in both dry powder inhaler, or DPI, and metered dose inhaler, or MDI, formulations for the maintenance treatment of COPD. Handheld DPI and MDI devices are the most common forms of drug delivery in non-hospitalized patients with COPD and are well suited for maintenance therapy. We believe the development of DPI and MDI formulations has the potential to significantly increase the market opportunity for RPL554, if approved, for the maintenance treatment of COPD. In addition, we may explore the development of RPL554 in these formulations for the treatment of asthma and other respiratory diseases. Following the completion of our DPI and MDI formulation process, we plan to commence pre-clinical studies for RPL554 in these formulations in 2018.

According to the World Health Organization, over one billion people suffer from chronic respiratory diseases. Among the most common of these afflictions is COPD, which is a progressive respiratory disease for which there is no cure. COPD damages the airways and the lungs and leads to shortness of breath, impacting a person's ability to perform daily activities. Chronic inflammation plays a central role in the pathology of the disease, and is particularly prominent in the airways of COPD patients. COPD includes chronic bronchitis, which refers to the inflammation of the lung and airways that results in coughing and sputum production, and emphysema, which refers to a destruction of distal lung tissue, or air sacs. In some cases, patients with COPD experience exacerbations, which are estimated to cause approximately 1.5 million emergency department visits, 687,000 hospitalizations and 129,000 deaths per year in the United States alone. According to the World Health Organization, COPD is the third leading cause of death globally, with 210 million people worldwide suffering from the disease. It is estimated that there are 24 million people with COPD in the United States, only half of whom have been diagnosed. Of those diagnosed with COPD in the United States, approximately 2 million suffer from severe or very severe forms of the disease. Total annual medical costs relating to COPD in the United States were estimated to be $32 billion in 2010 and are projected to rise to $49 billion in 2020. Global sales of drugs currently indicated for COPD were $10.6 billion in 2016 and are expected to grow to $15.6 billion in 2019.

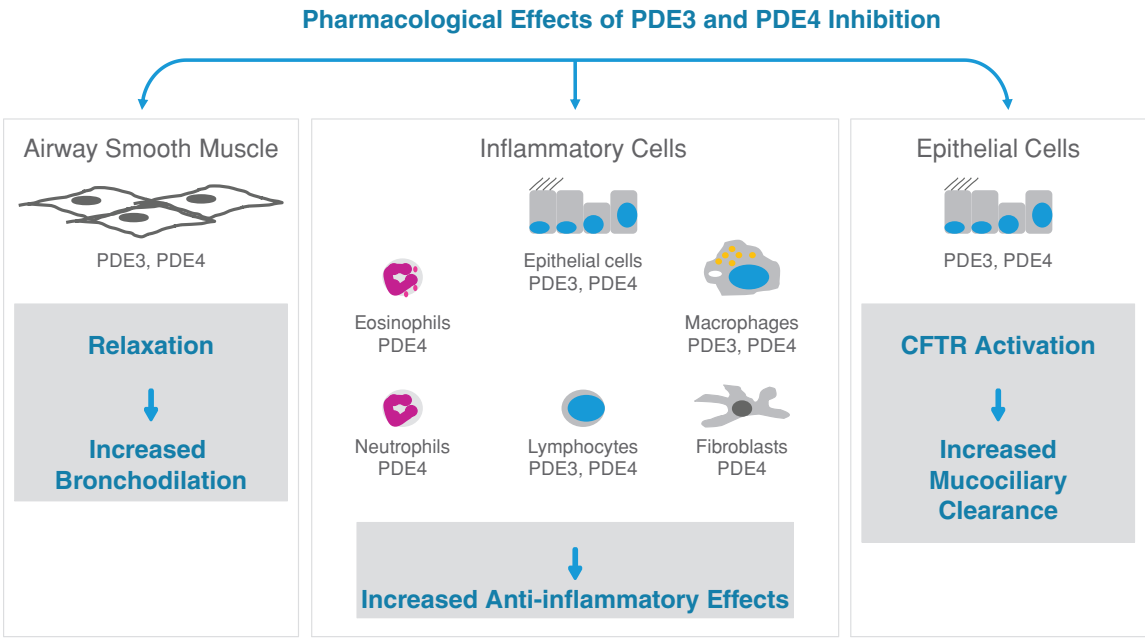
COPD patients are commonly treated with bronchodilators, which seek to relieve airway constriction and make it easier to breathe, and corticosteroids, which seek to reduce lung inflammation. For patients with more severe disease who experience recurrent exacerbations, and for whom inhaled corticosteroids are not effective, an oral formulation of a PDE4 inhibitor, which is an anti-inflammatory agent, may also be used as treatment. Despite the wide availability of these therapies, many COPD patients continue to suffer exacerbations and have continued respiratory symptoms, which limit their daily activities. Furthermore, current therapies have not demonstrated an ability to change the progressive decline in lung function or reduce the mortality associated with COPD. We believe there is an urgent and unmet medical need for new and more effective treatments for COPD to reduce the number and burden of symptoms, reduce exacerbations and establish a consistent and durable treatment response.

Cystic fibrosis is the most common fatal inherited disease in the United States and Europe. CF causes impaired lung function and is commonly associated with repeat and persistent lung infections due to the

inability to clear thickened phlegm, or mucus, from the lung. This condition often results in frequent exacerbations and hospitalizations. There is no cure for CF and the median age of death for CF patients is 37 years. CF is considered a rare, or orphan, disease by both the FDA and the EMA. According to the Cystic Fibrosis Foundation, more than 30,000 people in the United States and more than 70,000 people worldwide are living with CF and approximately 1,000 new cases of CF are diagnosed each year. The FDA and the EMA provide incentives for sponsors to develop products for orphan diseases, and we plan to seek orphan drug designation for RPL554 in treating CF. CF patients require lifelong treatment with multiple daily medications, frequent hospitalizations and, ultimately, lung transplants in some end-stage patients. The quality of life for CF patients is compromised as a result of spending significant time on self-care every day and frequent outpatient doctor visits and hospitalizations. CF patients take an average of seven medications daily. In the 12-month period ended June 30, 2016, global sales of drugs currently indicated for CF totaled $4.1 billion. The global market for CF drugs is expected to increase to $7.0 billion in 2020.

RPL554 is a first-in-class, inhaled, dual inhibitor of PDE3 and PDE4. Phosodiesterases, or PDEs, are well known and validated therapeutic targets, and many PDE inhibitors, with different specificities, are currently available in the market for other indications. PDE3 is present in airways and the lung, and inhibition of this enzyme is primarily responsible for the bronchodilatory action of RPL554. PDE4 is found in inflammatory and epithelial cells, and inhibition of this enzyme contributes to RPL554's anti-inflammatory activity. PDEs metabolize the critical signaling molecules, cyclic adenosine monophosphate, or cAMP, and cyclic guanosine monophosphate, or cGMP. By inhibiting PDE3 and PDE4, RPL554 increases the levels of cAMP and cGMP, resulting in bronchodilator and anti-inflammatory effects. RPL554 also stimulates the cystic fibrosis transmembrane conductance regulator, or 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 been observed to be more effective than inhibition of either PDE alone at relaxing airway smooth muscle cells and suppressing the activation and functions of pro-inflammatory cells residing in the lung, both of which are commonly understood to play a significant role in COPD and CF.

The figure below illustrates the three key mechanisms of action of RPL554 in respiratory diseases:



In our clinical trials, RPL554 has shown rapid onset and durable bronchodilation in healthy subjects and patients with COPD when inhaled from a nebulizer. In addition, RPL554 has been observed to be complementary and additive when administered as an add-on therapy to other currently marketed bronchodilators. Our most recent clinical trial of RPL554 was a Phase 2a clinical trial in 36 patients with COPD. Our primary objective in this clinical trial was to evaluate the improvement in lung function, as measured by FEV_1, and the duration of action of RPL554. We evaluated RPL554 administered as a single agent as compared to placebo and two commonly used bronchodilators, albuterol, also known as salbutamol and marketed as Ventolin, and ipratropium, marketed as Atrovent. We also evaluated RPL554 administered as an add-on therapy to either albuterol or ipratropium, in each case as compared to albuterol or ipratropium alone. We observed that RPL554 administered as a single agent produced statistically significant improvements in lung function, as measured by FEV_1, as compared to placebo, with a p-value of less than 0.001. P-value is a conventional statistical method for measuring the statistical significance of clinical results. A p-value of 0.05 or less represents statistical significance, meaning that there is a less than 1-in-20 likelihood that the observed results occurred by chance. We also observed clinically meaningful and statistically significant improvement in lung function, as measured by FEV_1, when RPL554 was administered as an add-on therapy to standard doses of albuterol and ipratropium as compared to standard doses of either bronchodilator alone. In this clinical trial, we observed the effect size, or peak improvement minus placebo improvement, was 51% higher for the add-on-therapy of RPL554 with albuterol as compared to albuterol alone, and 66% higher for the add-on-therapy of RPL554 with ipratropium as compared to ipratropium alone. In addition, RPL554 administered as an add-on therapy to either albuterol or ipratropium resulted in a statistically significant reduction in time of onset of bronchodilation as compared to albuterol or ipratropium alone.

RPL554 also has shown anti-inflammatory effects. In a Phase 1 clinical trial, 21 healthy evaluable subjects were treated with either RPL554 or placebo once daily for six days before airway challenge with aerosolized lipopolysaccharide, or LPS. LPS challenge induces an inflammatory response in the lung with a large proportion of neutrophils, which is a common type of white blood cell widely recognized as the most important inflammatory cell in COPD. LPS challenge is a well-validated and commonly used measure to assess the anti-inflammatory effects of novel compounds and is of particular relevance to drugs used in the treatment of COPD. Subjects treated with RPL554 were observed to have significantly lower absolute numbers of neutrophils in sputum collected six hours after LPS challenge, and a significant reduction in the absolute numbers of other inflammatory cells, including lymphocytes, macrophages and eosinophils, at the same time point. Eosinophils are prevalent in the lungs of some patients with COPD and in the vast majority of patients with asthma. These observations suggest that RPL554 also has the potential to target the chronic inflammatory processes in COPD, CF and other respiratory diseases, including asthma.

In addition, based on our pre-clinical studies, we believe that RPL554 has the potential to reduce the deleterious inflammation in CF patients, which is largely driven by neutrophils, reduce airway obstruction through bronchodilation and enhance mucociliary clearance through stimulation of the CFTR on airway epithelial cells. We believe the bronchodilator and anti-inflammatory properties of RPL554, combined with its ability to decrease mucus viscosity thereby improving mucociliary clearance, suggest that inhibition of PDE3 and PDE4 is an attractive therapeutic strategy to treat CF.

We have worldwide commercialization rights for RPL554. Our intellectual property portfolio includes five issued U.S. patents, four pending U.S. patent applications, 16 issued foreign patents in countries including China, Canada, Brazil, Japan, Mexico and Australia, and also including two issued European patents that have been validated in many European countries, including Germany, Italy, Spain, France and the United Kingdom, and 49 pending foreign applications in regions including Canada, Mexico, Asia and Europe, and also including two patent applications made under the Patent Cooperation Treaty, or PCT. These patents and patent applications include claims directed to RPL554 composition of matter, new dosage formulations and a crystalline polymorph, as well as methods of making and using RPL554 in the treatment of respiratory diseases, with expected expiry dates not earlier than between 2020 and 2037.

We were incorporated in February 2005 and are headquartered in the United Kingdom. Since September 2006, our ordinary shares have traded on AIM, a market of the London Stock Exchange, under the symbol "VRP". We have raised £74.6 million in gross proceeds from investors since such listing, of which £44.7 million was raised in our most recent private placement of equity securities in July 2016 with a number of European and U.S.-based healthcare specialist investment firms. Members of our management team and board of directors have extensive experience in large pharmaceutical and biotechnology companies in respiratory product development from drug discovery through commercialization and have played important roles in the development and commercialization of several approved respiratory treatments, including Symbicort, Daliresp/Daxas, Spiriva and Flutiform.

Our Product Candidate Pipeline

The following table depicts the potential indications for RPL554 and their current development status:

Indication	RPL554 Formulation	Pre-clinical	Phase 1	Phase 2	Phase 3	Anticipated Milestones
Maintenance treatment of COPD	Nebulizer					Commence 4-week Phase 2b clinical trial in the second half of 2017 and U.S. PK trial in mid-2017 Report Phase 2a top-line data in the fourth quarter of 2017
Treatment of acute COPD	Nebulizer					Commence Phase 2 clinical trial in the second half of 2018
CF	Nebulizer					Report Phase 2a top-line data in the first half of 2018
Maintenance treatment of COPD	DPI/MDI					Finalize formulation and commence pre-clinical studies in 2018
Treatment of asthma	DPI/MDI					Finalize formulation and commence pre-clinical studies in 2018

Our Strengths

We believe that our company has the following key distinguishing characteristics:

- ***Potential for multiple targeted indications, formulations and add-on therapies.*** We are developing RPL554 in a nebulized formulation for the maintenance treatment of COPD patients, as an add-on therapy to short-acting bronchodilators and other commonly used therapies for the treatment of hospitalized patients with acute exacerbations of COPD and the treatment of CF. We also are developing RPL554 in both DPI and MDI formulations for the maintenance treatment of COPD. In addition, we may explore the development of RPL554 in these formulations for the treatment of asthma and other respiratory diseases. Based on the favorable properties of RPL554 that we have observed in our clinical trials, we believe RPL554 has broad potential applicability in the treatment of other respiratory diseases, either as a single agent or as an add-on therapy.

- ***Observed clinical benefit as a single agent and as an add-on therapy with a favorable safety profile.*** We have completed eight Phase 1 and 2a clinical trials for RPL554 with 282 subjects enrolled. We have observed statistically significant improvements in lung function as compared to placebo, as well as clinically meaningful and statistically significant improvements in lung function when RPL554 is added to two commonly used bronchodilators as compared to either bronchodilator administered as a single agent. In addition, we observed a more rapid time of onset of bronchodilation when RPL554 was administered as an add-on therapy to albuterol or ipratropium. RPL554 also has shown anti-inflammatory effects and been well tolerated in our clinical trials, and has not been observed to result in the gastrointestinal or other side effects commonly associated with roflumilast, the only PDE4 inhibitor currently on the market approved for treatment of COPD. In addition, RPL554 has not been observed to result in any cardiovascular effects, other than a small increase in heart rate at the highest doses tested.

- ***Differentiated mechanism of action in a single compound.*** RPL554 is a first-in-class, inhaled, dual inhibitor of PDE3 and PDE4 that acts as both a bronchodilator and an anti-inflammatory agent in a single compound and stimulates the CFTR. Dual inhibition of PDE3 and PDE4 has been shown to be more effective than inhibition of either PDE alone at relaxing airway smooth muscle cells and suppressing the activation and functions of pro-inflammatory cells residing in the lung, both of which are commonly understood to play a significant role in COPD and CF. In addition, through this dual mechanism, RPL554 also stimulates the CFTR, which is important in the treatment of CF and potentially COPD. We believe that RPL554 has the potential to be a more effective and better tolerated treatment of COPD than existing treatments for COPD, including the approved PDE4 inhibitor.

- ***Established regulatory pathway and well-defined clinical endpoints.*** Our planned clinical trials for RPL554 for the maintenance treatment of COPD will be designed to evaluate the effect on FEV_1 and duration of action of our product candidate. These clinical endpoints are commonly used in clinical trials for respiratory diseases and have been used by other companies in obtaining FDA approval of drugs addressing respiratory diseases.

- ***Addressing significant market opportunities.*** Despite the availability of bronchodilators and anti-inflammatory corticosteroid or PDE4 inhibitor treatments for COPD, many patients continue to suffer from significant symptoms and may experience acute exacerbations leading to hospitalization. Furthermore, current therapies have not demonstrated an ability to change the progressive decline in lung function or reduce the mortality associated with COPD. We believe a large market opportunity with significant unmet medical need exists in COPD. We believe the properties of RPL554 make it attractive as an important and novel potential treatment of patients with COPD, as well as for patients with CF and asthma. We plan to seek orphan drug designation of RPL554 for the treatment of CF.

- ***Experienced management team.*** Members of our management team and board of directors have extensive experience in large pharmaceutical and biotechnology companies in respiratory product development from drug discovery through commercialization and have played important roles in the development and commercialization of several approved respiratory treatments. We believe that the experience of our management team and our network of relationships within the industry and medical community provides us with insight into product development and identification of other opportunities in the respiratory field.

Our Strategy

We intend to become a leading biopharmaceutical company focused on the treatment of respiratory diseases with significant unmet medical needs. The key elements of our strategy to achieve this goal include:

- ***Rapidly advance the development of nebulized RPL554 for the maintenance treatment of COPD.*** We intend to develop RPL554 for the maintenance treatment of COPD. We plan to commence a four-week Phase 2b dose ranging clinical trial to evaluate RPL554 for the maintenance treatment of COPD in the second half of 2017. In this trial, we plan to compare the use of RPL554 in a nebulized formulation to placebo in approximately 400 patients. We expect to report top-line data from this trial in the second half of 2018. In February 2017, we commenced a Phase 2a clinical trial of RPL554 for the maintenance treatment of COPD in the United Kingdom. This trial is evaluating RPL554 as an add-on therapy to tiotropium in approximately 30 patients. We expect to report top-line data from this trial in the fourth quarter of 2017. We also plan to commence a PK trial of RPL554 in approximately 12 healthy volunteers in the United States in mid-2017. We expect to report top-line data from this trial in the fourth quarter of 2017. In addition, we plan to commence a 12-week Phase 2b dose-ranging clinical trial of RPL554 for the maintenance treatment of COPD in the second half of 2018. In this trial, we plan to evaluate RPL554 as an add-on therapy to a long-acting bronchodilator in approximately 400 patients.

- ***Rapidly advance the development of nebulized RPL554 for the treatment of acute exacerbations of COPD.*** We also are developing RPL554 as an add-on therapy to short-acting bronchodilators and other commonly used therapies for the treatment of hospitalized patients with acute exacerbations of COPD. We plan to commence a Phase 2 clinical trial in the United States for RPL554 for this indication in approximately 150 patients in the second half of 2018.

- ***Develop RPL554 for the treatment of CF.*** In March 2017, we commenced a Phase 2a single-dose trial in the United Kingdom of RPL554 in up to ten CF patients to evaluate the PK and PD profile and tolerability of RPL554, as well as examine the effect on lung function. We expect to report top-line data from this trial in the first half of 2018. The results of this trial are expected to support dose selection for a proof-of-concept Phase 2b trial in Europe in approximately 100 patients with CF, which we plan to commence in 2018.

- ***Develop DPI and MDI formulations of RPL554.*** In addition to our nebulized formulation of RPL554, we are developing RPL554 in both DPI and MDI formulations for the maintenance treatment of COPD. We believe the development of DPI and MDI formulations has the potential to significantly increase the market opportunity for RPL554, if approved, for the maintenance treatment of COPD. In addition, we may explore the development of RPL554 in these formulations for the treatment of asthma and other respiratory diseases. Following the completion of our DPI and MDI formulation process, we plan to commence pre-clinical studies for RPL554 in these formulations in 2018.

- ***Pursue development of RPL554 in other forms of respiratory disease.*** We believe that RPL554's properties as an inhaled, dual inhibitor of PDE3 and PDE4 give it broad potential applicability in the treatment of other respiratory diseases. We may explore development of RPL554 to treat other forms of respiratory disease following development of RPL554 for the treatment of COPD and CF.

- ***Seek strategic collaborative relationships.*** We may seek strategic collaborations with market-leading biopharmaceutical companies to develop and commercialize RPL554. We believe these collaborations could provide significant funding to advance the development of RPL554 while allowing us to benefit from the development or commercialization expertise of our collaborators.

- ***Acquire or in-license product candidates for the treatment of respiratory diseases.*** We plan to leverage our respiratory disease expertise to identify and in-license or acquire additional clinical-stage

product candidates that we believe have the potential to become novel treatments for respiratory diseases with significant unmet medical needs.

RPL554 for the Treatment of COPD

Overview

Our product candidate, RPL554, is a first-in-class, inhaled, dual inhibitor of PDE3 and PDE4 that acts as both a bronchodilator and an anti-inflammatory agent in a single compound. We are not aware of any therapy in a single compound in clinical development or approved by the FDA or the EMA, for the treatment of respiratory diseases that acts as both a bronchodilator and anti-inflammatory agent. We believe RPL554 has the potential to be the first novel class of bronchodilator in over 40 years.

COPD Background

COPD is a progressive respiratory disease for which there is no cure. COPD damages the airways and the lungs and leads to shortness of breath, impacting a person's ability to work, exercise, sleep and perform other daily activities. Part of the pathology of the disease is chronic airway inflammation and constriction of airway muscles. Airflow limitation in COPD patients results from mucosal and airway inflammation and edema, or excess fluid in the airway walls, bronchoconstriction, increased secretions in the airways and loss of elastic recoil, or the ease with which the lung rebounds after having been stretched by inhalation. COPD includes chronic bronchitis, which refers to the inflammation of the lung and airways that results in coughing and sputum production, and emphysema, which refers to a destruction of distal lung tissue, or air sacs. In some cases, hospitalized patients with COPD experience acute exacerbations, which include rapid and prolonged worsening of symptoms.

According to the World Health Organization, COPD is the third leading cause of death globally, with 210 million people worldwide suffering from the disease. The U.S. Centers for Disease Control and Prevention, or CDC, estimates that there are 24 million people with COPD in the United States, only half of whom have been diagnosed. Of those diagnosed with COPD in the United States, approximately 2 million suffer from severe or very severe forms of the disease. Acute exacerbations or COPD are estimated to cause approximately 1.5 million emergency department visits, 687,000 hospitalizations and 129,000 deaths per year in the United States alone. According to the CDC, total annual medical costs relating to COPD in the United States were estimated to be $32 billion in 2010, and are projected to rise to $49 billion in 2020. An estimated 16.4 million days of work were lost due to COPD each year in the United States. Global sales of drugs currently indicated for COPD were $10.6 billion in 2016 and are expected to grow to $15.6 billion in 2019.

Current Treatment Landscape of COPD

There are no approved therapies for COPD that alter the progression, rate of decline of lung function or mortality of the disease. The goal of current COPD treatments is to alleviate symptoms, decrease the frequency and severity of exacerbations, and reduce limitations on daily activities. COPD patients are commonly treated with bronchodilators, which seek to relieve airway constriction and make it easier to breathe, and corticosteroids, which seek to reduce lung inflammation. For patients with more severe disease who experience recurrent exacerbations, and for whom inhaled corticosteroids are not effective, an oral formulation of a PDE4 inhibitor, which is an anti-inflammatory agent, is available and may be used as treatment. Antibiotic therapy has also been shown to have a small but important effect on clinical recovery and outcome in hospitalized patients with bacterial infections that resulted in an acute exacerbation of COPD.

Despite the availability of bronchodilators, anti-inflammatory corticosteroids, an anti-inflammatory PDE4 inhibitor and antibiotics for treatment of COPD, many patients continue to suffer from significant symptoms and may experience acute exacerbations leading to increased doses of medication and hospitalization. Following an acute exacerbation of COPD and subsequent hospitalization, it may take many weeks for a

patient's lung function to recover to pre-exacerbation levels. In addition, the rate of mortality of COPD patients within one year of hospitalization is approximately 20%, and patients with a need for hospital readmission have only a 20% five-year survival rate. Retrospective studies have demonstrated that more than 20% of patients discharged from hospital after an exacerbation of their COPD require readmission within 30 days of discharge. This has medical implications for the patient and is a financial burden for the healthcare system. We believe that increasing awareness of the problem of COPD patients returning for hospital treatment within 30 days of discharge has triggered a strong interest from industry, regulators and healthcare administrators and payors in optimizing the treatment of acute COPD exacerbations, both in the hospital setting and after patients are discharged.

For many COPD patients, a better and more effective maintenance treatment is required that can control their symptoms and reduce the risk of acute exacerbations. For patients that require hospitalization, essentially the same treatment modalities are used as in non-hospitalized patient treatment, however, they are often treated with higher doses, including with corticosteroids that are administered systemically rather than locally by inhalation. Acute medical treatment of COPD exacerbations has not changed in decades, with older, short-acting nebulized bronchodilators still used as a mainstay bronchodilator treatment in the acute hospital setting. This is despite hospitalizations for COPD being long, at about five days, expensive, and with a high mortality rate and high probability of hospital readmission. We believe there is an unmet medical need for an improved treatment approach.

Bronchodilators

Bronchodilators are the first-line therapy for the treatment of COPD patients. There are two existing classes of bronchodilators: beta2-agonists and anti-muscarinics. Long-acting versions of these bronchodilators, lasting 12 to 24 hours, are commonly used in the maintenance therapy of patients with COPD. Long-acting beta2-agonists, or LABAs, which are commonly used in combination with inhaled corticosteroids, include Advair (salmeterol and fluticasone), which had $2.4 billion in global sales in 2015, and Symbicort (formoterol and budesonide), which had $1.6 billion in global sales in 2015. Long-acting anti-muscarinics, or LAMAs, include Spiriva (tiotropium), which had $3.9 billion in global sales in 2015. In the United States, nebulized LABAs, which are only indicated for COPD, generated sales of $601 million in the 12-month period ending June 30, 2016. In addition to producing bronchodilation, beta2-agonists have been shown to improve mucociliary clearance in COPD patients, thereby potentially reducing mucus in the airways. LAMAs have a different mechanism of action and effect bronchodilation via different cell-surface receptors and through different intracellular pathways than LABAs. Studies with twice-daily LABAs indicate that clinically relevant improvements in dyspnea or health-related quality of life are only achieved by a minority of patients. Clinical data suggest that inhaled LAMAs may be somewhat more effective than LABAs in improving lung function of COPD patients. However, LAMAs have a relatively slow onset of action and both LABAs and LAMAs are contraindicated for acute use in the United States. Another limitation is a diminished effectiveness of beta2-agonists that can be experienced by some COPD patients over time. Some patients also have adrenergic side effects such as tremor or increased heart rate from existing beta2-agonists.

Short-acting versions of bronchodilators, lasting up to eight hours, are most commonly used to treat hospitalized patients who experience a worsening airway obstruction, including as a result of acute exacerbations of COPD. A short-acting beta2-agonist, or SABA, such as Ventolin (albuterol), which had $820 million in global sales in 2015, and a short-acting anti-muscarinic, or SAMA, such as Atrovent (ipratropium), which had $590 million in global sales in 2015, are typically used for relief of acute exacerbations of COPD. However, the response to bronchodilators can be highly variable in individual patients over time, and patients who are non-responders at one office visit may respond at a different visit. In addition, the frequent use of beta2-agonists can lead to reduced effectiveness of the drug due to the development of tolerance. As a consequence of this variability in responsiveness, a significant number of COPD patients are classified as non-responders to albuterol, the standard SABA used in the market. Based on screening visits in a large recent clinical trial conducted by GlaxoSmithKline, in which patients were

treated with albuterol once every three months over a 12-month period, the rate of classification of patients as responders per treatment was 24% as measured by American Thoracic Society, or ATS, criteria. Classification as a responder pursuant to ATS criteria requires at least a 12% and 200 ml increase in FEV_1. In addition, the rate of classification of patients as consistent responders, or responders at least three out of four times over the 12-month treatment period, was 14% as measured by ATS criteria. In another large study conducted by Boehringer Ingelheim, even when albuterol was combined with ipratropium, the rate of classification of patients as responders pursuant to the ATS criteria was just over 50%.

Bronchodilators can be delivered in a nebulized form or by a DPI or MDI if patients are able to use proper technique, which may be difficult during an exacerbation. As a result, acute COPD exacerbations are often treated with a nebulizer. A nebulizer is both convenient and effective in delivering a large dose. Use of a nebulizer to provide bronchodilation enhances delivery of the therapeutic to the airways of the patient. Patients with more severe COPD, who tend to suffer more frequent exacerbations, generally prefer treatment with a nebulizer as they view its perceived benefits, including greater confidence in effective drug administration and a reduced need to visit health care providers, as outweighing its perceived disadvantages, which include length of treatment administration and required cleaning. In addition, use of a nebulizer is generally preferred when administering larger doses in the hospital setting.

Beta2-agonists and anti-muscarinics can be used as single agents for the treatment of COPD, but studies have shown that their combined use leads to greater bronchodilation than each used as a single agent because these classes of bronchodilators have different mechanisms of action to improve lung function. Based on these findings, novel drugs combining a LABA and a LAMA in one inhaler device are being brought to market, such as Novartis' Utibro Breezhaler (indacaterol and glycopyrrolate), which had $260 million in global sales in 2015. However, many patients, and especially those with more severe disease, still need more effective bronchodilation to improve their symptoms. Additionally, LABAs and LAMAs, acting alone or in combination, do not treat the underlying inflammation present in COPD.

Corticosteroids

Corticosteroids are used for treatment in a range of diseases for their anti-inflammatory effect. However, corticosteroids do not affect neutrophils, which are widely recognized as the most important inflammatory cells in COPD. Corticosteroids have shown limited efficacy and are not approved as a stand-alone treatment for COPD. Inhaled corticosteroids are commonly administered together with LABAs for the maintenance treatment of COPD. When administered with LABAs, corticosteroids have been shown to improve lung function and reduce exacerbation rates. However, recent studies have shown that removing inhaled corticosteroids from this treatment regimen does not lead to increases in exacerbations in a majority of patients, implying that the combination is not effective in all patients. In addition, inhaled corticosteroids have been shown to decrease the immune response in some patients, which results in an increased incidence of pneumonia.

In the treatment of acute COPD exacerbations, corticosteroids are often administered systemically, either through injection or orally, in addition to high-dose bronchodilators. In this setting, corticosteroids may be effective in improving symptoms and lung function, reducing the rate of treatment failure and shortening the length of hospital stay. However, when given systemically, corticosteroids are known to be associated with side effects such as compromised adrenal gland function and reduced bone density.

PDE4 Inhibitors

PDE4 inhibitors have attracted recent attention for the treatment of COPD because PDE4 is broadly expressed in airways and in the lung. PDEs are well known and validated therapeutic targets, and many PDE inhibitors, with different specificities, are currently available in the market for other indications. PDE4 is found in inflammatory and epithelial cells, and inhibition of this enzyme contributes to RPL554's anti-inflammatory activity. PDE4 is the primary cAMP-hydrolyzing enzyme in inflammatory and immune cells, especially neutrophils, lymphocytes, macrophages and eosinophils, all of which are found in the lungs

of COPD patients. Inhibition of PDE4 leads to elevated cAMP levels in these cells, which results in anti-inflammatory effects due to the down-regulation of the inflammatory response.

The recently approved oral PDE4 inhibitor, roflumilast, has shown clinical efficacy as an oral therapeutic in the reduction of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations. The drug is an anti-inflammatory compound that decreases inflammation in a different manner than corticosteroids. However, roflumilast has only shown a modest improvement in lung function in COPD patients as compared to commonly used bronchodilators as it is not a direct bronchodilator. In addition, because of roflumilast's systemic exposure as an oral PDE4 inhibitor, its use has been limited due to frequent adverse side effects such as back pain, decreased appetite, diarrhea, dizziness, flu-like symptoms, headache, weight loss, nausea and vomiting.

Antibiotics

Antibiotic therapy has been shown to have a small but important effect on clinical recovery and outcome in patients with bacterial infections that resulted in an acute exacerbation of COPD. As a result, antibiotic therapy is often considered at the beginning of treatment of acute exacerbations of COPD. Hospitalized patients commonly receive intravenous treatment with an antibiotic and initial outpatient management of COPD may include oral antibiotics. However, the limited efficacy of and patient resistance to antibiotics represent significant drawbacks of this form of therapy for COPD patients.

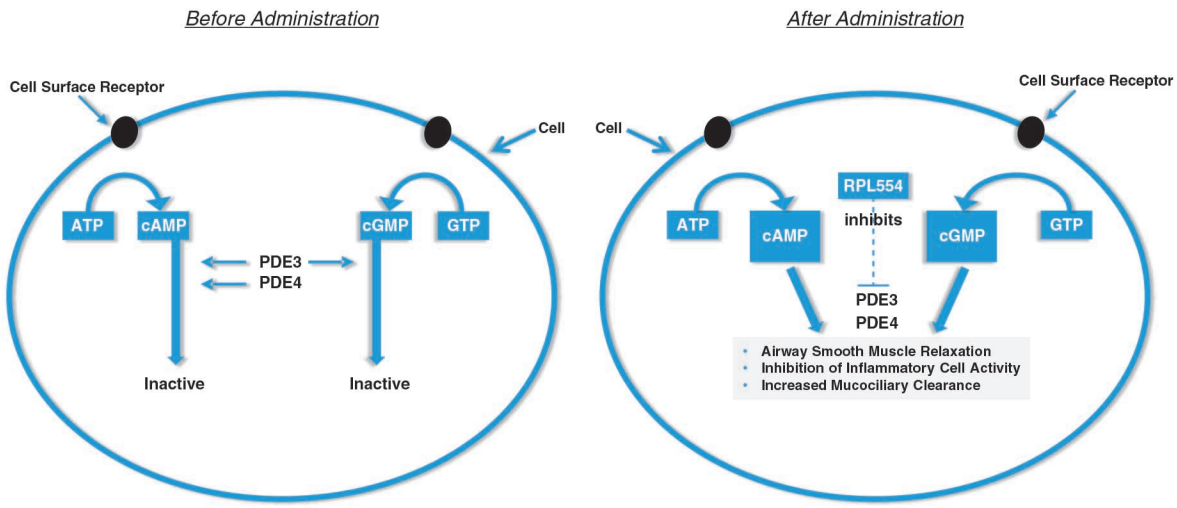
Our Solution

We believe that RPL554, as a first-in-class, inhaled, dual inhibitor of PDE3 and PDE4, which acts as both a bronchodilator and an anti-inflammatory in a single compound, if approved, has the potential to become an important and novel treatment and standard of care for patients with COPD. We are not aware of any therapy in a single compound in clinical development or approved by the FDA or the EMA, for the treatment of COPD that acts as both a bronchodilator and anti-inflammatory agent. Based on our clinical trials, we believe RPL554 has the potential to be a best-in-class bronchodilator for the treatment of COPD, both as a monotherapy and as an add-on therapy to existing bronchodilators.

PDEs are a family of over ten intracellular enzymes that regulate important cellular pathways in many different cell types. PDEs metabolize the critical signaling molecules cAMP and cGMP. By inhibiting PDE3 and PDE4, RPL554 increases the levels of these intracellular messengers resulting in bronchodilator and anti-inflammatory effects. Dual inhibition of PDE3 and PDE4 has been shown to be more effective than inhibition of either PDE alone at relaxing airway smooth muscle cells and suppressing the activation and functions of pro-inflammatory cells residing in the lung, both of which are commonly understood to play a significant role in COPD.

The figure below illustrates the mechanism of action of RPL554's dual inhibition of PDE3 and PDE4 in the treatment of COPD.

Mechanism of Action of RPL554 from PDE3 and PDE4 Inhibition



Previous attempts to develop PDE4 inhibitors for COPD, asthma and other indications have been limited by the resulting side effects, particularly to the gastrointestinal system, such as nausea, vomiting and weight loss. RPL554 is designed to maximize effectiveness and reduce the occurrence of adverse events by:

- relying on a chemical structure that is distinct from other PDE4 inhibitors and avoids gastrointestinal and other side effects typically associated with PDE4 inhibition;
- having high selectivity for PDE3 and PDE4 over other enzymes, including other PDE enzymes, and receptors to minimize off-target effects; and
- enabling delivery directly to the lung by inhalation, thereby maximizing pulmonary exposure to RPL554 while minimizing systemic distribution and related adverse events.

We believe RPL554 may offer significant advantages over currently approved therapies for COPD based on the following:

- ***Clinical benefit as an add-on therapy and as a single agent with a favorable safety profile.*** RPL554 has been evaluated in multiple randomized, controlled Phase 1 and Phase 2a clinical trials involving 282 subjects. In these trials, RPL554 has been observed to result in statistically significant improvements in lung function as compared to placebo. Our clinical trials also have shown clinically meaningful and statistically significant improvements in lung function when RPL554 is added to two commonly used bronchodilators as compared to either bronchodilator administered as a single agent. RPL554 has been well tolerated in our clinical trials, and has not been observed to result in the gastrointestinal or other side effects commonly associated with roflumilast, the only PDE4 inhibitor currently on the market approved for the treatment of COPD. In addition, RPL554 has not been observed to result in any cardiovascular effects, other than a small increase in heart rate at the highest doses tested.
- ***Bronchodilator and anti-inflammatory effects in one compound.*** RPL554 utilizes a novel mechanism of action that inhibits PDE3 and PDE4 to act as both a bronchodilator and an anti-inflammatory agent in a single compound. We are not aware of any therapy in a single compound in clinical development or approved by the FDA or the EMA, for the treatment of COPD that acts as both a bronchodilator and anti-inflammatory agent. Inhibition of PDE3 is largely responsible for the bronchodilatory effects of RPL554, while the inhibition of PDE4 is largely responsible for the

anti-inflammatory effects. By simultaneously targeting PDE3 and PDE4, we believe that RPL554 results in a more profound effect that addresses both airway constriction and chronic inflammation, which are the hallmarks of COPD. As a result, we believe RPL554, if approved, has the potential to become an important and novel treatment and standard of care for patients with COPD.

- ***Inhaled administration.*** We are developing RPL554 as an inhaled therapy, which we believe is advantageous for the treatment of COPD patients because it delivers high concentrations of RPL554 directly to the patient's airways, thereby potentially improving efficacy while minimizing some of the side effects resulting from the systemic exposure associated with orally administered bronchodilators and anti-inflammatory drugs. For example, roflumilast, the only currently marketed PDE4 inhibitor approved for the treatment of COPD, is administered orally and has been associated with adverse side effects such as back pain, decreased appetite, diarrhea, dizziness, flu-like symptoms, headache, weight loss, nausea and vomiting. In our clinical trials, RPL554 has been well tolerated and has not been associated with many of the adverse effects associated with roflumilast. In this inhaled form, we believe RPL554, if approved, would provide significant advantages over orally administered therapies and potentially lead to better and more effective treatment of COPD.
- ***Rapid onset of action.*** In our Phase 2a clinical trial for RPL554 completed in February 2016, we observed a rapid onset of bronchodilation when RPL554 was administered as an add-on therapy to each of ipratropium and albuterol, two currently marketed short-acting bronchodilators. The time of onset of action of ipratropium was approximately 20 minutes, while the time of onset of action for RPL554 was approximately 15 minutes. When RPL554 was administered as an add-on therapy to ipratropium, the time of onset was reduced by 75% to approximately five minutes as compared to ipratropium alone, which is similar to albuterol alone. When RPL554 was administered as an add-on therapy to albuterol, the time to onset was more rapid than with albuterol alone. We believe RPL554 has the potential to provide significant benefits as an add-on therapy to short-acting bronchodilators in the treatment of acute exacerbations of COPD due to its effect on time of onset of action.

We are developing RPL554 in a nebulized formulation for the maintenance treatment of COPD patients and as an add-on therapy to short-acting bronchodilators and other current standard-of-care therapies for the treatment of hospitalized patients with acute exacerbations of COPD. In our planned clinical trials, we intend to explore the possibility that treatment with RPL554, when used for the maintenance treatment, has the potential to improve recovery rates as measured by improved lung function and, when used for the treatment of acute exacerbations of COPD, has the potential to reduce symptoms concomitantly with a reduction of the 30-day hospital readmission rates. No current medication has been shown to reduce this re-hospitalization rate and currently marketed long-acting bronchodilators are contraindicated for acute use in the United States. Furthermore, current therapies have not demonstrated an ability to change the progressive decline in lung function or reduce the mortality associated with COPD. We intend to explore opportunities for RPL554 for the maintenance treatment and in the hospital setting for acute exacerbations in our planned clinical trials.

In addition to our nebulized formulation of RPL554, we are developing RPL554 in both DPI and MDI formulations for the maintenance treatment of COPD. We may also explore the development of RPL554 in these formulations for the treatment of asthma and other respiratory diseases. DPI and MDI devices are the most common forms of drug delivery in non-hospitalized patients with COPD and are well-suited for the maintenance therapy of COPD patients. We believe the development of DPI and MDI formulations has the potential to significantly increase the market opportunity for RPL554, if approved, for the maintenance treatment of COPD. Following the completion of our DPI and MDI formulation process, we plan to commence pre-clinical studies for RPL554 in these formulations in 2018.

Clinical Development

We have completed five Phase 1 and Phase 2a trials for RPL554 outside the United States, dosing 105 subjects with an initial proof-of-concept formulation. Data from the single and multiple dose trials using our initial proof-of-concept formulation suggest that RPL554, when inhaled across a range of doses, has the

potential to be an effective bronchodilator in patients with COPD and other respiratory diseases, including asthma, and has broncho-protective properties, such as reducing the hypersensitivity of asthmatic airways to inhaled irritants. In these trials, we observed RPL554 having a rapid onset of action and the magnitude of improvement in lung function, as measured by FEV_1, seemed to be at least as profound as that of other commonly used and approved bronchodilator drugs. We also observed that RPL554 had a potent anti-inflammatory effect in a number of pre-clinical studies and a clinical trial.

In 2014, we developed a new nebulized formulation of RPL554 for our ongoing development programs. We designed this formulation to have a broader dose range, improved PK profile and dosing regimen and neutral pH, as compared to the initial proof-of-concept formulation. This nebulized formulation of RPL554 is also stable and would be suitable for commercial use, if approved. We initiated the first Phase 1 clinical trial with this nebulized formulation in December 2014 and completed the trial in September 2015. The following table summarizes the Phase 1 and 2a clinical trials we have completed with our new nebulized formulation of RPL554, all of which have been conducted outside of the United States:

Summary of Completed RPL554 Clinical Trials with New Nebulized Formulation			
Trial Description	**Patient Population**	**RPL554 Dosage**	**Key Findings**
Phase 2a trial to assess the improvement in lung function, as measured by FEV_1, of RPL554 as an add-on treatment to each of albuterol and ipratropium Completion date: February 2016	36 moderate-to-severe COPD patients, males and females, age 52 - 70 1 location; United Kingdom	Single dose of RPL554 of 6 mg alone and as an add-on treatment to albuterol or ipratropium	■ Well tolerated following single dose of 6 mg of RPL554 alone and as add-on treatment ■ RPL554 alone was as effective a bronchodilator as either albuterol (200 μg) or ipratropium (40 μg) and was statistically significant as compared to placebo ■ RPL554 produced significant additive bronchodilation (>50% increase) when dosed with either albuterol (200 μg) or ipratropium (40 μg) as compared to albuterol or ipratropium, respectively, alone, and caused an additive and significant reduction in lung volumes and airway resistance ■ The time to onset of RPL554 when dosed with either albuterol (200 μg) or ipratropium (40 μg) was more rapid than with albuterol or ipratropium, respectively, alone
Phase 2a trial to assess the effect of single doses of RPL554 compared to albuterol and placebo on lung function, as measured by FEV_1, of patients with chronic asthma Completion date: January 2016	29 chronic asthmatic patients, males and females, age 20 - 62 2 locations; United Kingdom and Sweden	Single dose of 0.4 mg to 24 mg	■ Well tolerated following single dose of 0.4 mg to 24 mg ■ Improvement in lung function, as measured by FEV_1, observed with a magnitude that was comparable to the maximum effect observed with a dose of 7.5 mg of nebulized albuterol, or three times the recommended dose of albuterol
Phase 1 trial to assess the safety, tolerability and PK profile of single and multiple inhaled doses of RPL554 in healthy volunteers and stable COPD subjects Completion date: September 2015	Part A: 50 (35 RPL554 / 15 placebo) healthy subjects, males, age 19 - 48 Part B: 30 (21 RPL554 / 9 placebo) healthy subjects, males, age 19 - 46 Part C: 32 (23 RPL554 / 9 placebo) moderate COPD patients, males and females, age 49 - 73 1 location; United Kingdom	Part A: Single dose of 1.5 mg to 24 mg Part B: Multiple dose (twice daily for 5.5 days) of 6 mg to 24 mg Part C: Multiple dose (twice daily for 5.5 days) of 1.5 mg to 12 mg	■ Improvement in lung function, as measured by FEV_1, observed in healthy subjects and COPD patients ■ Part A: RPL554 was well tolerated and there was a dose dependent increase in lung function, as measured by FEV_1, of up to 360 mL (9%) from baseline ■ Part B: RPL554 was well tolerated and there was a sustained increase in FEV_1 ■ Part C: RPL554 was well tolerated and there was a significant increase in lung function, as measured by FEV_1, of up to 360 mL (24%) from baseline, with a duration of action of 12 hours

Phase 2a Clinical Trials

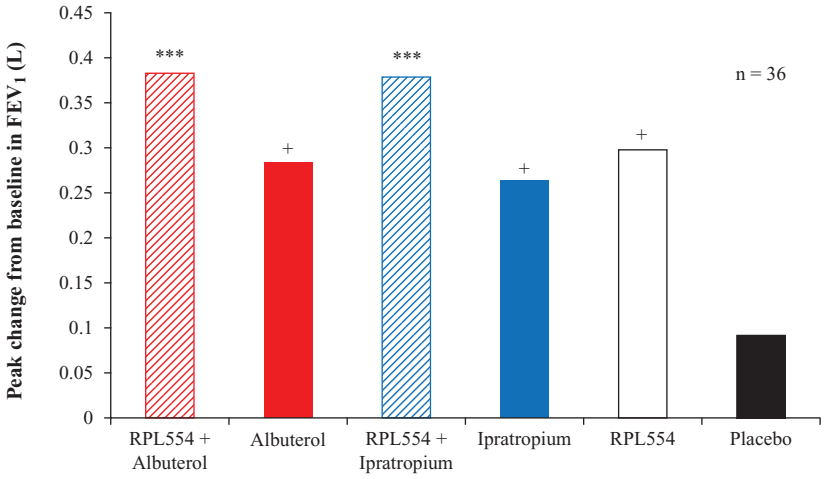
We have completed two Phase 2a clinical trials using our new nebulized formulation of RPL554.

In February 2016, we completed a single-dose, double-blinded, placebo-controlled, six-way cross-over Phase 2a clinical trial for RPL554 conducted in the United Kingdom. A total of 36 patients were randomized to receive each of the six treatments, which were albuterol, ipratropium, RPL554, placebo,

RPL554 as an add-on therapy to albuterol and RPL554 as an add-on therapy to ipratropium. The primary objective of this trial was to establish the improvement in lung function, as measured by FEV_1, of RPL554 as an add-on therapy to albuterol (200 μg), as an add-on therapy to ipratropium (40 μg) and as a single agent, each as compared to standard doses of each of albuterol and ipratropium alone and to placebo. The testing dose level for RPL554 was 6 mg. The secondary objective of this trial was to measure the change in residual lung volume, a measure of the volume of air trapped in the lung, airway conductance, a measure of the ease with which air moves down the airways, time of onset of action and safety and tolerability of RPL554.

In this clinical trial, RPL554 produced clinically meaningful and statistically significant improvement in lung function, as measured by FEV_1, as an add-on therapy to standard doses of each of albuterol and ipratropium as compared to standard doses of either bronchodilator alone. In this clinical trial, we observed the effect size, or peak improvement minus placebo improvement, was 51% higher for the add-on therapy of RPL554 with albuterol as compared to albuterol alone, and 66% higher for the add-on therapy of RPL554 with ipratropium as compared to ipratropium alone. We also observed in this trial that RPL554 as a single agent produced numerically greater improvements in lung function, as measured by FEV_1, as compared to albuterol or ipratropium alone, and statistically significant improvements as compared to placebo. These results are illustrated by the figure below.

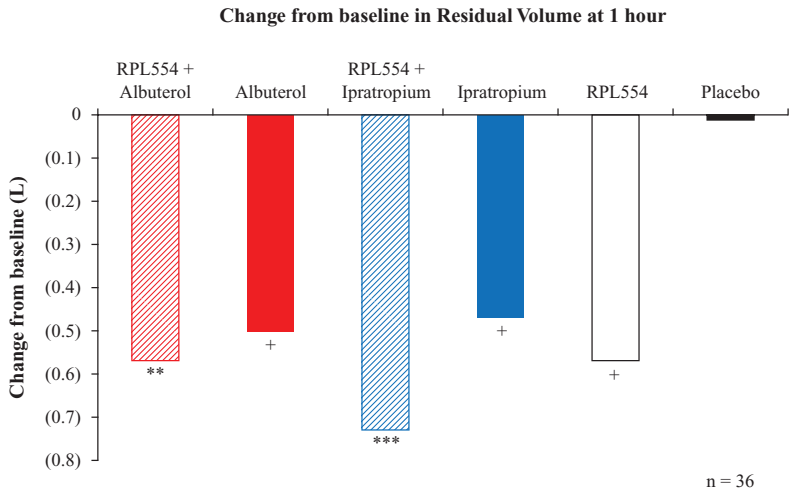
Improvement in Lung Function



*** p<0.001 vs. albuterol or ipratropium alone
\+ p<0.001 vs. placebo

In addition, patients treated with RPL554 as a single agent experienced numerically greater improvements in residual lung volume as compared to albuterol or ipratropium alone, and statistically significant improvements as compared to placebo. The add-on therapy of RPL554 with albuterol or ipratropium caused a statistically significant reduction in residual lung volume as compared to albuterol or ipratropium alone, suggesting that RPL554 treatment may reduce dyspnea, or shortness of breath, a major debilitating symptom of COPD. This reduction in residual lung volume as measured in liters is illustrated in the figure below.

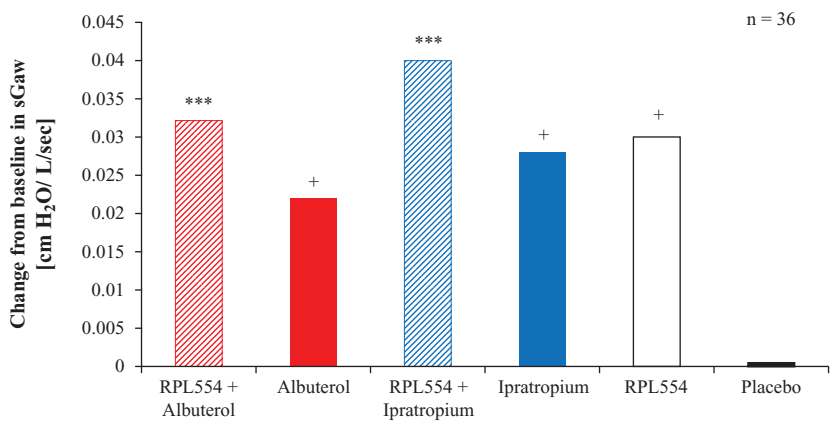
Reduction in Residual Lung Volume (Air Trapping)



** p=0.016 vs. albuterol alone at 1 hour timepoint
*** p<0.001 vs. ipratropium alone at 1 hour timepoint
+ p< 0.001 vs. placebo

Another important parameter in COPD is the resistance of the airways to airflow. The inverse of this is airway conductance. Similar to the effect on residual lung volume, patients treated with RPL554 as a single agent experienced numerically greater increases in airway conductance as compared to each of albuterol and ipratropium, and statistically significant improvements as compared to placebo. We also observed, that the administration of RPL554 as an add-on therapy to either albuterol or ipratropium resulted in a statistically significant increase in airway conductance as compared to albuterol or ipratropium alone, as illustrated in the figure below.

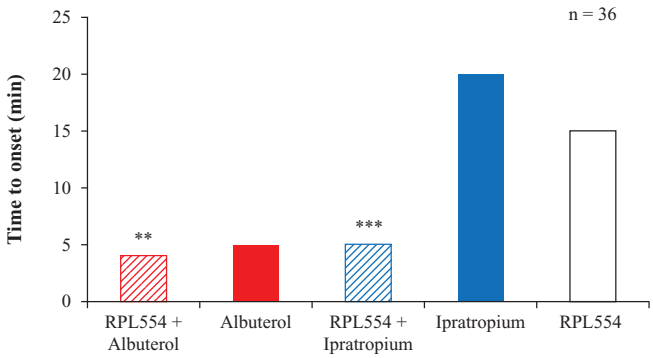
Improvement in Airway Conductance



*** p<0.001 vs. albuterol or ipratropium alone at 1 hour timepoint
+ p<0.001 vs. placebo at 1 hour time point

In this trial, the time of onset of action of ipratropium was approximately 20 minutes. The time of onset of action for RPL554 alone was approximately 15 minutes. When RPL554 was administered as an add-on therapy to ipratropium, the time of onset was reduced to approximately 5 minutes, which is similar to albuterol. In both cases, RPL554 as an add-on therapy resulted in a statistically significant reduction in time of onset as compared to ipratropium or albuterol alone. The time of onset in minutes is shown in the figure below.

Time of Onset of Bronchodilator Effect



** p<0.01 vs. albuterol alone

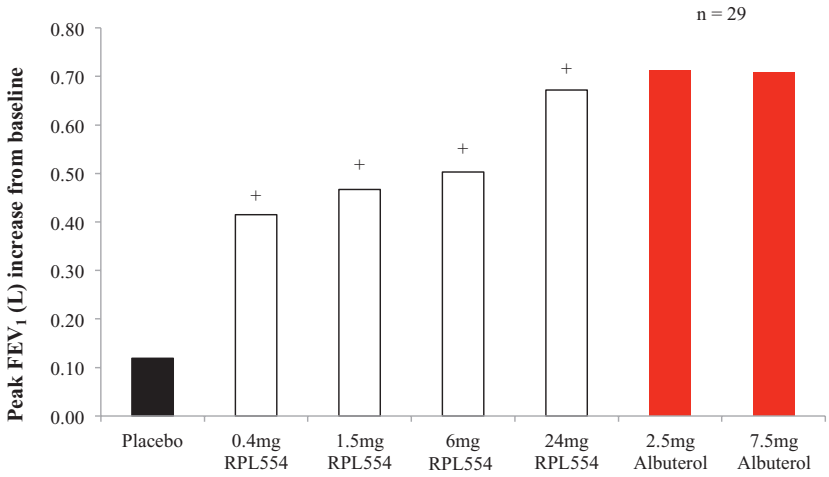
*** p<0.001 vs. ipratropium alone

Consistent with prior trials, RPL554 was well tolerated both alone and as an add-on therapy and was not observed to increase the incidence of any adverse event over standard bronchodilators when used alone. In addition, we did not observe the gastrointestinal or other side effects associated with roflumilast, the only PDE4 inhibitor currently on the market approved for the treatment of COPD. In this trial, RPL554 had no observed effect on cardiac function as measured by electrocardiograms, including QT intervals, a measure of time between certain waves in the heart's electrical cycle and measure of a potential cardiovascular adverse event. Finally, the serum levels of RPL554 were not affected by use of albuterol or ipratropium.

In January 2016, we completed a single-dose, double-blind, placebo-controlled, seven-way cross-over Phase 2a dose-finding trial of RPL554 in 29 male and female chronic asthma patients conducted in Sweden and the United Kingdom. The testing dose levels of RPL554 ranged from 0.4 mg to 24 mg, a sixty-fold range. The primary objective of this trial was to establish the improvement in lung function, as measured by FEV_1, of RPL554 as compared to albuterol and placebo. The secondary objective of this study was to assess the safety and tolerability of RPL554.

In this trial, all doses of RPL554 showed a dose-dependent and statistically significant improvement in lung function, as measured by FEV_1, with a p-value of less than 0.001, as compared to placebo. The maximum improvement in lung function, as measured by FEV_1, of RPL554 observed in this trial was comparable to the maximum effect observed with a dose of 7.5 mg, or three times the recommended dose, of nebulized albuterol. In this trial, RPL554 was well tolerated and there were no serious adverse events or adverse events of concern at any dose. RPL554 treatment resulted in no gastrointestinal adverse events or cardiovascular events of concern. The figure below illustrates improvement in lung function, as measured by FEV_1, as compared to albuterol and placebo.

Improvement in Lung Function Over a Sixty-fold Dose Range in Asthma Patients



\+ p<0.001 vs. placebo

Phase 1 Clinical Trials

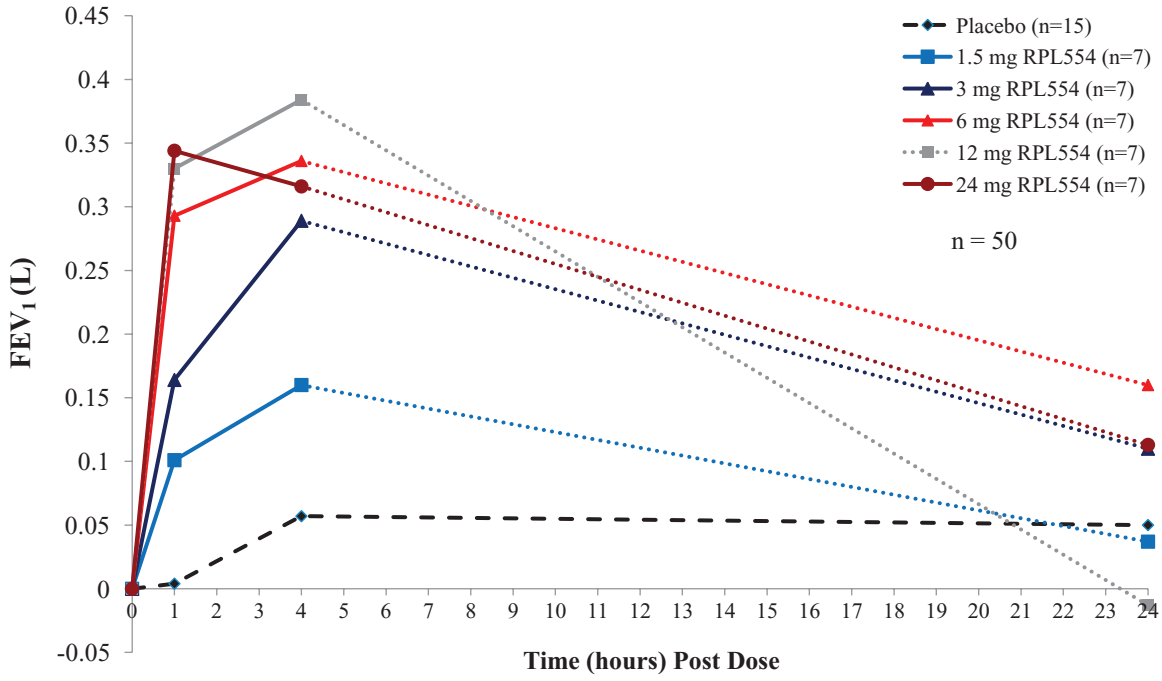
In September 2015, we completed a Phase 1 clinical trial that had three parts consisting of a single ascending dose, or SAD, trial in 50 healthy male subjects, a multiple ascending dose, or MAD, trial in 30 healthy male subjects and a MAD trial in 32 male and female patients with COPD. Doses in the SAD trial and the MAD trial with healthy subjects ranged from 6 mg to 24 mg, and doses in the MAD trial with COPD patients ranged from 1.5 mg to 12 mg. Each of the MAD trials continued for five and a half days with twice-daily dosing.

The primary objective of the SAD and MAD trials in healthy subjects was to assess the safety and tolerability of single and multiple doses of RPL554. The secondary objective of these trials was to measure the improvement in lung function, as measured by FEV_1, in healthy subjects receiving RPL554 as compared to placebo.

In the SAD and MAD trials in healthy subjects, RPL554 was well tolerated. In these trials, we also observed a longer residence time in the lung, lower peak plasma concentrations and a longer plasma half-life (10 to 12 hours) than our initial proof-of-concept formulation of RPL554, suggesting that twice-daily dosing is appropriate. The lung function testing in the SAD trial showed a dose-dependent improvement in lung

function, as measured by FEV_1, in these healthy individuals, despite none of them having asthma or COPD, as illustrated in the figure below.

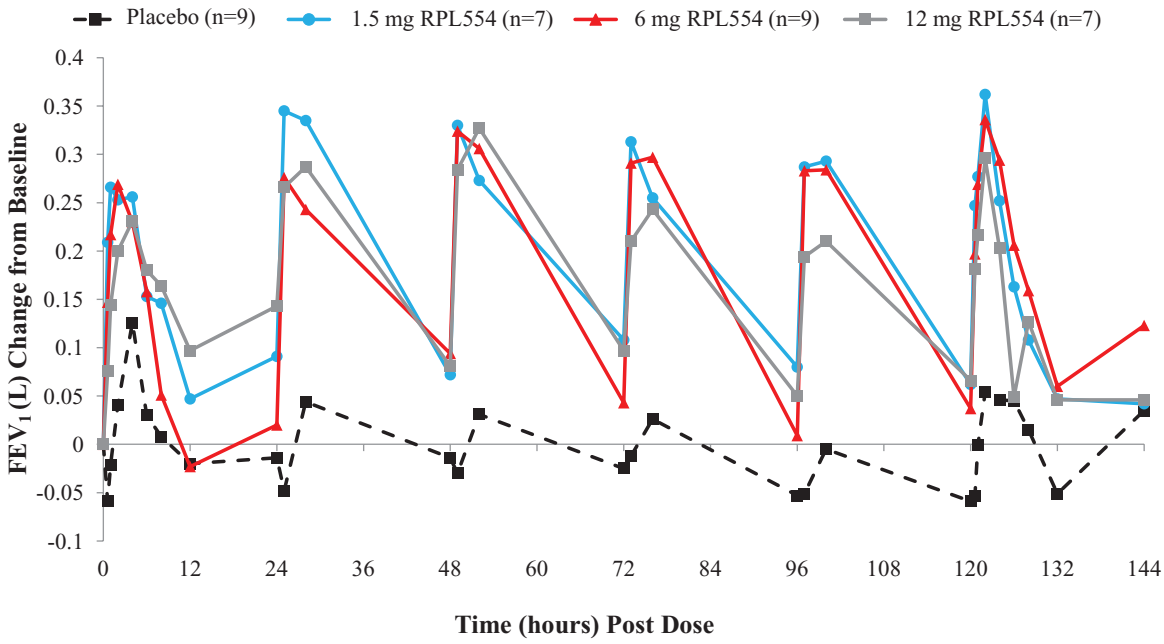
Improvement in Lung Function (FEV_1) in Healthy Subjects (SAD part)



Similarly, in the MAD trial in 30 healthy male subjects, RPL554 continued to show an increase in lung function compared to baseline on each day of the study, as measured by FEV_1, in these healthy individuals, despite none of them having asthma or COPD.

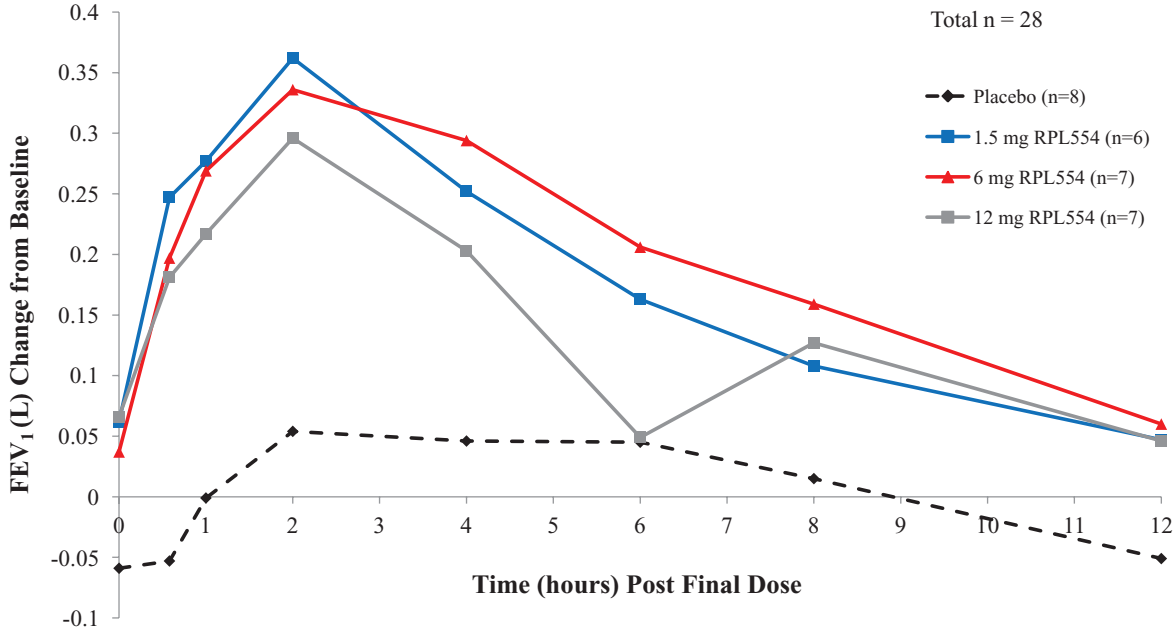
The primary objective of the third part of the trial, which was a MAD trial in 32 patients with moderate COPD, was to assess safety and tolerability and measure the PK profile of RPL554 in COPD patients receiving RPL554 as compared to placebo. The secondary objective was to assess the improvement in lung function, as measured by FEV_1, in these patients. In this clinical trial, RPL554 was well tolerated at all doses with no reports of serious adverse events or adverse events of concern. Specifically, we did not observe the gastrointestinal or other side effects associated with roflumilast, the only PDE4 inhibitor currently on the market approved for the treatment of COPD, and RPL554 was not observed to have any effect on cardiac function as measured by electrocardiograms, including QT intervals, and Holter monitoring, which uses a portable device that continuously measures and records the heart's activity for at least 24 hours. We also observed a statistically significant increase in lung function, as measured by FEV_1, with a p-value of less than 0.05, in patients receiving RPL554 in all dose groups as compared to placebo. The figure below illustrates a consistent increase in lung function compared to baseline with no evidence of reduction in effect level, as measured by FEV_1, on each day of the study.

Improvement in Lung Function (FEV_1) over Six Days of Dosing



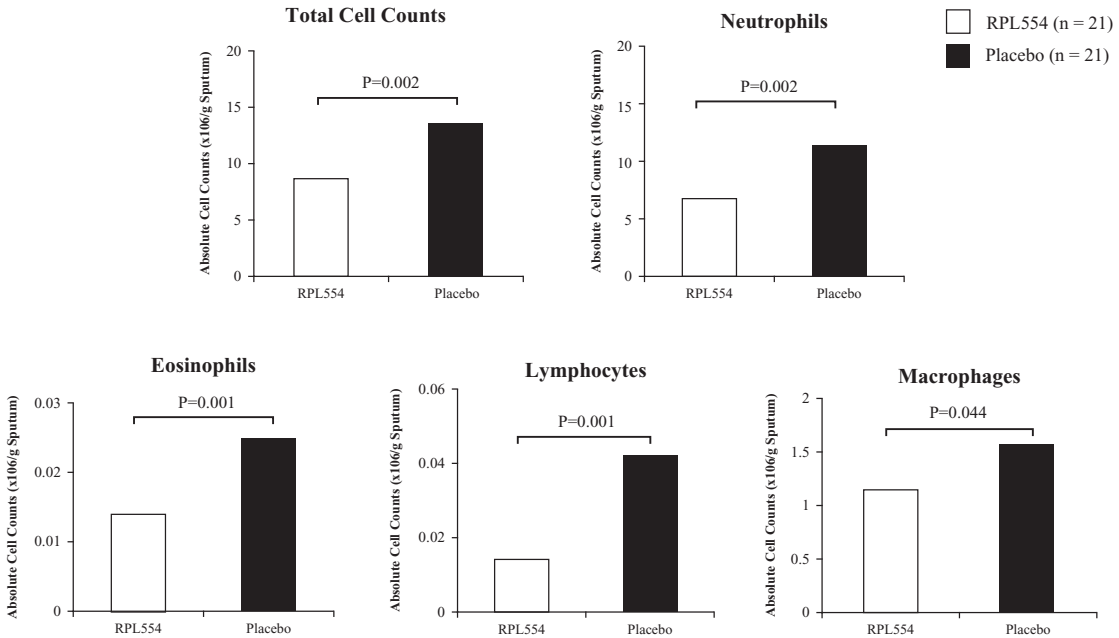
The figure below, which represents the effects of the final dose after five and a half days of treatment with RPL554, shows that patients with moderate COPD that were administered RPL554 experienced an improvement in lung function, as measured by FEV_1, and that the improvement peaked at two hours and continued through the 12-hour measurement period.

Improvement in Lung Function (FEV_1) over 12 Hours in COPD Patients



In May 2013, we completed a Phase 1 clinical trial in which 21 healthy evaluable subjects were treated with either our initial proof-of-concept formulation of RPL554 or placebo once daily for six days before airway challenge with aerosolized LPS. Subjects that were administered RPL554 had significantly lower absolute numbers of neutrophils in sputum collected six hours after LPS challenge, and a significant reduction in the absolute numbers of other inflammatory cells, including lymphocytes, macrophages and eosinophils, at the same time point. These observations suggest that RPL554 also has the potential to target the chronic inflammatory processes in COPD. The figure below illustrates the reduction in inflammatory cells observed in this trial as measured by absolute cell counts.

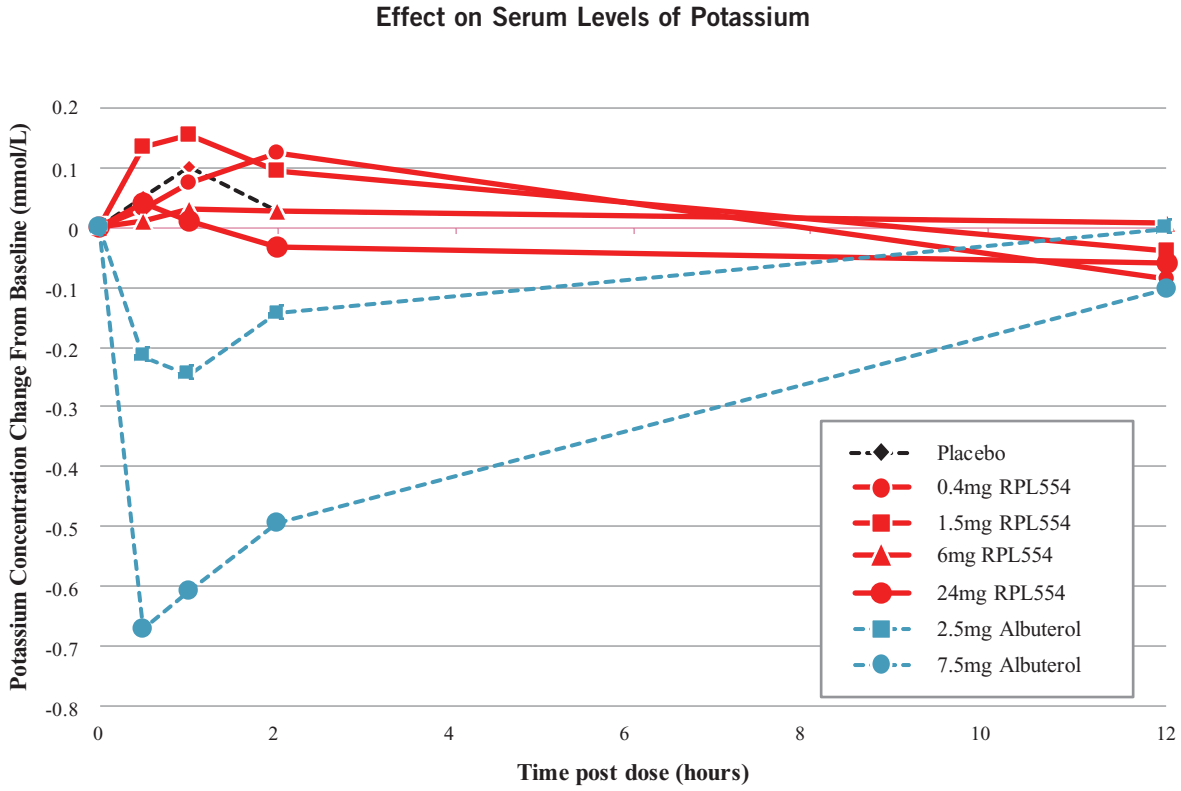
Reduction in Inflammatory Cells



Summary of Safety Results

RPL554 was well tolerated in each of our eight Phase 1 and 2a clinical trials at dose levels ranging from 0.4 mg to 24 mg. RPL554 was well tolerated both when administered alone and as an add-on therapy to commonly used bronchodilators. In our completed clinical trials, we did not observe any gastrointestinal adverse events or cardiovascular effects, other than a small increase in heart rate at the highest doses tested. RPL554 had no observed effect on cardiac function as measured by electrocardiograms, including QT intervals, a measure of time between certain waves in the heart's electrical cycle and measure of a potential cardiovascular adverse event. In addition, we did not observe an increase in incidence of any adverse event over commonly used bronchodilators when RPL554 was used alone. In these trials, some subjects experienced mild to moderate adverse reactions, including headache, dizziness, cough, heart palpitation, nausea, dry mouth, parenthesis (tingling), nasopharyngitis (throat irritation) and rash, which occurred with comparable frequency to placebo. No subjects had a serious adverse event.

The figure below illustrates the effects of RPL554 and albuterol on serum levels of potassium:



Clinical Development Plans

We plan to conduct several trials to support our plans to develop RPL554 in a nebulized formulation for the maintenance treatment of COPD and as an add-on therapy to short-acting bronchodilators and other commonly used therapies for the treatment of hospitalized patients with acute exacerbations of COPD. We also are developing RPL554 in both DPI and MDI formulations for the maintenance treatment of COPD. In addition, we may explore the development of RPL554 in these formulations for the treatment of asthma and other respiratory diseases.

- ***Maintenance treatment of COPD.*** We plan to commence a Phase 2b dose-ranging clinical trial for RPL554 for the maintenance treatment in approximately 400 patients with COPD in Europe in the second half of 2017. The Phase 2b clinical trial will be a four-week double-blind, placebo-controlled, parallel group trial. The primary endpoint is improvement in lung function, as measured by FEV_1, after dosing with RPL554 or placebo. We expect to report top-line data from the Phase 2b trial in the second half of 2018.

  We also plan to commence a Phase 2b dose-ranging clinical trial for RPL554 as an add-on therapy to a long-acting bronchodilator for maintenance treatment in approximately 400 patients with COPD in the second half of 2018. This Phase 2b clinical trial will be a 12-week double-blind, placebo-controlled trial. The primary endpoint is improvement in lung function, as measured by FEV_1, after dosing with RPL554 as an add-on treatment to tiotropium.

  We also plan to commence a single-dose PK trial of RPL554 in mid-2017 in approximately 12 healthy volunteers in the United States. The primary endpoint is to determine the amount of drug that is swallowed which makes it into systematic circulation, or oral bioavailability. We expect to report top-line data from the PK trial in the fourth quarter of 2017.

In February 2017, we commenced a Phase 2a clinical trial in the United Kingdom evaluating RPL554 in patients with COPD as an add-on therapy to tiotropium, an approved and widely used LAMA bronchodilator. Our Phase 2a clinical trial is a three day trial in approximately 30 COPD patients. In this trial, we plan to evaluate the improvement in lung function, as measured by FEV_1, and duration of effect of RPL554 or placebo as an add-on therapy to tiotropium. We expect to report top-line data from this trial in the fourth quarter of 2017. The data from these trials will also help inform the clinical development of RPL554 in the acute setting.

- ***Treatment of hospitalized patients with acute exacerbations of COPD.*** We plan to commence a Phase 2 clinical trial in the United States for RPL554 for the treatment of acute COPD patients requiring hospitalization in 2018. We plan to enroll approximately 150 patients in this Phase 2 clinical trial, which will be a double-blind, placebo-controlled, parallel group trial starting during the patients' hospitalization for COPD exacerbation and continuing for 30 days after discharge. RPL554 will be added to the standard-of-care treatment these patients receive. This trial will be designed to evaluate the efficacy and safety of RPL554 when administered for patients experiencing a COPD exacerbation requiring hospitalization.

The table below summarizes our planned clinical trial designs for RPL554 for the treatment of COPD.

Trial Description	Trial Design	Patient Population	Primary Endpoint	Secondary Endpoints	Anticipated Milestones
Phase 2a trial to determine efficacy and safety of RPL554 administered as add-on therapy to tiotropium for maintenance treatment of COPD	Double-blind, placebo-controlled, three-way cross-over, three-day trial Dosing: Two doses (twice-daily)	Approximately 30 stable COPD patients, age 40 - 75, with FEV_1 between 40% and 80% of predicted normal levels	■ FEV_1: peak and AUC over 12 hours	■ PK profile ■ Safety ■ Plethysmography measuring the volume of air in the lungs ■ Cardiovascular effects	Commenced in February 2017, with top-line data expected in the fourth quarter of 2017
Phase 1 PK trial to determine oral bioavailability of the compound	Dosing: Single dose	Approximately 12 healthy volunteers	■ Oral bioavailability	■ Tolerability ■ Safety	Planned commencement in mid-2017, with top-line data expected in the fourth quarter of 2017
Phase 2b trial to determine efficacy, safety and dose-response of RPL554 for maintenance treatment of COPD	Double-blind, placebo-controlled, parallel group, four-week trial Dosing: Four doses (twice-daily)	Approximately 400 COPD patients, age 40 - 75, with FEV_1 of 40% to 80% of predicted normal levels. All long-acting bronchodilators will be withheld	■ FEV_1: peak and AUC over 12 hours	■ FEV_1 24 hours after the previous dose, or FEV_1 trough ■ COPD daily symptoms ■ St George's Respiratory Questionnaire (SGRQ), a COPD health status score ■ Dyspnea scale ■ Safety	Planned commencement in the second half of 2017, with top-line data expected in the second half of 2018

Trial Description	Trial Design	Patient Population	Primary Endpoint	Secondary Endpoints	Anticipated Milestones
Phase 2b trial to determine efficacy, safety and dose-response of RPL554 administered as add-on therapy to a long-acting bronchodilator for maintenance treatment of COPD	Double-blind, placebo-controlled, 12-week trial Dosing: Two to three doses (twice-daily)	Approximately 400 COPD patients, age 40 - 75, with moderate to very severe COPD	■ FEV_1 24 hours after the previous dose, or FEV_1 trough ■ FEV_1: peak	■ FEV_1: AUC over 12 hours ■ COPD daily symptoms ■ St George's Respiratory Questionnaire (SGRQ), a COPD health status score ■ Dyspnea scale ■ Safety	Planned commencement in the second half of 2018
Phase 2 trial to determine efficacy and safety of RPL554 for acute COPD exacerbation requiring hospitalization	Double-blind, placebo-controlled, parallel group trial starting during hospitalization and continuing for 30 days after discharge Dosing: Two doses (twice-daily)	Approximately 150 patients, age 40 - 80	■ FEV_1: peak	■ COPD symptoms ■ Length of stay in hospital ■ 30-day hospital re-admission rate	Planned commencement in the second half of 2018

Additional Development Programs

In addition to our nebulized formulation of RPL554, we are developing RPL554 in both DPI and MDI formulations for the maintenance treatment of COPD. In addition, we may explore the development of RPL554 in these formulations for the treatment of asthma and other respiratory diseases. DPI and MDI inhaler devices are the most common forms of drug delivery in non-hospitalized patients with COPD and are well-suited for the maintenance therapy of COPD patients. We believe the development of DPI and MDI formulations has the potential to significantly increase the market opportunity for RPL554, if approved, for the maintenance treatment of COPD. Following the completion of our DPI and MDI formulation process, we plan to commence pre-clinical studies for RPL554 in these formulations in 2018.

RPL554 for the Treatment of Cystic Fibrosis

Overview

We plan to evaluate RPL554 for the treatment of CF. We believe RPL554, if approved, has the potential to be an important and novel treatment and standard of care for patients with CF based on its favorable properties observed to date.

CF Background

CF is the most common fatal inherited disease in the United States and Europe. CF causes impaired lung function and is commonly associated with repeat and persistent lung infections due to the inability to clear thickened mucus from the lung. This condition often results in frequent exacerbations and hospitalizations. There is no cure for CF and the median age of death for CF patients is 37 years. CF is considered a rare, or orphan, disease by both the FDA and the EMA. According to the Cystic Fibrosis Foundation, more than 30,000 people in the United States and more than 70,000 people worldwide are living with CF and approximately 1,000 new cases of CF are diagnosed each year. We plan to seek orphan drug designation for RPL554 in treating CF. CF patients require lifelong treatment with multiple daily medications, frequent hospitalizations and, ultimately, lung transplants in some end-stage patients. The quality of life for CF patients is compromised as a result of spending significant time on self-care every day and frequent

outpatient doctor visits and hospitalizations. CF patients take an average of seven medications daily. In the 12-month period ended June 30, 2016, global sales of drugs currently indicated for CF totaled $4.1 billion. The global market for CF drugs is expected to increase to $7.0 billion in 2020.

CF is caused by mutations in a gene that encodes the CFTR protein. The CFTR protein channel regulates the movement, or efflux, of specific ions such as chloride in and out of the cells of organs like the lungs, pancreas and gastrointestinal tract. Through regulation of these ions, the amount of salts in the fluid both inside and outside the cell remains balanced. In CF patients, however, the CFTR protein is defective and cannot perform its normal function of transporting ions across the cell membrane, resulting in an environment characterized by thick mucus in vital organs such as the lung, the pancreas and the gastrointestinal tract.

The lack of functional CFTR in CF patients is particularly problematic in the lungs, where the build-up of thick mucus obstructs parts of the lung, allows bacteria to grow unfettered and impairs the functionality of the local immune system. Of all the manifestations of CF, chronic pulmonary disease is the most critical and is characterized by a combination of airway obstruction, infection and inflammation such that more than 90% of all CF patients die of respiratory failure, and thus have a shortened life expectancy.

Current Treatment Landscape of CF

Until recently, approved therapies to treat CF patients have been designed to treat the symptoms of CF, by preventing and controlling infections that occur in the lungs, rather than address the underlying cause. Accordingly, antibiotics are frequently used along with mucus-thinning drugs. A significant portion of CF patients are prescribed bronchodilators, although no bronchodilator is currently approved by the FDA for the treatment of patients with CF. For patients with certain gene mutations, a new medication called ivacaftor, or Kalydeco, which is a CFTR potentiator, is used to improve CFTR function and thereby improve lung function. A combination drug consisting of ivacaftor and lumacaftor, or Orkambi, which is a CFTR corrector, can be used in a somewhat broader group of CF patients with partly different gene mutations. While not indicated specifically for CF, high doses of ibuprofen also have been studied in CF patients and have demonstrated some anti-inflammatory efficacy resulting in a beneficial effect on the annual rate of decline of FEV_1. However, CF patients commonly experience adverse events from ibuprofen, including gastrointestinal and liver side effects, and as a result it is infrequently used. However, it demonstrates that an anti-inflammatory medication in CF might change the course of the disease. There is currently no anti-inflammatory medication which is approved to treat the underlying inflammation in CF.

Despite the recent approval of the two novel targeted therapies, Kalydeco and Orkambi, for patients with CF, only a subset of CF patients is indicated for treatment with these two therapies. As a result, we believe CF remains a significant unmet medical need. If we obtain orphan drug designation and FDA approval for this indication, RPL554 may be entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for this indication for a period of seven years, except in limited circumstances.

Our Solution

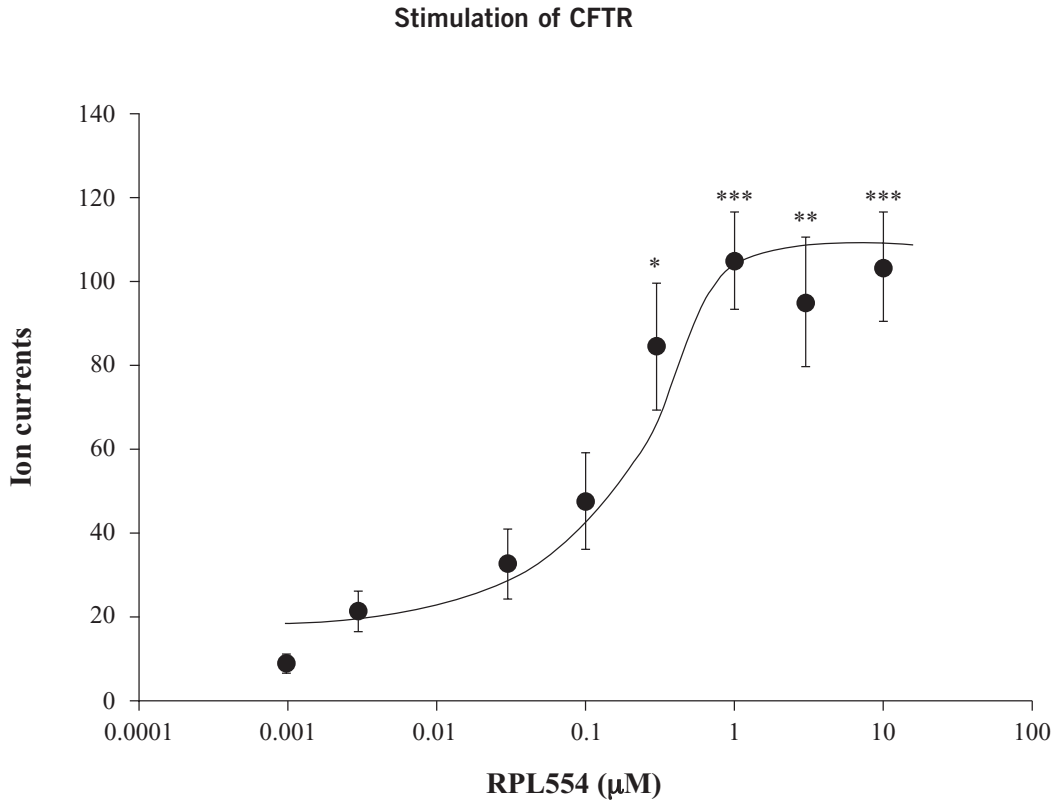
By inhibiting PDE3 and PDE4, RPL554 increases the levels of cAMP and CGMP, resulting in bronchodilator and anti-inflammatory effects, and stimulates the CFTR. CFTR stimulation leads to improved electrolyte balance in the lung and thinning of the mucus, which facilitates mucociliary clearance and leads to improved lung function and potentially a reduction in lung infections. Dual inhibition of PDE3 and PDE4 has been observed to be more effective than inhibition of either PDE alone at relaxing airway smooth muscle cells and suppressing the activation and functions of pro-inflammatory cells residing in the lung, both of which are commonly understood to play a significant role in CF.

In our pre-clinical studies, RPL554 has been observed to stimulate the CFTR, as well as increase ciliary beat frequency, a key parameter determining the rate of mucus clearance, in primary airway cells and to

improve electrolyte balance in the lung. Based on available data, we believe that RPL554 has the potential to inhibit deleterious inflammation, reduce airway obstruction through bronchodilation and enhance mucociliary clearance through stimulation of the CFTR on airway epithelial cells, thereby making it an attractive therapy for the treatment of CF.

Pre-clinical Studies

In a series of pre-clinical studies we conducted, RPL554 was observed to stimulate the CFTR. As shown in the figure below, administration of increasing concentrations of RPL554 resulted in improvement in CFTR function, as measured by ion currents in a human bronchial-epithelial cell line.

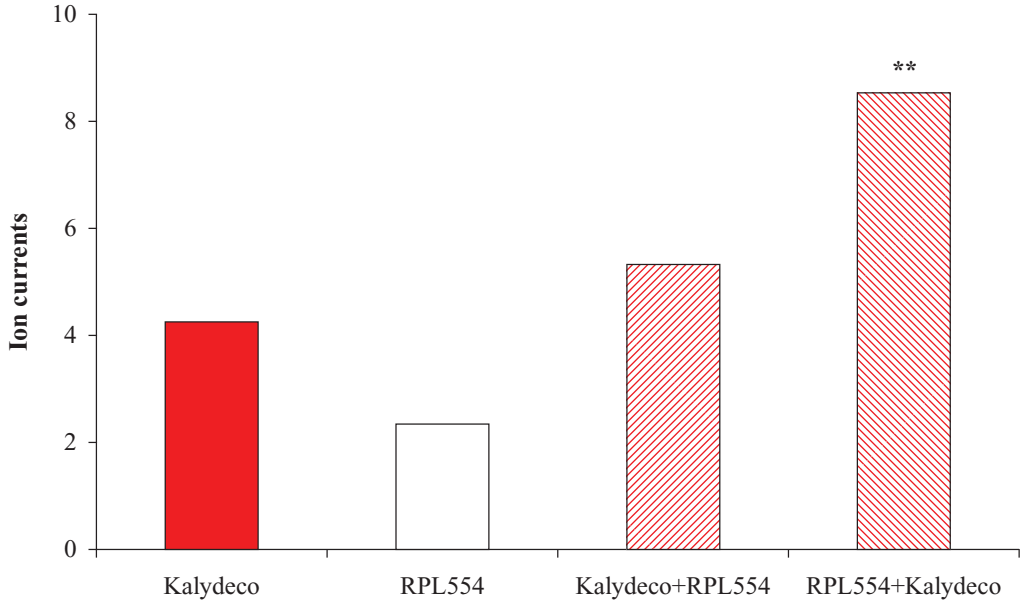


* p<0.05
** p<0.01
*** p<0.001

Furthermore, in a pre-clinical study comparing RPL554 to Kalydeco, both compounds increased CFTR activity in cells from a CF patient with the mutation that is appropriate for treatment with Kalydeco. When RPL554 was administered before Kalydeco, it had an additive effect, which was smaller when the

compounds were delivered in the reverse order. This stimulatory effect on the CFTR, as measured by ion currents, is shown in the figure below.

Stimulation of CFTR

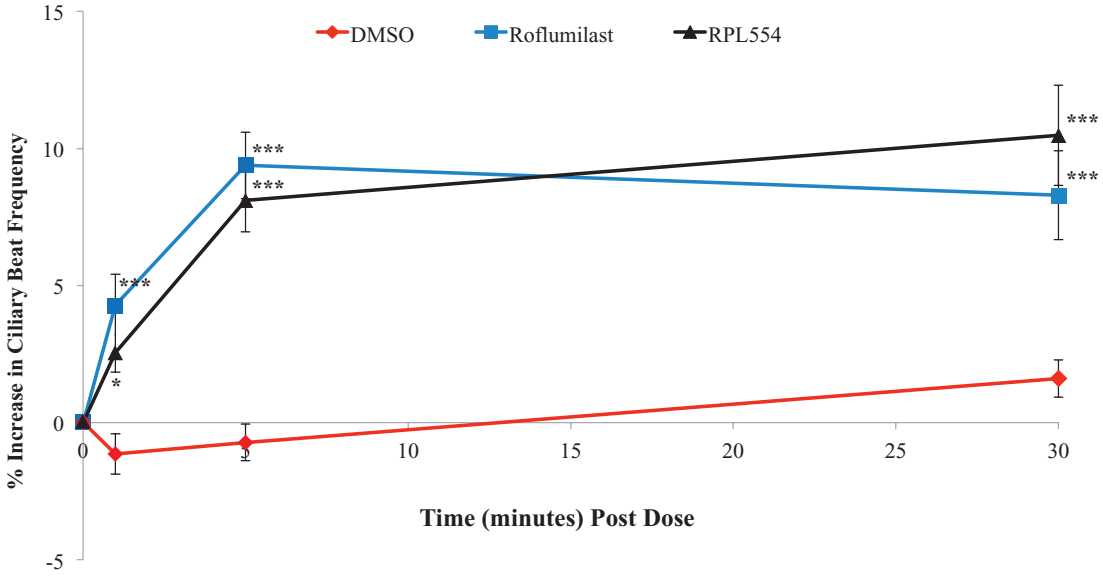


** $p<0.01$ vs. Kalydeco alone

In addition, in a pre-clinical study RPL554 was observed to increase ciliary beat frequency in primary human airway cells at similar levels to the PDE4 inhibitor, roflumilast. We believe RPL554 may increase

ciliary beat frequency and therefore promote mucociliary clearance in CF patients. This is illustrated in the figure below.

Increased Ciliary Beat Frequency



* p<0.05 vs. DMSO (control) measured 1, 5 and 30 mins post dose
*** p<0.001 vs. DMSO (control) measured 1, 5 and 30 minutes post dose

We believe this pre-clinical data, combined with the anti-inflammatory and bronchodilator effects of RPL554, suggest that RPL554 is appropriate for clinical trials for, and may prove effective in the treatment of, CF patients.

Clinical Development Plans

In March 2017, we commenced a Phase 2a single-dose trial in the United Kingdom evaluating RPL554 in up to ten CF patients in the United Kingdom. This trial is evaluating the PK and PD profile and tolerability of RPL554 in patients with CF, as well as the effect on lung function. We expect to report top-line data from this trial in the first half of 2018. The results of this trial are expected to support dose selection for a proof-of-concept Phase 2b trial in Europe in approximately 100 patients with CF, which we plan to commence in 2018.

The table below summarizes our planned clinical trials for RPL554 for the treatment of CF.

Trial Description	Trial Design	Patient Population	Primary Endpoints	Secondary Endpoints	Anticipated Milestones
Phase 2a PK and PD trial to evaluate tolerability in CF patients and examine effect on lung function and inflammatory biomarkers	Double-blind, placebo-controlled, cross-over trial Dosing: Single dose	Up to 10 CF patients, age 18 years and older, with FEV_1 between 40% and 80% of predicted normal levels	■ PK profile ■ Safety	■ FEV_1: peak and AUC	Commenced in March 2017, with top-line data expected in the first half of 2018
Phase 2b proof-of-concept trial to determine the efficacy and safety of RPL554 in CF patients	Double-blind, placebo-controlled, three way, parallel group trial Dosing: Multiple dose (twice-daily)	Approximately 100 CF patients, age 18 and older, with FEV_1 between 40% and 90% of predicted normal levels All CFTR mutations	■ FEV_1: peak	■ FEV_1 trough ■ Inflammation biomarkers ■ Exacerbations ■ Safety	Planned commencement in 2018

Vernalis Agreement

In February 2005, Rhinopharma Limited, or Rhinopharma, entered into an assignment and license agreement with Vernalis Development Limited, or Vernalis, which we refer to as the Vernalis Agreement. In 2006, we acquired Rhinopharma and all of its rights and obligations under the Vernalis Agreement. Pursuant to the Vernalis Agreement, Vernalis assigned to us all of its rights to certain patents and patent applications relating to RPL554 and related compounds, or the Vernalis Patents. We cannot further assign the Vernalis Patents to a third party without Vernalis' prior consent. Vernalis also granted to us an exclusive, worldwide, royalty-bearing license under certain Vernalis know-how to develop, manufacture and commercialize products, or the Licensed Products, based on PDE inhibitors developed using Vernalis Patents, Vernalis know-how and the physical stock of certain compounds, including RPL554, which we refer to as the Program IP, in the treatment of human or animal allergic or inflammatory disorders. Pursuant to the Vernalis Agreement, we must maintain the Vernalis Patents and use commercially reasonable and diligent efforts to develop and commercialize the Licensed Products.

Under the Vernalis Agreement, we are obligated to pay Vernalis 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 Vernalis Patents or Vernalis know-how, excluding royalties. We must also pay Vernalis, on a Licensed Product-by-Licensed Product and country-by-country basis, a low to mid-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 Vernalis 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 Vernalis Agreement continues until terminated by either party in accordance with its terms. Either party may terminate the Vernalis Agreement for an uncured material breach, bankruptcy or insolvency of the other party. We may terminate the Vernalis Agreement upon 90 days' prior written notice. Vernalis may terminate

the Vernalis Agreement if we notify Vernalis of our intention to abandon any Vernalis Patents or allow any Vernalis Patents to lapse. Upon termination of the Vernalis Agreement, we must cease use of any Program IP and assign the Vernalis Patents and any improvements thereto back to Vernalis.

Manufacturing

We have no experience in product candidate formulation or manufacturing. We rely on, and expect to continue to rely, on third-party contract manufacturing organizations, or CMOs, for the supply of current good manufacturing practices specified by the FDA, or cGMP, clinical trial materials of RPL554 and any future product candidates, as well as for commercial quantities of RPL554 and any future product candidates, if approved. We currently do not have any agreements for the commercial production of raw materials. While we may contract with other CMOs in the future, we currently contract with only one pharmaceuticals CMO for the manufacture of RPL554 drug substance. For RPL554 drug product in our nebulized formulation, we currently have two CMOs. We believe that the RPL554 manufacturing process can be transferred to a number of other CMOs for the production of clinical and commercial supplies of RPL554 in the ordinary course of business.

Manufacturing of any product candidate is subject to extensive regulations that impose various procedural and documentation requirements governing recordkeeping, manufacturing processes and controls, personnel, quality control and quality assurance, among others. We expect that all of our CMOs will manufacture RPL554 under cGMP conditions. cGMP is a regulatory standard for the production of pharmaceuticals to be used in humans.

Commercialization, Sales and Marketing

We have not yet defined our sales, marketing or commercialization strategy for RPL554. Our commercial strategy may include the use of strategic collaborators, distributors, a contract sales force, or the establishment of our own commercial and specialty sales force. We plan to further evaluate these alternatives as we continue the clinical development of RPL554.

Competition

We consider RPL554's current closest potential competitors in the nebulized maintenance treatment of COPD in the U.S. market to be Brovana, a long-acting beta2-agonist bronchodilator marketed by Sunovion, and Perforomist, a long-acting beta2-agonist bronchodilator marketed by Mylan. Neither drug, however, provides an anti-inflammatory effect. We consider RPL554's current closest potential competitors in the DPI/MDI maintenance treatment of COPD to be Symbicort, a combination of a long-acting beta2-agonist bronchodilator and inhaled corticosteroid marketed by AstraZeneca, Spiriva, a long-acting anti-muscarinic bronchodilator marketed by Boehringer Ingelheim, Advair, a combination of a long-acting beta2-agonist bronchodilator and inhaled corticosteroid marketed by GlaxoSmithKline, Utibron Neohaler, a combination of a long-acting beta2-agonist and long-acting anti-muscarinic bronchodilator marketed by Novartis, Breo, a combination of a long-acting beta2-agonist bronchodilator and inhaled corticosteroid marketed by GlaxoSmithKline, and Anoro, a combination of a long-acting beta2-agonist bronchodilator and long-acting anti-muscarinic bronchodilator marketed by GlaxoSmithKline.

We compete directly with biotechnology and pharmaceutical companies that focus on the treatment of respiratory diseases. We also face competition from academic research institutions, governmental agencies and other various public and private research institutions. We expect to face increasingly intense competition as new technologies become available. Any product candidates, including RPL554, that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Many of our competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources than we do. Mergers and acquisitions in the pharmaceutical and

biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining top qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

The key competitive factors affecting the success of RPL554, if approved, are likely to be its efficacy, safety, dosing convenience, price, the effectiveness of companion diagnostics in guiding the use of related therapeutics, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Our commercial opportunity could be reduced or eliminated if 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 effects than any products that we may develop. Our competitors may also obtain FDA, EMA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Even if RPL554 achieves marketing approval, it may be priced at a significant premium over competitive products if any have been approved by then.

Intellectual Property

We strive to protect and enhance the proprietary technologies, inventions and improvements that we believe are important to our business, including seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties. Our policy is to seek to protect our proprietary position by, among other methods, pursuing and obtaining patent protection in the United States and in jurisdictions outside of the United States 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 March 31, 2017, our patent portfolio consisted of five issued U.S. patents, four pending U.S. patent applications, 16 issued foreign patents and 49 pending foreign applications including two patent applications made under the PCT. These patents and patent applications include claims directed to RPL554 composition of matter, new dosage formulations and a crystalline polymorph, as well as methods of making and using RPL554 in the treatment of respiratory diseases, with expected expiry dates not earlier than between 2020 and 2037.

The patent portfolio relating to RPL554 includes eight patent families:

- The first of these patent families relates to RPL554 per se. As of March 31, 2017, this patent family includes granted patents in Australia, Brazil, Canada, China, Europe, Japan, Mexico as well as four granted patents in the United States. We expect patents in this family to expire in March 2020.
- The second of these patent families relates to a crystalline polymorph of RPL554. As of March 31, 2017, this patent family included granted patents in Australia, China, Europe, Indonesia, Japan, Malaysia, Mexico, Russia, the United States and Taiwan and patent applications in Canada, Israel, Japan, South Korea, Philippines, Thailand and the Gulf Cooperation Council. We expect patents in this family to expire in August 2031.
- The third of these patent families relates to the combination of RPL554 with a beta-adrenergic receptor agonist. As of March 31, 2017, this patent family included patent applications in Canada, Europe and the United States. We expect patents in this family to expire in March 2034.
- The fourth of these patent families relates to the combination of RPL554 with an M3-muscarinic receptor antagonist. As of March 31, 2017, this patent family included patent applications in Australia, Canada, China, Europe, Israel, India, Japan, South Korea, Mexico, Russia, Thailand and the United States. We expect patents in this family to expire in March 2034.
- The fifth of these patent families relates to certain specific salts of RPL554. As of March 31, 2017, this patent family included a pending PCT application designating all contracting states. We expect patents in this family to expire in February 2036.

- The sixth of these patent families relates to use of RPL554 to treat certain diseases associated with the function of CFTR (including CF). As of March 31, 2017, this patent family included patent applications in Australia, Canada, Europe, Israel, Mexico, Russia, the United States and South Africa. We expect patents in this family to expire in May 2035.
- The seventh of these patent families relates to an inhalable formulation of RPL554. As of March 31, 2017, this patent family included patent applications in Australia, Brazil, Canada, China, Europe Indonesia, Israel, India, Japan, South Korea, Mexico, Malaysia, New Zealand, the Philippines, Singapore, South Africa, Thailand, and the United States. We expect patents in this family to expire in September 2035.
- The eighth of these patent families relates to a new compound related to RPL554 and to processes useful for the production of RPL554 and related compounds. As of March 31, 2017, this patent family included an unpublished Great Britain priority application. We expect patents in this family to expire in July 2037.

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 "Risk Factors — Risks Related to Intellectual Property and Information Technology."

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 drug 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.

U.S. Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or 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 approve pending NDAs, 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 pre-clinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an investigational new drug application, or IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, 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, or GCP, requirements to establish the safety and efficacy of the proposed drug product for each indication;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- 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, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and
- FDA review and approval of the NDA.

Pre-clinical Studies

Pre-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 pre-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. Some pre-clinical testing may continue even after the IND is submitted. 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 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. 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 sequential phases, which may overlap or be combined:

- Phase 1: The drug 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 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 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.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Special Protocol Assessment

The special protocol assessment, or SPA, process is designed to facilitate the FDA's review and approval of drugs by allowing the FDA to evaluate issues related to the adequacy of certain clinical trials, including Phase 3 clinical trials that are intended to form the primary basis for a drug product's efficacy claim in an NDA. Upon specific request by a clinical trial sponsor, the FDA will evaluate the protocol and respond to a sponsor's questions regarding, among other things, primary efficacy endpoints, trial conduct and data analysis, within 45 days of receipt of the request.

The FDA ultimately assesses whether the protocol design and planned analysis of the trial are acceptable to support regulatory approval of the product candidate with respect to effectiveness of the indication studied. All agreements and disagreements between the FDA and the sponsor regarding an SPA must be clearly documented in an SPA letter or the minutes of a meeting between the sponsor and the FDA.

Even if the FDA agrees to the design, execution and analyses proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its agreement under the following circumstances:

- public health concerns emerge that were unrecognized at the time of the protocol assessment;
- the director of the review division determines that a substantial scientific issue essential to determining safety or efficacy has been identified after testing has begun;

- a sponsor fails to follow a protocol that was agreed upon with the FDA; or
- the relevant data, assumptions, or information provided by the sponsor in a request for SPA change, are found to be false statements or misstatements, or are found to omit relevant facts.

A documented SPA may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if FDA and the sponsor agree in writing to modify the protocol and such modification is intended to improve the study.

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. Under the Prescription Drug User Fee Act, or PDUFA, 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.

In addition, under the Pediatric Research Equity Act of 2003, or PREA, as amended and reauthorized, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements.

The FDA may also require submission of a risk evaluation and mitigation strategy, or REMS, plan to ensure that the benefits of the drug outweigh its risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

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.

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.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

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 and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

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.

Foreign Government Regulation

To the extent that any of our product candidates, once approved, are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals.

In order to market our future products in the EEA (which is comprised of the 28 Member States of the EU plus Norway, Iceland and Liechtenstein) and many other foreign jurisdictions, we must obtain separate regulatory approvals. More concretely, in the EEA, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations:

- the Community 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 of the European Medicines Agency, or EMA, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products and medicinal products indicated for the treatment of 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; 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 above described procedures, before granting 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.

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 marketing authorization. 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 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, marketing authorization applications for new medicinal products not authorized have to include the results of studies conducted in the pediatric population, in compliance with a pediatric investigation plan, or PIP, agreed with the EMA's Pediatric Committee, or PDCO. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization 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. Once the marketing authorization 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 protection certificate extension. For orphan-designated medicinal products, the 10-year period of market exclusivity is extended to 12 years.

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.

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.

Additionally, the intent standard under the U.S. federal Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, to a stricter standard 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, the ACA codified case law that a claim including items or services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. 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 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. 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 civil monetary penalties of up to an aggregate of $150,000 per year and up to an aggregate of $1 million per year 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, or HITECH, and their respective implementing regulations, including the Final HIPAA Omnibus Rule published on January 25, 2013, impose specified requirements relating to the privacy, security and transmission of individually identifiable health information held by covered entities and their business associates. Among other things, HITECH made HIPAA's security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. 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. 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. 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 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; subjected drug manufacturers to new annual fees based on pharmaceutical companies' share of sales to federal healthcare programs; created a new Patient Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; creation of the Independent Payment Advisory Board, once empaneled, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs; and establishment of a Center for Medicare Innovation at the CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending. 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. For example, in January 2017, the U.S. House of Representatives and Senate passed legislation, which, if signed into law, would repeal certain aspects of the ACA. In addition, Congress could consider subsequent legislation to replace those elements of the ACA if so repealed.

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. 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 by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This 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 2025 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 bills 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 once approved or additional pricing pressures.

Employees

As of March 31, 2017, we had 12 employees. None of our employees is subject to a collective bargaining agreement or represented by a trade or labor union.

Facilities

Our principal office is located at 3 More London Riverside, London SE1 2RE, United Kingdom, where we lease office space. We lease a portion of this office space under two leases that terminate on November 30, 2017 and the remainder of the office space under a lease that terminates on December 31, 2017. We also lease office space in White Plains, New York. We intend to add new facilities as we add employees, and we believe that suitable additional or substitute space will be available as needed to accommodate any such expansion of our operations.

Legal Proceedings

We are not subject to any material legal proceedings.

Executive Officers and Directors

The following table presents information about our executive officers and directors, including their ages as of the date of this prospectus:

Name	Age	Position
Executive Officers		
Jan-Anders Karlsson, Ph.D.	62	Chief Executive Officer and Director
Piers Morgan	50	Chief Financial Officer
Kenneth Newman, M.D.	59	Chief Medical Officer
Peter Spargo, Ph.D.	55	Senior Vice President, Chemistry Manufacturing and Controls
Claire Poll	50	Legal Counsel
Richard Hennings	47	Commercial Director
Non-Executive Directors		
David Ebsworth, Ph.D.(1)(2)(3)	62	Chairman of the Board
Ken Cunningham, M.D.(2)	64	Director
Rishi Gupta(2)	39	Director
Mahendra Shah, Ph.D.(3)	72	Director
Andrew Sinclair, Ph.D.(1)	45	Director
Vikas Sinha(1)	53	Director
Anders Ullman, M.D., Ph.D.(3)	61	Director

(1) Audit Committee member

(2) Remuneration Committee member

(3) Governance Committee member

The current business addresses for our executive officers and board of directors is c/o Verona Pharma plc, 3 More London Riverside, London SE1 2RE, the United Kingdom.

The following are brief biographies of our executive officers and directors:

Jan-Anders Karlsson, Ph.D. Dr. Karlsson has served as our Chief Executive Officer and on our board of directors since June 2012. From January 2005 to May 2012, Dr. Karlsson was the Chief Executive Officer of S*BIO Pte Ltd, a biotechnology company in Singapore. Previously to S*BIO, Dr. Karlsson was Executive Vice President and head of Pharma Global Research at Bayer HealthCare AG in Germany. Dr. Karlsson received an M.Sc. in pharmacy from Uppsala University and a Doctor of Medical Science (Ph.D.) in clinical experimental pharmacology from the University of Lund.

Piers Morgan. Mr. Morgan has served as our Chief Financial Officer since September 2016. From November 2015 to September 2016, Mr. Morgan was an independent consultant. From May 2014 to November 2015, Mr. Morgan was the Chief Executive Officer of C4X Discovery plc, a biotechnology company. Prior to C4X, Mr. Morgan co-founded uniQure N.V., a biotechnology company, in Amsterdam, where he served as Chief Financial Officer from December 2009 to May 2014. Mr. Morgan is a member of the Institute of Chartered Accountants in England and Wales and received an M.A. in law and management studies from the University of Cambridge.

Kenneth Newman, M.D. Dr. Newman has served as our Chief Medical Officer since January 2015. From December 2013 to December 2014, Dr. Newman was Chief Development Officer at Mesoblast Inc., a

biotechnology company. From 2010 to November 2013, Dr. Newman was Chief Medical Officer of Acton Pharmaceuticals, Inc., a specialty respiratory pharmaceutical company, which was acquired by Meda Pharmaceuticals, Inc. Dr. Newman received an M.D. from the University of Texas Health Science Center at Houston and an M.B.A. in management from the University of Cincinnati College of Business.

Peter Spargo, ***Ph.D.*** Dr. Spargo has served as our Senior Vice President, Chemistry Manufacturing and Controls since May 2014. From January to October 2015, Dr. Spargo also served as Senior Vice President, CMC at Spinifex Pharmaceuticals Inc., a biotechnology company, that was acquired by Novartis International AG. From 2011 to 2013, Dr. Spargo was Senior Vice President, CMC at Creabilis SA, a pharmaceutical company. Dr. Spargo received an M.A. in natural sciences and a Ph.D. in synthetic organic chemistry from Cambridge University.

Claire Poll. Ms. Poll has served as Legal Counsel since September 2016. From September 2015 to August 2016, Ms. Poll served as an advisor to us on legal, general corporate and financing matters. She also served as an Executive Director on our board of directors from September 2006 until September 2015. Ms. Poll received a Bachelor of Laws from the University of Western Australia and a Diploma in Applied Finance and Investment from the Securities Institute of Australia.

Richard Hennings. Mr. Hennings has served as our Commercial Director since March 2017. From May 2016 to March 2017, Mr. Hennings was the Global Marketing Director for AstraZeneca UK Limited, a biopharmaceutical company. Since July 2015, Mr. Hennings has been a director of Hennings Consulting Ltd., where he consults with healthcare organizations on commercial strategy. From January 2012 to June 2015, Mr. Hennings held various positions at Gilead Sciences, Inc., a biopharmaceutical company, most recently as Commercial Director — EMEA Planning & Operations. Mr. Hennings received a bachelor's degree in applied chemistry from the University of Portsmouth.

David Ebsworth, Ph.D. Dr. Ebsworth has served as the Non-Executive Chairman of our board of directors since December 2014. From October 2009 to August 2014, Dr. Ebsworth served as Chief Executive Officer of Vifor Pharma, based in Zürich, the specialty pharma division of Galenica AG Group, a pharmaceutical wholesaler and retailer, and as a member of Galenica's Executive Committee. In 2012, Dr. Ebsworth was also named as Chief Executive Officer of Galenica and as Chairman of Galenica's Executive Committee, positions he held until August 2014. Dr. Ebsworth received a Ph.D. in industrial relations from the University of Surrey.

Ken Cunningham, M.D. Dr. Cunningham has served as a Non-Executive Director on our board of directors since September 2015. Dr. Cunningham serves as the non-executive chairman of the board of directors of Abzena plc and non-executive member of the board of directors of Xention Pharma Ltd. Dr. Cunningham received an M.D. from St. Mary's, Imperial College, London University.

Rishi Gupta. Mr. Gupta has served as a Non-Executive Director on our board of directors since July 2016. Since 2002, Mr. Gupta has held various positions at OrbiMed Advisors LLC, a global healthcare investment firm, where he is currently a Private Equity Partner. Mr. Gupta currently is a member of the board of directors of Symbiomix Therapeutics, LLC, Dimension Therapeutics, Inc., Avitide, Inc. and Turnstone Biologics Inc. Mr. Gupta received an A.B. in biochemical sciences from Harvard College and a J.D. from the Yale Law School.

Mahendra Shah, Ph.D. Dr. Shah has served as a Non-Executive Director on our board of directors since July 2016. Since March 2010, Dr. Shah has served as a Managing Director of Vivo Capital, a healthcare investment firm. Dr. Shah is also the founder and Executive Chair of Semnur Pharmaceuticals, Inc., a specialty pharmaceutical company. Dr. Shah serves as a member of the board of directors of Fortis Inc., Crinetics Pharmaceuticals, Inc., Essentialis Therapeutics LLC, and Impel Neuropharma, Inc. In addition, Dr. Shah serves on the board of directors of private companies in the biopharmaceutical and biotechnology

industries. Dr. Shah received his Ph.D. in industrial pharmacy from St. John's University and a Master's Degree in Pharmacy from L.M. College of Pharmacy in Gujarat, India.

Andrew Sinclair, Ph.D. Dr. Sinclair has served as a Non-Executive Director on our board of directors since July 2016. Since 2008, Dr. Sinclair has held various positions at Abingworth LLP, a life sciences investment group, where he is currently a Partner and Portfolio Manager. Dr. Sinclair is a member of the Institute of Chartered Accountants in England and Wales and received a Ph.D. in chemistry and genetic engineering at the BBSRC Institute of Plant Science, Norwich, and a B.Sc. in microbiology from King's College London.

Vikas Sinha. Mr. Sinha has served as a Non-Executive Director on our board of directors since September 2016. From 2005 to 2016, Mr. Sinha has served as the Chief Financial Officer of Alexion Pharmaceuticals, Inc., a biotechnology company. Mr. Sinha holds a master's degree in business administration from the Asian Institute of Management. He is also a qualified chartered accountant from the Institute of Chartered Accountants of India and a Certified Public Accountant in the United States.

Anders Ullman, M.D., Ph.D. Dr. Ullman has served as a Non-Executive Director on our board of directors since September 2015. From 2013 to 2014, Dr. Ullman was the Executive Vice President and Head of Research and Development in the BioScience business unit of Baxter International Inc., a healthcare company, which became Baxalta Inc. From 2007 to 2013, Dr. Ullman was Executive Vice President, Head of Research and Development at Nycomed Pharma Private Limited, which was acquired by Takeda Pharmaceutical Company Limited. Dr. Ullman received an M.D. and a Ph.D. in clinical pharmacology from the University of Gothenburg.

Foreign Private Issuer Exemption

As a "foreign private issuer," as defined by the SEC, we are permitted to follow home country corporate governance practices, instead of certain corporate governance practices required by NASDAQ for domestic issuers. While we voluntarily follow most NASDAQ corporate governance rules, we intend to follow U.K. corporate governance practices in lieu of NASDAQ corporate governance rules as follows:

- We do not intend to follow NASDAQ Rule 5620(c) regarding quorum requirements applicable to meetings of shareholders. Such quorum requirements are not required under English law. In accordance with generally accepted business practice, our articles of association provide alternative quorum requirements that are generally applicable to meetings of shareholders.
- We do not intend to follow NASDAQ Rule 5605(b)(2), which requires that independent directors regularly meet in executive session, where only independent directors are present. Our independent directors may choose to meet in executive session at their discretion.

Although we may rely on certain home country corporate governance practices, we must comply with NASDAQ's Notification of Noncompliance requirement (Rule 5625) and the Voting Rights requirement (Rule 5640). Further, we must have an audit committee that satisfies Rule 5605(c)(3), which addresses audit committee responsibilities and authority, and consists of committee members that meet the independence requirements of Rule 5605(c)(2)(A)(ii).

We intend to take all actions necessary for us to maintain compliance as a foreign private issuer under the applicable corporate governance requirements of the Sarbanes-Oxley Act of 2002, the rules adopted by the SEC and NASDAQ's listing standards.

Because we are a foreign private issuer, our directors and senior management are not subject to short-swing profit and insider trading reporting obligations under Section 16 of the Exchange Act. They will, however, be subject to the obligations to report changes in share ownership under Section 13 of the Exchange Act and related SEC rules.

Composition of our Board of Directors

Our board of directors currently consists of eight members. Our board of directors has determined that seven of our eight directors, Ken Cunningham, M.D., David Ebsworth, Ph.D., Rishi Gupta, Mahendra Shah, Ph.D., Andrew Sinclair, Ph.D., Vikas Sinha and Anders Ullman, M.D., Ph.D., do not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of director and that each of these directors is "independent" as that term is defined under the rules of NASDAQ. There are no family relationships among any of our directors or executive officers.

In accordance with our Articles of Association, one-third of our directors retire from office at every annual general meeting of shareholders. Retiring directors are eligible for re-election and, if no other director is elected to fill his or her position and the director is willing, shall be re-elected by default. See "Description of Share Capital and Articles of Association — Articles of Association — Directors — Rotation of Directors."

We have relationship agreements with entities affiliated with each of Mr. Gupta and Drs. Shah and Sinclair, pursuant to which each such individual has been designated as a member of our board of directors. The relationship agreements will continue in effect after the global offering. See "Related Party Transactions — Relationship Agreements" for a description of these agreements.

Committees of our Board of Directors

Our board of directors has three standing committees: an Audit Committee, a Remuneration Committee and a Governance Committee.

Audit Committee of the Board

The audit committee, which consists of David Ebsworth, Ph.D., Andrew Sinclair, Ph.D. and Vikas Sinha, assists the board in overseeing our accounting and financial reporting processes and the audits of our financial statements. Mr. Sinha serves as Chairman of the committee. The audit committee consists exclusively of members of our board who are financially literate, and Mr. Sinha and Drs. Ebsworth and Sinclair are each considered an "audit committee financial expert" as defined by applicable SEC rules and has the requisite financial sophistication as defined under the applicable NASDAQ rules and regulations. Our board has determined that all of the members of the audit committee satisfy the "independence" requirements set forth in Rule 10A-3 under the Exchange Act. The audit committee will be governed by a charter that complies with NASDAQ rules.

The audit committee's responsibilities will include:

- recommending the appointment of the independent auditor to the general meeting of shareholders;
- the appointment, compensation, retention and oversight of any accounting firm engaged for the purpose of preparing or issuing an audit report or performing other audit services;
- pre-approving the audit services and non-audit services to be provided by our independent auditor before the auditor is engaged to render such services;
- evaluating the independent auditor's qualifications, performance and independence, and presenting its conclusions to the full board on at least an annual basis;
- reviewing and discussing with the executive officers, the board and the independent auditor our financial statements and our financial reporting process; and
- approving or ratifying any related person transaction (as defined in our related person transaction policy) in accordance with our related person transaction policy.

The audit committee will meet as often as one or more members of the audit committee deem necessary, but in any event will meet at least four times per year. The audit committee will meet at least once per year with our independent accountant, without our executive officers being present.

Remuneration Committee of the Board

The remuneration committee, which consists of Ken Cunningham, M.D., David Ebsworth, Ph.D. and Rishi Gupta, assists the board in determining executive officer compensation. Dr. Cunningham serves as Chairman of the committee. Under SEC and NASDAQ rules, there are heightened independence standards for members of the remuneration committee, including a prohibition against the receipt of any compensation from us other than standard board member fees. Although foreign private issuers are not required to meet this heightened standard, as of the date of this prospectus, all of our expected remuneration committee members meet this heightened standard.

The remuneration committee's responsibilities will include:

- identifying, reviewing and proposing policies relevant to executive officer compensation;
- evaluating each executive officer's performance in light of such policies and reporting to the board;
- analyzing the possible outcomes of the variable remuneration components and how they may affect the remuneration of the executive officers;
- recommending any equity long-term incentive component of each executive officer's compensation in line with the remuneration policy and reviewing our executive officer compensation and benefits policies generally; and
- reviewing and assessing risks arising from our compensation policies and practices.

Governance Committee of the Board

The governance committee, which consists of David Ebsworth, Ph.D., Mahendra Shah, Ph.D. and Anders Ullman, M.D., Ph.D., assists our board in identifying individuals qualified to become members of our board and executive officers consistent with criteria established by our board and in developing our corporate governance principles. Dr. Ebsworth will serve as Chairman of the governance committee.

The governance committee's responsibilities will include:

- drawing up selection criteria and appointment procedures for board members;
- reviewing and evaluating the size and composition of our board and making a proposal for a composition profile of the board at least annually;
- recommending nominees for election to our board and its corresponding committees;
- assessing the functioning of individual members of board and executive officers and reporting the results of such assessment to the board; and
- developing and recommending to the board rules governing the board, reviewing and reassessing the adequacy of such rules governing the board and recommending any proposed changes to the board.

Code of Business Conduct and Ethics

In connection with the global offering, we have adopted a Code of Business Conduct and Ethics that covers a broad range of matters including the handling of conflicts of interest, compliance issues and other corporate policies such as equal opportunity and non-discrimination standards.

Compensation

Executive Officer Remuneration

The following table sets forth the approximate remuneration paid during the year ended December 31, 2016 to our current executive officers.

Name and Principal Position	Salary (£)	Bonus[1] (£)	Option Awards[2] (£)	All Other Compensation (£)	Total (£)
Jan-Anders Karlsson, Ph.D. Chief Executive Officer	220,833	230,000	281,479	87,974[3]	820,286
Piers Morgan[4] Chief Financial Officer	52,778	15,750	49,360	12,251[5]	130,139
Kenneth Newman, M.D. Chief Medical Officer	258,369	93,216	145,643	39,972[6]	537,200
Peter Spargo, Ph.D. Senior Vice President of Chemistry Manufacturing and Controls	127,521	44,650	56,591	22,639[7]	251,401
Claire Poll Legal Counsel	46,667	16,300	40,480	130,076[8]	233,523
Richard Hennings[9] Commercial Director	—	—	—	—	—

(1) Amount shown reflects bonuses awarded for achievement of performance goals in 2016.

(2) Amount shown represents the aggregate grant date fair value of option awards granted in 2016 measured using the Black Scholes model. For a description of the assumptions used in valuing these awards, see note 19 to our Annual Consolidated Financial Statements included elsewhere in this prospectus.

(3) Amount shown represents National Insurance and health benefits payments and pension contributions made by us.

(4) Mr. Morgan began his employment with us on September 26, 2016.

(5) Amount shown represents National Insurance and pension contributions made by us.

(6) Amount shown represents health benefits payments made by us.

(7) Amount shown represents National Insurance payments made by us.

(8) Amount shown represents National Insurance payments made by us (from start of her employment on October 1, 2016) and consulting fees earned by Ms. Poll in 2016 for corporate managerial services provided to us as a consultant. These fees were paid in accordance with the letter agreement that we entered into with Ms. Poll on September 21, 2015, which is further described below in the section entitled "— Executive Officer Employment Agreements — Claire Poll."

(9) Mr. Hennings began his employment with us on March 27, 2017.

Executive Officer Employment Agreements

Jan-Anders Karlsson, Ph.D.

We entered into an employment agreement with Dr. Karlsson on April 30, 2012, which was subsequently amended. This agreement, as amended, entitles Dr. Karlsson to receive an annual base salary of £250,000, or such higher rate as may be agreed in writing, and a target annual bonus opportunity of 66% of his annual base salary (potentially extending to up to 132%), with the amount of any such bonus based on annual performance criteria to be agreed between us and Dr. Karlsson. By June 1, 2017, Dr. Karlsson is required to invest an amount equal to £130,000 in our company through the purchase of our ordinary shares. Dr. Karlsson is also entitled to participate in a workplace pension scheme that we contribute to on his behalf. See "— Pension, Retirement or Similar Benefits" below.

Either party may terminate the employment agreement by giving the other party not less than 12 months' written notice, provided that we may terminate Dr. Karlsson at any time with immediate effect for cause or by giving written notice to Dr. Karlsson that we shall pay, in lieu of notice, his basic salary during the 12 months following termination, a pro-rated full discretionary bonus and any other contractual benefits prevailing at the time when such notice is given. The employment agreement provides that, upon a change of control, Dr. Karlsson is entitled to receive his full discretionary bonus (without an obligation to purchase ordinary shares) and full accelerated vesting of any outstanding, unvested equity awards under our share and share option schemes. See "— Equity Compensation Arrangements" below. If payments to Dr. Karlsson would constitute a "parachute payment" within the meaning of Section 280G of the Internal Revenue Code of 1986, as amended, or the Code, and would be subject to the excise tax imposed by Section 4999 of the Code, then such payment would be reduced to either (i) the largest portion of the payment that would result in no portion of the payment being subject to the excise tax or (ii) the largest portion of the payment, whichever of (i) or (ii) would result in Dr. Karlsson's receipt, on an after-tax basis, of the greater amount of the payment. Additionally, in order to minimize the effect of the different rates of U.S. and U.K. income tax rates, Dr. Karlsson is entitled to receive a payment from us to leave him in a net after-tax position substantially equivalent to what he would experience if he were only subject to U.K. taxes during the period of his employment with us. Dr. Karlsson's employment agreement also contains restrictive covenants pursuant to which he has agreed to refrain from competing with us or soliciting our customers or prospective customers for a period of six months following his termination of employment.

Kenneth Newman, M.D.

We entered into an offer letter with Dr. Newman on December 15, 2014, which was subsequently amended, pursuant to which he agreed to serve as our Chief Medical Officer, effective January 1, 2015. This agreement entitles Dr. Newman to receive an annual base salary of $340,000 and a target annual bonus opportunity of 40% of his annual base salary, with the amount of any such bonus based on performance criteria for our company and his individual performance, as determined by the board of directors in its sole discretion. Dr. Newman's offer letter also entitled him to receive a stock option to purchase 250,000 of our ordinary shares, which vests in full upon the earlier of (a) the third anniversary of the grant date or (b) a change of control. The offer letter with Dr. Newman also provides that, for so long as Dr. Newman is eligible for medical continuation coverage under the Consolidated Omnibus Budget Reconciliation Act, or COBRA, from his previous employer or until we establish a health insurance plan in which he is eligible to participate, Dr. Newman will receive reimbursement for monthly premiums paid for such medical continuation coverage and reimbursement for any premiums he pays for private long-term disability insurance (up to $800 per month).

If Dr. Newman's employment is terminated by us without "Cause" or by Dr. Newman for "Good Reason" (as each such term is defined in his offer agreement), then, subject to his signing and not revoking a general release of claims, he is entitled to receive (i) six months of base salary continuation, (ii) six months of continued payment of premiums for continued medical coverage under COBRA, (iii) a pro-rated portion of the annual bonus that he otherwise would have earned in the year of termination based on actual performance in such year and (iv) if the date of termination occurs within the six-month period immediately preceding the third anniversary of the date of grant of the stock option to purchase 250,000 of our ordinary shares, such stock option will vest in full. The offer agreement also provides that, if Dr. Newman's employment is terminated by us without Cause or by Dr. Newman for Good Reason, in either case within 12 months following a change of control, then, subject to his signing and not revoking a general release of claims, he is entitled to receive (i) nine months of base salary continuation, (ii) nine months of continued payment of premiums for continued medical coverage under COBRA, and (iii) a pro-rated portion of the annual bonus that he would otherwise have earned in the year of termination based on actual performance in such year. If payments to Dr. Newman would constitute a "parachute payment" within the meaning of Section 280G of the Code, and would be subject to the excise tax imposed by Section 4999 of the Code, then such payment would be reduced to either (i) the largest portion of the payment that would result in no portion of the payment being subject to the excise tax or (ii) the largest portion of the payment, whichever

of (i) or (ii) would result in Dr. Newman's receipt, on an after-tax basis, of the greater amount of the payment.

Piers Morgan

We entered into an employment agreement with Mr. Morgan on September 24, 2016, which was subsequently amended, pursuant to which he agreed to serve as our Chief Financial Officer. This agreement entitles Mr. Morgan to receive an annual base salary of £200,000, or such higher rate as may be agreed in writing, and a target annual bonus opportunity of 35% (potentially extending to up to 50%) of his salary, with the amount of any such bonus based on performance criteria for our company and his individual performance, as determined by our board of directors in its sole discretion. Within 12 months after receiving any such bonus payment, Mr. Morgan is expected to invest an amount equal to 25% of the bonus (net of income tax paid by Mr. Morgan) in our company through the purchase of our ordinary shares. Pursuant to this agreement, on September 16, 2016, Mr. Morgan received an option to purchase 300,000 of our ordinary shares with an exercise price of £2.04 per ordinary share, which vests in equal proportions on the first, second and third anniversary of the grant date of September 26, 2016.

Either party may terminate the employment agreement by giving the other party not less than six months' written notice, provided that we may terminate Mr. Morgan at any time with immediate effect for cause or by giving written notice to Mr. Morgan that we shall pay, in lieu of notice, his basic salary during the six months following termination, a pro-rated full discretionary bonus and any other contractual benefits prevailing at the time when such notice is given. The employment agreement provides that, upon a change of control, Mr. Morgan is entitled to receive his full discretionary bonus (without an obligation to purchase ordinary shares) and full accelerated vesting of any outstanding, unvested equity awards under our share and share option schemes. If payments to Mr. Morgan would constitute a "parachute payment" within the meaning of Section 280G of the Code, and would be subject to the excise tax imposed by Section 4999 of the Code, then such payment would be reduced to either (i) the largest portion of the payment that would result in no portion of the payment being subject to the excise tax or (ii) the largest portion of the payment, whichever of (i) or (ii) would result in Mr. Morgan's receipt, on an after-tax basis, of the greater amount of the payment. Additionally, in order to minimize the effect of the different rates of U.S. and U.K. income tax rates, Mr. Morgan is entitled to receive a payment from us to leave him in a net after-tax position substantially equivalent to what he would experience if he were only subject to U.K. taxes during the period of his employment with us. Mr. Morgan's employment agreement also contains restrictive covenants pursuant to which he has agreed to refrain from competing with us or soliciting our customers or prospective customers for a period of six months following his termination of employment.

Peter Spargo, Ph.D.

We entered into an employment agreement with Dr. Spargo on April 1, 2014, which was subsequently amended. Pursuant to this agreement, Dr. Spargo agreed to serve as our Senior Vice President, Chemistry Manufacturing and Controls, effective April 1, 2014. This agreement, as amended, entitles Dr. Spargo to receive an annual base salary of £154,570 and a target annual bonus opportunity of up to 35% of his annual base salary, with the amount of any such bonus based primarily on annual performance criteria to be agreed between us and Dr. Spargo.

Either party may terminate the employment agreement by giving the other party not less than six months' written notice, provided that we may terminate Dr. Spargo at any time with immediate effect for cause or by giving written notice to Dr. Spargo that we shall pay, in lieu of notice, his basic salary during the six months following termination, a pro-rated full discretionary bonus and any other contractual benefits prevailing at the time when such notice is given. The employment agreement provides that, upon a change of control, Dr. Spargo is entitled to receive his full discretionary bonus and full accelerated vesting of any outstanding, unvested equity awards under our share and share option schemes. If payments to Dr. Spargo would constitute a "parachute payment" within the meaning of Section 280G of the Code, and would be subject to the excise tax imposed by Section 4999 of the Code, then such payment would be reduced to either (i) the largest portion of the payment that would result in no portion of the payment being subject to the

excise tax or (ii) the largest portion of the payment, whichever of (i) or (ii) would result in Dr. Spargo's receipt, on an after-tax basis, of the greater amount of the payment. Dr. Spargo's employment agreement also contains restrictive covenants pursuant to which he has agreed to refrain from competing with us or soliciting our customers or prospective customers for a period of six months following his termination of employment.

Claire Poll

We entered into an agreement for consulting services with Ms. Poll on March 28, 2007, or the Poll Consulting Agreement, pursuant to which Ms. Poll provided corporate managerial services to us. We also entered into an agreement for director services with Ms. Poll on March 28, 2007 pursuant to which Ms. Poll served on our board of directors or the Poll Director Services Agreement. Pursuant to a letter agreement that we entered into with Ms. Poll on September 21, 2015, Ms. Poll retired from our board of directors and the Poll Director Services Agreement was terminated, effective September 10, 2015. The letter agreement further provided that an annual aggregate remuneration of £70,000 payable under both the Poll Consulting Agreement and Poll Director Services Agreement would be paid under the Poll Consulting Agreement.

We entered into an employment agreement with Ms. Poll on October 1, 2016 pursuant to which Ms. Poll agreed to serve as our Legal Counsel. This agreement entitles Ms. Poll to receive an annual base salary of £140,000, or such higher rate as may be agreed in writing, and a target annual bonus opportunity of 35% of her annual base salary, with the amount of any such bonus based primarily on annual performance criteria to be agreed to between us and Ms. Poll. Pursuant to this agreement, on September 13, 2016, Ms. Poll received an option to purchase a total of 200,000 of our ordinary shares with an exercise price of £1.89 per ordinary share, which vests in equal proportions on the first three anniversaries of the date of grant.

Either party may terminate the employment agreement by giving the other party not less than six months' written notice, provided that we may terminate Ms. Poll at any time with immediate effect for cause or by giving written notice to Ms. Poll that we shall pay, in lieu of notice, her basic salary during the six months following termination, a pro-rated full discretionary bonus and any other contractual benefits prevailing at the time when such notice is given. The employment agreement provides that, upon a change of control, Ms. Poll is entitled to receive her full discretionary bonus and full accelerated vesting of any outstanding, unvested equity awards under our share and share option schemes. If payments to Ms. Poll would constitute a "parachute payment" within the meaning of Section 280G of the Code, and would be subject to the excise tax imposed by Section 4999 of the Code, then such payment would be reduced to either (i) the largest portion of the payment that would result in no portion of the payment being subject to the excise tax or (ii) the largest portion of the payment, whichever of (i) or (ii) would result in Ms. Poll's receipt, on an after-tax basis, of the greater amount of the payment. Ms. Poll's employment agreement also contains restrictive covenants pursuant to which she has agreed to refrain from competing with us or soliciting our customers or prospective customers for a period of six months following her termination of employment.

Richard Hennings

We entered into an employment agreement with Mr. Hennings on March 27, 2017. This agreement entitles Mr. Hennings to receive an annual base salary of £155,000, or such higher rate as may be agreed in writing, and a target annual bonus opportunity of up to 35% of his annual base salary, with the amount of any such bonus based on annual performance criteria to be agreed between us and Mr. Hennings. Mr. Hennings is also entitled to participate in a workplace pension scheme that we contribute to on his behalf. See "— Pension, Retirement or Similar Benefits" below. Pursuant to his employment agreement, Mr. Hennings has been granted, subject to the terms and conditions described below under the heading "— Equity Compensation Arrangements — 2017 Incentive Award Plan — 2017 Grants," (a) an option to purchase a total of 160,000 of our ordinary shares with an exercise price equal to our NASDAQ listing price on the date of grant and (b) restricted share units with a grant date fair value of approximately £40,000.

Either party may terminate the employment agreement by giving the other party not less than six months' written notice. The employment agreement provides that, upon a change of control, Mr. Hennings is entitled to receive his full discretionary bonus and full accelerated vesting of any outstanding, unvested equity awards under our share and share option schemes. If payments to Mr. Hennings would constitute a "parachute payment" within the meaning of Section 280G of the Code, and would be subject to the excise tax imposed by Section 4999 of the Code, then such payment would be reduced to either (i) the largest portion of the payment that would result in no portion of the payment being subject to the excise tax or (ii) the largest portion of the payment, whichever of (i) or (ii) would result in Mr. Hennings' receipt, on an after-tax basis, of the greater amount of the payment. Additionally, in order to minimize the effect of the different rates of U.S. and U.K. income tax rates, Mr. Hennings is entitled to receive a payment from us to leave him in a net after-tax position substantially equivalent to what he would experience if he were only subject to U.K. taxes during the period of his employment with us. Mr. Hennings' employment agreement also contains restrictive covenants pursuant to which he has agreed to refrain from competing with us or soliciting our customers or prospective customers for a period of six months following his termination of employment.

Equity Compensation Arrangements

We have issued option grants under two option schemes, the Unapproved Share Option Scheme, or the Unapproved Scheme, adopted by our board of directors on September 18, 2006, and the EMI Option Scheme, or the EMI Scheme, adopted by our board of directors on July 24, 2012. Discussions in this section regarding the Unapproved Scheme or the EMI Scheme that refer to our board of directors include any designated committee of our board of directors. Once the New Incentive Plan (as defined below) is adopted, no further awards will be made under either the unapproved Scheme or EMI Scheme.

EMI Option Scheme

Under the EMI Scheme, eligible employees are granted tax-efficient options to purchase our ordinary shares. Options may be granted to eligible employees who are contracted to work for us or a qualifying subsidiary for at least 25 hours a week, or, if less than 25 hours a week, for at least 75% of their working time. The options granted under the EMI Scheme are exercisable at a price and in accordance with a vesting schedule determined by our board of directors at the time of grant and expire 10 years from the date of grant.

Unapproved Share Option Scheme

Under the Unapproved Scheme, we grant non-tax-qualifying options to purchase our ordinary shares. Options may be granted to employees, directors or consultants to acquire our ordinary shares at a price determined by our board of directors. In general, the options granted under the Unapproved Scheme are exercisable at a price and in accordance with the vesting period determined by our board of directors at the date of grant and expire 10 years from the date of grant.

Certain Transactions

Under the EMI Scheme and the Unapproved Scheme, if certain changes are made in, or events occur with respect to, our ordinary shares (including any capitalization, sub-division, reduction or other variation of our ordinary shares), any outstanding awards may be adjusted in terms of the number of ordinary shares subject to an option and the exercise price as our board of directors may determine appropriate on a fair and reasonable basis. In the event of certain corporate transactions, including a change of control, scheme of arrangement, merger, demerger or liquidation, the vesting and exercisability of all options will accelerate and, to the extent not exercised, will lapse within certain time periods defined in the applicable plan rules.

Amendment and Termination

Our board of directors may at any time amend the rules of the EMI Scheme or the Unapproved Scheme in any manner, except that no amendment may be made if, in the reasonable opinion of our board of directors, it would materially abrogate or adversely affect the subsisting rights of an option holder regarding existing options, unless the amendment is made either (i) with the written consent of the number of option holders

that hold options to acquire 50% of the ordinary shares that would be delivered if all options granted and subsisting under the scheme, as applicable, were exercised; or (ii) by a resolution at a meeting of option holders passed by not less than 50% of the option holders holding options under the scheme, as applicable, who attend and vote either in person or by proxy. The EMI Scheme and the Unapproved Scheme are discretionary and may be suspended or terminated by us at any time. Suspension or termination will not affect any options granted under the schemes to the extent that they are subsisting at the date of the suspension or termination.

The following table summarizes the options that we granted to our directors and executive officers under the EMI Scheme and Unapproved Scheme in 2016:

Name	Ordinary Shares Underlying Options	Exercise Price Per Share (£)	Grant Date	Expiration Date
Jan-Anders Karlsson, Ph.D.	100,000	2.00	February 9, 2016	February 9, 2026
	100,000	3.30	February 9, 2016	February 9, 2026
	500,000	1.80	August 3, 2016	August 3, 2026
Piers Morgan	300,000	2.04	September 26, 2016	September 26, 2026
Kenneth Newman, M.D.	60,000	2.00	February 9, 2016	February 9, 2026
	200,000	1.80	August 3, 2016	August 3, 2026
Peter Spargo, Ph.D.	20,000	2.00	February 9, 2016	February 9, 2026
	100,000	1.80	August 3, 2016	August 3, 2026
Claire Poll	200,000	1.89	September 13, 2016	September 13, 2026
Richard Hennings	—	—	—	—
Patrick Humphrey, D.Sc.[1]	—	—	—	—
David Ebsworth, Ph.D.	—	—	—	—
Ken Cunningham, M.D.	—	—	—	—
Rishi Gupta	—	—	—	—
Mahendra Shah, Ph.D.	—	—	—	—
Vikas Sinha	—	—	—	—
Andrew Sinclair, Ph.D.	—	—	—	—
Anders Ullman, M.D., Ph.D.	—	—	—	—

[1] Patrick Humphrey resigned from our board of directors, effective April 15, 2017.

2017 Incentive Award Plan

We have adopted the 2017 Incentive Award Plan, or the New Incentive Plan, under which we may grant cash and equity-based incentive awards to eligible service providers in order to attract, retain and motivate the persons who make important contributions to us. The material terms of the New Incentive Plan are summarized below. Except where the context indicates otherwise, references hereunder to our ordinary shares shall be deemed to include a number of ADSs equal to an ordinary share.

Eligibility and Administration

Our employees, consultants and directors, and employees and consultants of our subsidiaries are eligible to receive awards under the New Incentive Plan. The New Incentive Plan is administered by our board of directors, which may delegate its duties and responsibilities to one or more committees of our directors and/or officers (referred to collectively as the plan administrator below), subject to the limitations imposed under the New Incentive Plan, stock exchange rules and other applicable laws. The plan administrator has the authority to take all actions and make all determinations under the New Incentive Plan, to interpret the New Incentive Plan and award agreements and to adopt, amend and repeal rules for the administration of the New Incentive Plan as it deems advisable. The plan administrator also has the authority to determine which eligible service providers receive awards, grant awards, set the terms and conditions of all awards

under the New Incentive Plan, including any vesting and vesting acceleration provisions, and designate whether such awards will cover our ordinary shares or ADSs, subject to the conditions and limitations in the New Incentive Plan.

Sub-Plan

The New Incentive Plan authorizes the administrator to establish one or more sub-plans. Immediately after the New Incentive Plan was established, the administrator established a sub-plan. The sub-plan incorporates all of the terms of the New Incentive Plan, except that only employees of ours (or our subsidiaries) will be eligible to receive awards under the sub-plan. Consultants and directors who are not also employees are not eligible to receive awards under the sub-plan. Awards under the sub-plan count towards the total number of shares available for issuance under the New Incentive Plan. The sub-plan is an "employees' share scheme" for the purposes of the U.K. Companies Act 2006 and it is anticipated that all awards that are to be made to employees will be made under the sub-plan rather than the New Incentive Plan itself.

Shares Available for Awards

An aggregate of 6,333,000 of our ordinary shares are initially available for issuance under the New Incentive Plan. The number of shares initially available for issuance will be increased by an annual increase on January 1 of each calendar year beginning in 2018 and ending in and including 2027 equal to the least of (A) 4% of our ordinary shares outstanding on the final day of the immediately preceding calendar year and (B) a smaller number of shares determined by our board of directors. Pursuant to the terms of the New Incentive Plan, awards may be issued under the New Incentive Plan covering ADSs in lieu of the number of our ordinary shares that such ADSs represent. No more than 5,000,000 shares may be issued under the New Incentive Plan upon the exercise of incentive options. Shares issued under the New Incentive Plan may be authorized but unissued shares, shares purchased on the open market, treasury shares or ADSs.

If an award under the New Incentive Plan, the EMI Option Scheme, the Unapproved Share Option Scheme or any prior equity incentive plan, expires, lapses or is terminated, exchanged for cash, surrendered, repurchased, canceled without having been fully exercised or forfeited, any unused shares subject to the award will, as applicable, become or again be available for new grants under the New Incentive Plan. Awards granted under the New Incentive Plan in substitution for any options or other equity or equity-based awards granted by an entity before the entity's merger or consolidation with us or our acquisition of the entity's property or stock will not reduce the shares available for grant under the New Incentive Plan, but will count against the maximum number of shares that may be issued upon the exercise of incentive options.

Awards

The New Incentive Plan provides for the grant of options, share appreciation rights, or SARs, restricted shares, dividend equivalents, restricted share units, or RSUs, and other share or cash based awards. All awards under the New Incentive Plan will be set forth in award agreements, which will detail the terms and conditions of awards, including any applicable vesting and payment terms and post-termination exercise limitations. A brief description of each award type follows.

Options and SARs. Options provide for the purchase of our ordinary shares in the future at an exercise price set on the grant date. SARs entitle their holder, upon exercise, to receive from us an amount equal to the appreciation of the shares subject to the award between the grant date and the exercise date. The plan administrator will determine the number of shares covered by each option and SAR, the exercise price of each option and SAR and the conditions and limitations applicable to the exercise of each option and SAR.

Restricted Shares and Restricted Share Units. Restricted shares are an award of nontransferable ordinary shares that remain forfeitable unless and until specified conditions are met and which may be subject to a purchase price. RSUs are contractual promises to deliver our ordinary shares in the future, which may also remain forfeitable unless and until specified conditions are met and may be accompanied by the right to receive the equivalent value of dividends paid on our ordinary shares prior to the delivery of the underlying

shares. The plan administrator may provide that the delivery of the shares underlying RSUs will be deferred on a mandatory basis or at the election of the participant. The terms and conditions applicable to restricted shares and RSUs will be determined by the plan administrator, subject to the conditions and limitations contained in the New Incentive Plan.

Other Share or Cash Based Awards. Other share or cash based awards are awards of cash, fully-vested our ordinary shares and other awards valued wholly or partially by referring to, or otherwise based on, our ordinary shares or other property. Other share or cash based awards may be granted to participants and may also be available as a payment form in the settlement of other awards, as standalone payments and as payment in lieu of compensation to which a participant is otherwise entitled. The plan administrator will determine the terms and conditions of other share or cash based awards, which may include any purchase price, performance goal, transfer restrictions and vesting conditions.

Performance Criteria

The plan administrator may select performance criteria for an award to establish performance goals for a performance period. Performance criteria under the New Incentive Plan may include, but are not limited to, the following: net earnings or losses (either before or after one or more of interest, taxes, depreciation, amortization, and non-cash equity-based compensation expense); gross or net sales or revenue or sales or revenue growth; net income (either before or after taxes) or adjusted net income; profits (including but not limited to gross profits, net profits, profit growth, net operation profit or economic profit), profit return ratios or operating margin; budget or operating earnings (either before or after taxes or before or after allocation of corporate overhead and bonus); cash flow (including operating cash flow and free cash flow or cash flow return on capital); return on assets; return on capital or invested capital; cost of capital; return on shareholders' equity; total shareholder return; return on sales; costs, reductions in costs and cost control measures; expenses; working capital; earnings or loss per share; adjusted earnings or loss per share; price per share or dividends per share (or appreciation in or maintenance of such price or dividends); regulatory achievements or compliance; implementation, completion or attainment of objectives relating to research, development, regulatory, commercial, or strategic milestones or developments; market share; economic value or economic value added models; division, group or corporate financial goals; customer satisfaction/ growth; customer service; employee satisfaction; recruitment and maintenance of personnel; human resources management; supervision of litigation and other legal matters; strategic partnerships and transactions; financial ratios (including those measuring liquidity, activity, profitability or leverage); debt levels or reductions; sales-related goals; financing and other capital raising transactions; cash on hand; acquisition activity; investment sourcing activity; and marketing initiatives, any of which may be measured in absolute terms or as compared to any incremental increase or decrease. Such performance goals also may be based solely by reference to the company's performance or the performance of a subsidiary, division, business segment or business unit of the company or a subsidiary, or based upon performance relative to performance of other companies or upon comparisons of any of the indicators of performance relative to performance of other companies. When determining performance goals, the plan administrator may provide for exclusion of the impact of an event or occurrence which the plan administrator determines should appropriately be excluded, including, without limitation, non-recurring charges or events, acquisitions or divestitures, changes in the corporate or capital structure, events unrelated to the business or outside of the control of management, foreign exchange considerations, and legal, regulatory, tax or accounting changes.

Certain Transactions

In connection with certain corporate transactions and events affecting our ordinary shares, including a change in control, another similar corporate transaction or event, another unusual or nonrecurring transaction or event affecting us or its financial statements or change in any applicable laws or accounting principles, the plan administrator has broad discretion to take action under the New Incentive Plan to prevent the dilution or enlargement of intended benefits, facilitate the transaction or event or give effect to the change in applicable laws or accounting principles. This includes canceling awards for cash or property, accelerating the vesting of awards, providing for the assumption or substitution of awards by a successor

entity, adjusting the number and type of shares subject to outstanding awards and/or with respect to which awards may be granted under the New Incentive Plan and replacing or terminating awards under the New Incentive Plan. In addition, in the event of certain non-reciprocal transactions with our shareholders, the plan administrator will make equitable adjustments to the New Incentive Plan and outstanding awards as it deems appropriate to reflect the transaction. Pursuant to the terms of their individual employment agreements, awards granted under the New Incentive Plan to certain of our executives may become fully vested and exercisable upon a change in control.

Plan Amendment and Termination

Our board of directors may amend or terminate the New Incentive Plan at any time; however, no amendment, other than an amendment that increases the number of shares available under the New Incentive Plan, may materially and adversely affect an award outstanding under the New Incentive Plan without the consent of the affected participant and shareholder approval will be obtained for any amendment to the extent necessary to comply with applicable laws. Further, the plan administrator cannot, without the approval of our shareholders, amend any outstanding option or SAR to reduce its price per share or cancel any outstanding option or SAR in exchange for cash or another award under the New Incentive Plan with an exercise price per share that is less than the exercise price per share of the original option or SAR. The New Incentive Plan will remain in effect until the tenth anniversary of its effective date unless earlier terminated by our board of directors. No awards may be granted under the New Incentive Plan after its termination.

Non-U.S. Participants, Claw-Back Provisions, Transferability and Participant Payments

The plan administrator may modify awards granted to participants who are non-U.S. nationals or employed outside the United States or establish sub-plans or procedures to address differences in laws, rules, regulations or customs of such foreign jurisdictions. All awards will be subject to any company claw-back policy as set forth in such claw-back policy or the applicable award agreement. Except as the plan administrator may determine or provide in an award agreement, awards under the New Incentive Plan are generally non-transferrable, except by will or the laws of descent and distribution, or, subject to the plan administrator's consent, pursuant to a domestic relations order, and are generally exercisable only by the participant. With regard to tax withholding obligations arising in connection with awards under the New Incentive Plan, and exercise price obligations arising in connection with the exercise of options under the New Incentive Plan, the plan administrator may, in its discretion, accept cash, wire transfer or cheque, our ordinary shares that meet specified conditions, a promissory note, a "market sell order," such other consideration as the plan administrator deems suitable or any combination of the foregoing.

2017 Grants

In connection with the global offering, we approved a grant to each of our current executive officers and Vikas Sinha, effective upon the pricing of the global offering, of an option and an RSU under the New Incentive Plan. The number of ordinary shares subject to the options and RSUs will be determined by dividing the values shown in the table below by a Black-Scholes value formula on the date of grant based on the offering price per ordinary share in the European private placement. In applying the Black-Scholes model, assumptions are made on inputs such as time to maturity (5.5-7.0 years), annualized volatility (71.31%-73.08%), dividend rate (0.00%) and risk free rate (0.42%-0.62%). Based on an offering price of £1.32 per ordinary share in the European private placement, the aggregate number of ordinary shares subject to these grants would be approximately 4,300,000 ordinary shares underlying options and approximately 1,050,000 ordinary shares underlying RSUs. Pursuant to the terms of the New Incentive Plan, awards may be issued under the New Incentive Plan covering ADSs in lieu of the number of our ordinary shares that such ADSs represent.

Name	Amount of Ordinary Shares Underlying Options	Amount of Restricted Share Units
Jan-Anders Karlsson, Ph.D.	£1,160,000	£290,000
Piers Morgan	£ 672,000	£168,000
Ken Newman, M.D.	$ 852,000	$213,000
Peter Spargo, Ph.D.	£ 456,000	£114,000
Claire Poll	£ 408,000	£102,000
Richard Hennings	—[1]	£ 40,000
Vikas Sinha	£ 100,000	—

[1] Mr. Hennings will receive an option for 160,000 ordinary shares.

The options and RSUs (other than those granted to Messrs. Hennings and Sinha) will vest as to 50% of the ordinary shares in three substantially equal annual installments following the grant date and as to 50% of the ordinary shares in four substantially equal annual installments following the grant date. The options and RSUs granted to Messrs. Hennings and Sinha will vest in three substantially equal annual installments following the grant date.

Non-Employee Directors Remuneration

The following table sets forth the remuneration paid during 2016 to our current non-employee directors:

Name	Annual Fees (£)	Total (£)
David Ebsworth, Ph.D.	124,000	124,000
Ken Cunningham, M.D.	30,000	30,000
Rishi Gupta	12,500	12,500
Patrick Humphrey, D.Sc[1]	30,000	30,000
Mahendra Shah, Ph.D.	12,500	12,500
Andrew Sinclair, Ph.D.	12,500	12,500
Vikas Sinha	9,083	9,083
Anders Ullman, M.D., Ph.D.	30,000	30,000

[1] Patrick Humphrey resigned from our board of directors, effective April 15, 2017.

Non-Employee Director Service Contracts

The remuneration of the non-executive directors is determined by our board as a whole, based on a review of current practices in other companies. We have entered into service contracts with our directors for their services, which are subject to a three-month termination period.

Pension, Retirement or Similar Benefits

We operate a defined contribution pension scheme which is available to all employees. The total amount set aside or accrued by us to provide pension, retirement or similar benefits to our current directors and our executive officers with respect to 2016 was £16,417, which represents contributions made by us in 2016 in respect of a defined contribution scheme in which Dr. Karlsson and Mr. Morgan participated.

Employees

As of December 31, 2016, 2015 and 2014, we had 11, nine and seven employees, respectively. All of our employees were based in the United Kingdom, except that, as of December 31, 2016, 2015 and 2014, we had one to four employees based outside of the United Kingdom. All of our employees were engaged in either administrative or research & development functions. None of our employees are covered by a collective bargaining agreement.

Insurance and Indemnification

To the extent permitted by the U.K. Companies Act 2006, we are empowered to indemnify our directors against any liability they incur by reason of their directorship. We maintain directors' and officers' insurance to insure such persons against certain liabilities. We expect to enter into a deed of indemnity with each of our directors and executive officers.

In addition to such indemnification, we provide our directors and executive officers with directors' and officers' liability insurance.

Insofar as indemnification of liabilities arising under the Securities Act may be permitted to our board, executive officers, or persons controlling us pursuant to the foregoing provisions, we have been informed that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

PRINCIPAL SHAREHOLDERS

The following table sets forth information relating to the beneficial ownership of our ordinary shares as of March 31, 2017 by:

- each person, or group of affiliated persons, that beneficially owns 3% or more of our outstanding ordinary shares;
- each member of our board of directors and each of our other executive officers; and
- all board members and executive officers as a group.

The number of ordinary shares beneficially owned by each entity, person, board member or executive officer is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power as well as any shares that the individual has the right to acquire within 60 days of March 31, 2017 through the exercise of any option, warrant or other right. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all ordinary shares held by that person.

The percentage of ordinary shares beneficially owned before the global offering and shareholder private placement is computed on the basis of 51,361,064 of our ordinary shares outstanding as of March 31, 2017. The percentage of ordinary shares beneficially owned after the offering is based on the number of our ordinary shares outstanding before the offering as provided above plus (i) 47,399,001 ordinary shares (including 46,144,000 ordinary shares in the form of ADSs) that we are offering in the global offering, and assuming no exercise of the underwriters' option to purchase additional ADSs from us and (ii) 254,099 ordinary shares we expect to issue and sell in the shareholder private placement. Ordinary shares that a person has the right to acquire within 60 days of March 31, 2017 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all board members and executive officers as a group. We have included in these calculations ordinary shares which are subject to outstanding warrants that become exercisable upon the closing of the global offering. As of March 31, 2017, 1,696,191 ordinary shares, representing 3.30% of our issued and outstanding ordinary shares, were held by three U.S. record holders. Unless otherwise indicated below, the address for each beneficial owner listed is c/o Verona Pharma plc, 3 More London Riverside, London SE1 2RE UK.

Our existing institutional investors affiliated with certain of our directors have indicated an interest in purchasing up to an aggregate of approximately $23 million (or the pounds sterling equivalent) in the global offering on the same terms as the other purchasers in the global offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no securities offered in the global offering to any of these investors or any of these investors may determine to purchase more, less or no securities offered in the global offering. The following table does not reflect any potential purchases by these investors or their affiliated entities.

Name and address of beneficial owner	Number of Shares Beneficially Owned Before Offering	Percentage of Shares Beneficially Owned	
		Before Offering	After Offering
3% or Greater Shareholders:			
Novo A/S[1]	8,233,691	15.5%	8.2%
Vivo Capital affiliates[2]	8,177,785	15.4	8.1
OrbiMed Private Investments VI, LP[3]	6,537,786	12.3	6.5
Growth Equity Opportunities Fund IV, LLC[4]	6,193,691	11.7	6.1
Abingworth Bioventures VI, LP[5]	4,914,774	9.3	4.9
Arix Bioscience Holdings Ltd affiliates[6]	3,916,493	7.5	3.9
Aviva plc and subsidiaries[7]	3,288,448	6.4	3.3
Biodiscovery 4 FCPI[8]	3,096,846	5.9	3.1
Tekla Capital affiliates[9]	3,096,845	5.9	3.1
Aisling Capital IV, LP[10]	2,064,563	4.0	2.1
BBHISL Nominees Ltd. A/C 121624[11]	2,028,708	3.9	2.0
HSBC Global Custody Nominee (UK) Ltd A/C: 944287[12]	1,801,618	3.5	1.8
Executive Officers and Directors:			
Jan-Anders Karlsson, Ph.D.[13]	499,150	*	*
Piers Morgan	—	—	—
Kenneth Newman, M.D.[14]	186,667	*	*
Claire Poll[15]	170,000	*	*
Richard Hennings	—	—	—
Peter Spargo, Ph. D.[16]	86,333	*	*
Ken Cunningham, M.D.	—	—	—
David Ebsworth, Ph.D.[17]	122,574	*	*
Rishi Gupta	—	—	—
Patrick Humphrey, D.Sc.[18]	20,000	*	*
Mahendrah Shah, Ph.D.	—	—	—
Andrew Sinclair, Ph.D.[19]	—	—	—
Vikas Sinha	—	—	—
Anders Ullman, M.D., Ph.D.	—	—	—
All executive officers and directors as a group (14 persons)	1,084,724	2.1	1.1

* Indicates beneficial ownership of less than 1% of the total outstanding ordinary shares.

(1) Consists of (a) 6,464,065 ordinary shares held directly by Novo A/S, or Novo, and (b) warrants to purchase 1,769,626 ordinary shares that vest upon the closing of the global offering held directly by Novo. The board of directors of Novo A/S, or the Novo Board, has shared investment and voting control over the securities held by Novo and may exercise such control only with the support of a majority of the Novo Board. As such, no individual member of the Novo Board is deemed to hold any beneficial ownership or reportable pecuniary interest in the securities held by Novo. Beneficial ownership information is based on information known to us and a Form TR-1 provided to us on January 11, 2017. Novo's mailing address is Tuborg Havnevej 19, Hellerup, G7 2900, Denmark.

(2) Consists of (a) 1,252,791 ordinary shares held directly by Vivo Ventures Fund VI, L.P., or Vivo VI, (b) warrants to purchase 370,871 ordinary shares that vest upon the closing of the global offering held directly by Vivo VI, (c) 9,178 ordinary shares held directly by Vivo Ventures VI Affiliates Fund, L.P., or Vivo Affiliates VI, (d) warrants to purchase 2,717 ordinary shares that vest upon the closing of the global offering held directly by Vivo Affiliates VI, (e) 4,940,206 ordinary shares held directly by Vivo Ventures Fund VII L.P., or Vivo VII, (f) warrants to purchase 1,462,477 ordinary shares that vest upon the closing of the global offering held directly by Vivo VII, (g) 107,671 ordinary shares held directly by Vivo Ventures VII Affiliates Fund, L.P., or Vivo Affiliates VII, and (h) warrants to purchase 31,874 ordinary shares that vest upon the closing of the global offering held directly by Vivo Affiliates VII. Vivo Ventures VI, LLC , or Vivo Ventures VI, is the sole general partner

of Vivo VI and Vivo Affiliates VI. Vivo Ventures VII, LLC, or Vivo Ventures VII, is the sole general partner of Vivo VII and Vivo Affiliates VII. Vivo Ventures VI and Vivo Ventures VII disclaim beneficial ownership of all shares held by Vivo VI, Vivo Affiliates VI, Vivo VII and Vivo Affiliates VII except to the extent of any pecuniary interest therein. The managing members of Vivo Ventures VI are Drs. Albert Cha, Edgar Engleman and Frank Kung, each of whom may be deemed to have shared voting and dispositive power of the shares held by Vivo VI and Vivo Affiliates VI. The managing members of Vivo Ventures VII are Drs. Albert Cha, Edgar Engleman, Frank Kung, Chen Yu and Mr. Shan Fu, each of whom may be deemed to have shared voting and dispositive power of the shares held by Vivo VII and Vivo Affiliates VII. Mahendra Shah, the Managing Director of Vivo Capital, is a member of our Board of Directors and disclaims beneficial ownership of these shares except to the extent of his pecuniary interest arising as a result of his employment by Vivo Capital. Beneficial ownership information is based on information known to us and Forms TR-1 provided to us on August 3, 2016. Vivo Capital's mailing address is 505 Hamilton Avenue, Suite 200, Palo Alto, CA 94301.

(3) Consists of (a) 4,669,847 ordinary shares held directly by OrbiMed Private Investments VI, LP, or OrbiMed VI, and (b) warrants to purchase 1,867,939 ordinary shares that vest upon the closing of the global offering held directly by OrbiMed VI. OrbiMed Capital GP VI LLC, or GP VI, is the general partner of OrbiMed VI. OrbiMed Advisors LLC, or OrbiMed Advisors, is the managing member of GP VI. Samuel D. Isaly is the managing member of and owner of a controlling interest in OrbiMed Advisors. By virtue of such relationships, GP VI, OrbiMed Advisors and Mr. Isaly may be deemed to have voting and investment power with respect to the shares held by OrbiMed VI and as a result may be deemed to have beneficial ownership of such shares. Rishi Gupta, an employee of OrbiMed Advisors, is a member of our Board of Directors. Each of GP VI, OrbiMed Advisors, Mr. Isaly and Mr. Gupta disclaims beneficial ownership of the shares held by OrbiMed VI, except to the extent of its or his pecuniary interest therein, if any. Beneficial ownership information is based on information known to us and a Form TR-1 provided to us on August 1, 2016. OrbiMed Advisors' mailing address is 601 Lexington Avenue, 54th Floor, New York, NY 10022.

(4) Consists of (a) 4,424,065 ordinary shares held directly by Growth Equity Opportunities Fund IV, LLC, or GEO, and (b) warrants to purchase 1,769,626 ordinary shares that vest upon the closing of the global offering held directly by GEO. New Enterprise Associates 15, L.P., or NEA 15, is the sole member of GEO. NEA Partners 15, L.P., NEA Partners 15, is the sole general partner of NEA 15. NEA 15 GP, LLC, or NEA 15 LLC, is the sole general partner of NEA Partners 15. Peter J. Barris, Forest Baskett, Anthony Florence, Jr., Krishnu Kolluri, David M. Mott, Scott D. Sandell, Peter Sonsini, Jon Sakoda, Ravia Viswanthan and Henry Weller are the managers of NEA 15 LLC. NEA 15, NEA Partners 15, NEA 15 LLC and the managers of NEA 15 LLC share voting and dispositive power with regard to the securities held by GEO. Each of NEA 15, NEA Partners 15 and NEA 15 LLC as well as each of the managers of NEA 15 LLC disclaims beneficial ownership of all shares held by GEO except to the extent of their actual pecuniary interest therein. Beneficial ownership information is based on information known to us and a Form TR-1 provided to us on August 1, 2016. GEO's mailing address is 1954 Greenspring Drive, Suite 600, Timonium, MD 21093-4135.

(5) Consists of (a) 3,510,553 ordinary shares held directly by Abingworth Bioventures VI, LP, or Abingworth VI, and (b) warrants to purchase 1,404,221 ordinary shares that vest upon the closing of the global offering held directly by Abingworth VI. Abingworth Bioventures VI GP LP, or Abingworth GP VI, serves as general partner of Abingworth VI. Abingworth General Partner VI LLP, or Abingworth General Partner VI, serves as general partner of Abingworth GP VI. Abingworth General Partner VI has delegated to Abingworth LLP, all investment and dispositive power over the securities held by Abingworth VI. An Abingworth LLP investment committee comprised of Stephen Bunting, Timothy Haines, Kurt von Emster and Genghis Lloyd-Harris approves investment and voting decisions of Abingworth VI by a majority vote, and no individual member has the sole control or voting power over the securities held by Abingworth VI. Abingworth GP VI, Abingworth General Partner VI, Abingworth LLP and each of Stephen Bunting, Timothy Haines, Kurt von Emster and Genghis Lloyd-Harris disclaim beneficial ownership of securities held by Abingworth VI, except to the extent, if any of their pecuniary interest therein. Beneficial ownership information is based on information known to us and a Form TR-1 provided to us on August 1, 2016. Abingworth VI's mailing address is 38 Jermyn Street, London SW1Y 6DN, United Kingdom.

(6) Consists of (a) 1,290,352 ordinary shares held directly by Arix Bioscience Holdings Ltd, or Arix, (b) warrants to purchase 516,141 ordinary shares that vest upon the closing of the global offering held directly by Arix and (c) 2,110,000 ordinary shares held directly by Wales Life Sciences Investment Fund, or WLSIF. Arthurian Life Sciences Ltd, or Arthurian, is the general partner of WLSIF and a wholly owned subsidiary of Arix. Beneficial ownership information is based on information known to us and a Form TR-1 provided to us on August 3, 2016 and January 3, 2017. Arix's mailing address is 20 Berkeley Square, London W1J 6EQ, United Kingdom.

(7) Aviva Group Holdings Limited, or Aviva Holdings, is a wholly-owned subsidiary of Aviva plc. Aviva Investors Holdings Limited, or Aviva Investors, is a wholly-owned subsidiary of Aviva Holdings. Aviva Investors Global Services Limited, or Aviva Global Services, is a wholly-owned subsidiary of Aviva Investors. Aviva Life Holdings UK Limited, or Aviva Life, is a wholly-owned subsidiary of Aviva Holdings. Friends Life FPG Limited, or Friends FPG, is a wholly-owned subsidiary of Aviva Life. Friends

Life FPL Limited, or Friends FPL, is a wholly-owned subsidiary of Friends FPG. Friends Life Limited, or Friends Life, is a wholly-owned subsidiary of Friends FPL. Friends Life and Pensions Limited, or Friends Pensions, is a wholly-owned subsidiary of Friends Life. Friends Provident International Limited, or Friends Provident, is a wholly-owned subsidiary of Friends Pensions. The voting rights for these common shares are controlled and managed by Aviva Global Services and Friends Provident. Beneficial ownership information is based on information known to us and a Form TR-1 provided to us on August 5, 2016. Aviva plc's mailing address is St. Helen's, 1 Undershaft, London EC3P 3DQ, United Kingdom.

(8) Consists of (a) 2,212,033 ordinary shares held directly by Biodiscovery 4 FCPI, or Biodiscovery, and (b) warrants to purchase 884,813 ordinary shares that vest upon the closing of the global offering held directly by Biodiscovery. Beneficial ownership information is based on information known to us and a Form TR-1 provided to us on August 2, 2016.

(9) Consists of (a) 1,282,978 ordinary shares held directly by Tekla World Healthcare Fund, or Tekla World, (b) warrants to 513,192 purchase ordinary shares that vest upon the closing of the global offering held directly by Tekla World, (c) 929,053 ordinary shares held directly by Tekla Life Science Investors, or Tekla Life, and (d) warrants to purchase 371,622 ordinary shares that vest upon the closing of the global offering held directly by Tekla Life. Tekla Capital Management LLC, or Tekla Capital, is an investment adviser registered pursuant to Section 203 of the Investment Advisers Act of 1940 and is the investment adviser of Tekla World and Tekla Life, each of which is a registered investment company pursuant to Section 8 of the Investment Company Act of 1940. Each of Tekla Capital and Daniel R. Omstead, through his control of Tekla Capital, has sole power to dispose of the shares beneficially owned by Tekla World and Tekla Life. Neither Tekla Capital nor Daniel R. Omstead has the sole power to vote or direct the vote of the shares beneficially owned by Tekla World and Tekla Life, which power resides in each fund's Board of Trustees. Tekla Capital carries out the voting of the shares under written guidelines established by each fund's Board of Trustees. Beneficial ownership information is based on information known to us and a Schedule 13G filed with the Securities and Exchange Commission on February 13, 2017. Tekla Capital's mailing address is 100 Federal Street, 19th Floor, Boston, MA 02110.

(10) Consists of (a) 1,474,688 ordinary shares held directly by Aisling Capital IV, LP, or Aisling, and (b) warrants to purchase 589,875 ordinary shares that vest upon the closing of the global offering held directly by Aisling. This information is based on information known to us.

(11) Consists of (a) 1,805,944 ordinary shares held directly by BBHISL Nominees Ltd. A/C 121624, or BBHISL and (b) warrants to purchase 222,764 ordinary shares that vest upon the closing of the global offering held directly by BBHISL. Beneficial ownership information is based on information known to us.

(12) Consists of (a) 1,376,000 ordinary shares held directly by HSBC Global Custody Nominee (UK) Ltd A/C: 944287, or Hargreave Hale, and (b) warrants to purchase 425,618 ordinary shares that vest upon closing of the global offering held directly by Hargreave Hale. Beneficial ownership information is based on information known to us.

(13) Consists of (a) 89,150 ordinary shares and (b) 410,000 options to purchase ordinary shares that are or will be immediately exercisable within 60 days of March 31, 2017.

(14) Consists of 186,667 options to purchase ordinary shares that are or will be immediately exercisable within 60 days of March 31, 2017.

(15) Consists of (a) 95,000 ordinary shares and (b) 75,000 options to purchase ordinary shares that are or will be immediately exercisable within 60 days of March 31, 2017.

(16) Consists of (a) 13,000 ordinary shares and (b) 73,333 options to purchase ordinary shares that are or will be immediately exercisable within 60 days of March 31, 2017.

(17) Consists of (a) 104,285 ordinary shares, (b) warrants to purchase 4,916 ordinary shares that vest upon the closing of the global offering and (c) 13,373 ordinary shares that Dr. Ebsworth has agreed to purchase in the shareholder private placement, based on the offering price per ordinary share in the European private placement of £1.32.

(18) Consists of 20,000 options to purchase ordinary shares that are or will be immediately exercisable within 60 days of March 31, 2017. Patrick Humphrey resigned from our board of directors, effective April 15, 2017.

(19) Dr. Sinclair is a Partner and Portfolio Manager at Abingworth LLP. Dr. Sinclair does not have voting or dispositive power over any of the shares directly held by Abingworth VI referenced in footnote (6) above. Dr. Sinclair's business address is 38 Jermyn Street, London SW1Y 6DN, United Kingdom.

RELATED PARTY TRANSACTIONS

The following is a description of related party transactions we have entered into since January 1, 2014 with any members of our board of directors or executive officers and the holders of more than 5% of our ordinary shares.

Participation in the Global Offering

Our existing institutional investors affiliated with certain of our directors have indicated an interest in purchasing up to an aggregate of approximately $23 million (or the pounds sterling equivalent) of the securities offered in the global offering on the same terms as the other purchasers in the global offering. Based on the offering price of £1.32 per ordinary share, these investors would purchase up to an aggregate of 13,609,467 (including ordinary shares in the form of ADSs) of the 47,399,001 shares in the global offering based on these indications of interest. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no securities offered in the global offering to any of these investors, or any of these investors may determine to purchase more, less or no securities offered in the global offering. The underwriters will receive the same underwriting discount on any securities purchased by these investors as they will on any other securities sold to the public in the global offering.

Shareholder Private Placement

Our chairman of the board of directors and an existing shareholder have agreed to purchase an aggregate of approximately £335,400 (or the U.S. dollar equivalent) of our ordinary shares in a private placement separate from the global offering, contingent on and concurrent with the completion of the global offering at a price per share equal to the offering price per ordinary share in the European private placement. The underwriters will serve as placement agents for such shareholder private placement and receive a placement agent fee equal to a percentage of the total purchase price of the private placement shares, which percentage will be equal to the percentage discount the underwriters will receive on shares sold in this global offering. The closing of this global offering is not conditioned upon the closing of such shareholder private placement.

Ordinary Share and Warrant Placement

In July 2016, we issued an aggregate of 31,115,926 Units to new and existing institutional and other investors at a price of £1.4365 per Unit for an aggregate purchase price of £44.7 million, or the July Placement. Each Unit represented one ordinary share and a warrant to purchase 0.4 of an ordinary share at a price of £1.7238. Each warrant is exercisable beginning upon the closing of the global offering and will expire on the fifth anniversary of the closing of the global offering.

The following table sets forth the aggregate number of our ordinary shares issued to our 5% or greater shareholders and their affiliates and one of our directors in the July Placement.

Participants[1]	Ordinary Shares	Warrants
Arix Bioscience plc	1,290,352	516,140
Vivo Capital affiliates[2]	4,669,846	1,867,939
OrbiMed Private Investments VI, LP[3]	4,669,847	1,867,939
Growth Equity Opportunities Fund IV, LLC	4,424,065	1,769,626
Novo A/S	4,424,065	1,769,626
Abingworth Bioventures VI, LP[4]	3,510,553	1,404,221
David Ebsworth, Ph.D.	104,284	4,916

(1) For further information, see "Principal Shareholders."

(2) Includes Vivo Ventures Fund VII, L.P., Vivo Ventures VII Affiliates Fund, L.P., Vivo Ventures Fund VI, L.P., and Vivo Ventures Fund VI Affiliates Fund, L.P., or collectively, Vivo Capital. Mahendra Shah, a member of our board of directors, is a Managing Director of Vivo Capital.

(3) Rishi Gupta, a member of our board of directors, is a Private Equity Partner at OrbiMed LLC.

(4) Andrew Sinclair, a member of our board of directors, is a Partner and Portfolio Manager at Abingworth LLP.

Registration Rights Agreement

In connection with the July Placement, we entered into a registration rights agreement that provided certain shelf and demand registration rights to Abingworth Bioventures VI, LP, or Abingworth, Growth Equity Opportunities Fund IV, LLC, OrbiMed Private Investments VI, LP, or OrbiMed, and Vivo Capital, with respect to our ordinary shares currently held by them and issuable to them upon the exercise of our warrants, which rights are described below.

Shelf Registration Rights

At any time beginning not later than the later of (i) 180 days following the date of this prospectus or (ii) five business days after the expiration of the lock-up agreement entered into by our directors, officers, and securityholders in connection with the global offering, or the Commencement Date, we are required to file a shelf registration covering the resale of all of the registrable securities under the registration rights agreement pursuant to Rule 415 under the Securities Act (or any successor or similar rule), to use commercially reasonable efforts to have the registration statement declared effective as promptly as practicable and to maintain an effective shelf registration until all of the registrable securities pursuant to the registration rights agreement shall have been sold under such shelf registration or cease to be registrable securities. These registration rights are subject to specified conditions and limitations.

Demand Registration Rights

At any time after the Commencement Date, the holders of at least a majority of the registrable securities have the right to demand that we effect an underwritten public offering of the registrable securities pursuant to an effective registration statement under the Securities Act. These registration rights are subject to specified conditions and limitations including the right of the underwriters, if any, to limit the number of shares included in any such registration under specified circumstances. Upon such a request, we are required to use commercially reasonable efforts to effect the public offering.

Expenses of Registration

We will pay all expenses relating to any registration under the registration rights agreement, other than selling commission, discounts or brokerage fees and stock transfer taxes, subject to specified conditions and limitations.

Termination of Registration Rights

The registration rights granted under the registration rights agreement shall terminate upon the earlier to occur of (i) the fifth anniversary of the closing of the global offering and (ii) the date on which there are no registrable securities remaining pursuant to the registration rights agreement.

Relationship Agreements

In June 2016, we entered into relationship agreements with each of Vivo Capital, OrbiMed, Arix Bioscience plc and Arthurian Life Sciences SPV GP Limited, or Arix and Arthurian, and Abingworth, each of which hold 5% or more of our ordinary shares, pursuant to which our relationship with such parties is regulated and their influence over our corporate actions and activities, and the outcome of general matters pertaining to us, are limited. Pursuant to the relationship agreements, we also agreed to appoint representatives designated by Vivo Capital, OrbiMed, Arix and Arthurian, and Abingworth to our board of directors, who are Dr. Mahendra Shah, Mr. Rishi Gupta, Dr. Ken Cunningham and Dr. Andrew Sinclair, respectively. The relationship Agreement with Arix and Arthurian was terminated in January 2017. The

obligations of the parties under the remaining respective relationship agreements will continue in effect after the global offering, and the respective appointment rights under the remaining relationship agreements will automatically terminate upon (i) Vivo Capital, OrbiMed or Abingworth (or any of their associates), as applicable, ceasing to beneficially hold 6.5% of our issued ordinary shares, or (ii) our ordinary shares ceasing to be admitted to AIM. In addition, each of the relationship agreements will automatically terminate upon the first date which Vivo Capital, OrbiMed, or Abingworth, as applicable, cease to have certain rights and obligations under the relationship agreements.

Management Rights Letter

In June 2016, we entered into a management rights letter with Novo A/S, or Novo, which holds more than 5% of our ordinary shares, pursuant to which Novo may designate a non-voting observer to our board of directors. This agreement will terminate upon the earlier of the closing of the global offering or when Novo ceases to hold 50% of our ordinary shares held by Novo upon the closing of the July Placement.

Agreement with Arthurian Life Sciences

In March 2014, we entered into a subscription and shareholders agreement, or the Arthurian Agreement, with Arthurian pursuant to which Arthurian purchased through the Wales Life Sciences Investment Fund LP, or WLSIF, 4,200,000 ordinary shares at a price per share of £1.1 for total aggregate proceeds of £4.6 million. Under the Arthurian Agreement, we agreed to locate and conduct some of our business in Wales and to engage Simbec-Orion Group, or Simbec-Orion, a contract research organization, to conduct three of our clinical studies.

Agreements with Our Executive Officers & Directors

We have entered into employment agreements with certain of our executive officers and service agreements with our non-employee directors. See "Management — Compensation."

Indemnification Agreements

We have entered into indemnification agreements with each of our directors and executive officers. See "Management — Insurance and Indemnification."

Related Person Transaction Policy

In connection with the global offering, we have adopted a related person transaction policy.

DESCRIPTION OF SHARE CAPITAL AND ARTICLES OF ASSOCIATION

General

We were incorporated as a public limited company with the legal name Isis Resources plc under the laws of England and Wales on February 24, 2005 with the company number 5375156. In September 2006, we acquired Rhinopharma Limited, a company incorporated under the laws of the province of British Columbia, Canada and changed our name to Verona Pharma plc. Our registered office is One Central Square, Cardiff, CF10 1FS. The principal legislation under which we operate and our shares are issued is the Companies Act 2006.

As of March 31, 2017, our issued share capital was £2,568,053. The nominal value of our ordinary shares is £0.05 per share. Each issued ordinary share is fully paid.

Ordinary Shares

In accordance with the Articles, the following summarizes the rights of holders of our ordinary shares:

- each holder of our ordinary shares is entitled to one vote per ordinary share on all matters to be voted on by shareholders generally;
- the holders of the ordinary shares shall be entitled to receive notice of, attend, speak and vote at our general meetings; and
- holders of our ordinary shares are entitled to receive such dividends as are recommended by our directors and declared by our shareholders.

Registered Shares

We are required by the Companies Act 2006 to keep a register of our shareholders. Under English law, the ordinary shares are deemed to be issued when the name of the shareholder is entered in our share register. The share register therefore is prima facie evidence of the identity of our shareholders, and the shares that they hold. The share register generally provides limited, or no, information regarding the ultimate beneficial owners of our ordinary shares. Our share register is maintained by our registrar, Computershare Investor Services plc.

Holders of our ADSs will not be treated as one of our shareholders and their names will therefore not be entered in our share register. The depositary, the custodian or their nominees will be the holder of the shares underlying our ADSs. For discussion on our ADSs and ADS holder rights see "Description of American Depository Shares" in this prospectus. Holders of our ADSs have a right to receive the ordinary shares underlying their ADSs as discussed in "Description of American Depository Shares" in this prospectus.

Under the Companies Act 2006, we must enter an allotment of shares in our share register as soon as practicable and in any event within two months of the allotment. We will perform all procedures necessary to update the share register to reflect the ordinary shares being sold in the global offering and shareholder private placement, including updating the share register with the number of ordinary shares to be issued to the depositary upon the closing of the U.S. offering. We also are required by the Companies Act 2006 to register a transfer of shares (or give the transferee notice of and reasons for refusal) as soon as practicable and in any event within two months of receiving notice of the transfer.

We, any of our shareholders or any other affected person may apply to the court for rectification of the share register if:

- the name of any person, without sufficient cause, is wrongly entered in or omitted from our register of members; or

- there is a default or unnecessary delay in entering on the register the fact of any person having ceased to be a member or on which we have a lien, provided that such refusal does not prevent dealings in the shares taking place on an open and proper basis.

Preemptive Rights

English law generally provides shareholders with preemptive rights when new shares are issued for cash; however, it is possible for the articles of association, or shareholders in general meeting, to exclude preemptive rights. Such an exclusion of preemptive rights may be for a maximum period of up to five years from the date of adoption of the articles of association, if the exclusion is contained in the articles of association, or from the date of the shareholder resolution, if the exclusion is by shareholder resolution. In either case, this exclusion would need to be renewed by our shareholders upon its expiration (i.e., at least every five years). On July 22, 2016, our shareholders approved the exclusion of preemptive rights for a period of five years from the date of approval, which exclusion will need to be renewed upon expiration (i.e., at least every five years) to remain effective, but may be sought more frequently for additional five-year terms (or any shorter period). On February 8, 2017, our shareholders approved the exclusion of preemptive rights for the allotment of ordinary shares in connection with the global offering.

Options

As of March 31, 2017, there are options to purchase 2,804,000 ordinary shares outstanding with a weighted average exercise price of £1.90 per share. The options lapse after ten years from the date of the grant.

Warrants

As of March 31, 2017, there are warrants to subscribe for 12,646,370 ordinary shares outstanding, exercisable at a weighted average exercise price of £1.7174 per share. In connection with the July Placement, we issued warrants to purchase up to 12,446,370 ordinary shares at an exercise price of £1.7238 per ordinary share. Each warrant is exercisable beginning upon the closing of the global offering and will expire on the fifth anniversary of the closing of the global offering. On August 6, 2014, we issued warrants to subscribe for 200,000 ordinary shares to our nominated advisor, which are exercisable at a weighted average exercise price of £1.317 per share and expire on August 5, 2018.

Capital Reorganization

On February 10, 2017, we effected a 50-for-one share consolidation in which we consolidated every 50 existing ordinary shares of nominal value £0.001 each in our issued share capital into one ordinary shares of nominal value £0.05 each.

Articles of Association

Shares and Rights Attaching to Them

Objects

The objects of our company are unrestricted.

Share Rights

Subject to any special rights attaching to shares already in issue, our shares may be issued with or have attached to them any preferred, deferred or other special rights or privileges or be subject to such restrictions as we may resolve by ordinary resolution of the shareholders or decision of our board.

Voting Rights

Without prejudice to any special rights, privileges or restrictions as to voting rights attached to any shares forming part of our share capital from time to time, the voting rights attaching to shares are as follows:

- on a show of hands, every shareholder who (being an individual) is present in person and (being a corporation) is present by a duly authorized representative shall have one vote;
- on a show of hands, each proxy present in person has one vote for and one vote against a resolution if the proxy has been duly appointed by more than one shareholder and the proxy has been instructed by one or more of those shareholders to vote for the resolution and by one or more other of those shareholders to vote against it;
- on a show of hands, each proxy present in person has one vote for and one vote against a resolution if the proxy has been duly appointed by more than one shareholder entitled to vote on the resolution and either: (1) the proxy has been instructed by one or more of those shareholders to vote for the resolution and has been given any discretion by one or more other of those shareholders to vote and the proxy exercises that discretion to vote against it; or (2) the proxy has been instructed by one or more of those shareholders to vote against the resolution and has been given any discretion by one or more other of those shareholders to vote and the proxy exercises that discretion to vote for it; and
- on a poll every shareholder who is present in person or by proxy shall have one vote for each share of which he is the holder.

At any general meeting a resolution put to the vote of the meeting shall be decided on a show of hands unless a poll is demanded. Subject to the provisions of the Companies Act 2006, as described in "Differences in Corporate Law — Voting Rights" in this prospectus, a poll may be demanded by:

- the chairman of the meeting;
- at least five shareholders present in person or by proxy and entitled to vote;
- any shareholder(s) present in person or by proxy and representing in the aggregate not less than one-tenth of the total voting rights of all shareholders having the right to attend and vote at the meeting (excluding the shares held in treasury); or
- any shareholder(s) present in person or by proxy and holding shares conferring a right to attend and vote at the meeting on which there have been paid up sums in the aggregate equal to not less than one-tenth of the total sums paid up on all shares conferring that right (excluding the shares held in treasury).

Restrictions on Voting

No shareholder shall be entitled to vote at any general meeting or at any separate class meeting in respect of any share held by him unless all calls or other sums payable by him in respect of that share have been paid.

The board may from time to time make calls upon the shareholders in respect of any money unpaid on their shares and each shareholder shall (subject to at least 14 days' notice specifying the time or times and place of payment) pay at the time or times so specified the amount called on his shares.

Dividends

We may by ordinary resolution of shareholders declare dividends out of profits available for distribution in accordance with the respective rights of shareholders but no such dividend shall exceed the amount recommended by the directors. The board may from time to time pay shareholders such interim dividends as appear to the board to be justified by our profits and, if at any time, our share capital is divided into different classes the board may pay such interim dividends in respect of those shares which confer on the holders thereof deferred or non-preferential rights with regard to dividends.

Subject to any special rights attaching to or the terms of issue of any share, all dividends shall be declared and paid according to the amounts paid up on the shares and shall be apportioned and paid pro rata

according to the amounts paid up on the shares during any part or parts of the period in respect of which the dividend is paid.

No dividend or other moneys payable by us on or in respect of any share shall bear interest against us. Any dividend unclaimed after a period of 12 years from the date such dividend became due for payment shall, if the Board so resolved, be forfeited and shall revert to us.

Dividends may be declared or paid in any currency and the board may decide the rate of exchange for any currency conversions that may be required, and how any costs involved are to be met, in relation to the currency of any dividend.

Any general meeting declaring a dividend may by ordinary resolution of shareholders, upon the recommendation of the board, direct payment or satisfaction of such dividend wholly or in part by the distribution of specific assets other than cash, and in particular of paid up shares or debentures of any other company. The directors may, if authorized by ordinary resolution of shareholders, offer any holders of ordinary shares the right to elect to receive in lieu of a dividend an allotment of ordinary shares credited as fully paid up, subject to such exclusions as the Board may deem necessary or desirable.

No shareholder shall be entitled to receive any dividend or other distribution in respect of any share held by him unless all calls or other sums payable by him in respect of that share have been paid.

Change of Control

There is no specific provision in our articles of association that would have the effect of delaying, deferring or preventing a change of control.

Distributions on Winding Up

On a winding up, the liquidator may, with the consent by a special resolution of shareholders and any other resolution of the shareholders (excluding us to the extent we are a shareholder by virtue only of our holding of shares as treasury shares) in proportion to their shareholdings in specie or in kind or sanction of the court required by the Companies Act 2006 and/or the Insolvency Act 1986, divide amongst the shareholders the whole or any part of our assets (whether they shall consist of property of the same kind or not) and may set such values as he deems fair upon any property to be divided and may determine how such division shall be carried out as between the shareholders or different classes of shareholder. The liquidator may vest the whole or any part of such assets in trustees upon such trusts for the benefit of the shareholders as the liquidator shall think fit, but no shareholder shall be compelled to accept any shares or other assets upon which there is any liability or potential liability.

Variation of Rights

All or any of the rights and restrictions attached to any class of shares issued may be altered, added to or revoked with the consent in writing of the holders of not less than three-fourths in nominal value of the issued shares of that class (excluding any shares held as treasury shares) or by special resolution passed at a separate general meeting of the holders of such shares, subject to the Companies Act 2006 and the terms of their issue. The Companies Act 2006 provides a right to object to the variation of the share capital by the shareholders who did not vote in favor of the variation. Should an aggregate of 15% of the shareholders of the issued shares in question apply to the court to have the variation cancelled, the variation shall have no effect unless and until it is confirmed by the court.

Alteration to Share Capital

We may, by ordinary resolution of shareholders, consolidate and divide all or any of our share capital into shares of larger amount than our existing shares, or sub-divide our shares or any of them into shares of a smaller amount. We may, by special resolution of shareholders, confirmed by the court, reduce our share capital or any capital redemption reserve or any share premium account in any manner authorized by the Companies Act 2006. We may redeem or purchase all or any of our shares as described in "—Other U.K. Law Considerations — Purchase of Own Shares."

Preemption Rights

In certain circumstances, our shareholders may have statutory preemption rights under the Companies Act 2006 in respect of the allotment of new shares as described in "— Preemptive Rights" and "— Differences in Corporate Law — Preemptive Rights" in this prospectus.

Transfer of Shares

Any certificated shareholder may transfer all or any of his shares by an instrument of transfer in the usual common form or in any other manner which is permitted by the Companies Act 2006 and approved by the board. Any written instrument of transfer shall be signed by or on behalf of the transferor and (in the case of a partly paid share) the transferee.

All transfers of uncertificated shares shall be made in accordance with and subject to the provisions of the Uncertificated Securities Regulations 2001 and the facilities and requirements of its relevant system. The Uncertificated Securities Regulations 2001 permit shares to be issued and held in uncertificated form and transferred by means of a computer-based system.

The board may decline to register any transfer of any share:

- which is not a fully paid share;
- to a person known to be a minor, bankrupt or person who is mentally disordered or a patient for the purpose of any statute relating to mental health;
- to an entity which is not a natural or legal person;
- unless any written instrument of transfer, duly stamped, is lodged with us at our registered office or such other place as the board may appoint accompanied by the certificate for the shares to which it relates;
- unless there is provided such evidence as the board may reasonably require to show the right of the transferor to make the transfer and if the instrument of transfer is executed by some other person on his behalf, the authority of that person to do so;
- where the transfer is in respect of more than one class of share; and
- in the case of a transfer to joint holders, the number of joint holders to whom the share is to be transferred exceeds four.

If the board declines to register a transfer it shall, as soon as practicable and in any event within two months after the date on which the transfer is lodged, send to the transferee notice of the refusal, together with reasons for the refusal.

CREST

To be traded on AIM, securities must be able to be transferred and settled through the CREST system. CREST is a computerized paperless share transfer and settlement system which allows securities to be transferred by electronic means, without the need for a written instrument of transfer. The Articles are consistent with CREST membership and, amongst other things, allow for the holding and transfer of shares in uncertificated form.

Shareholder Meetings

Annual General Meetings

In accordance with the Companies Act 2006, we are required in each year to hold an annual general meeting in addition to any other general meetings in that year and to specify the meeting as such in the notice convening it. The annual general meeting shall be convened whenever and wherever the board sees fit, subject to the requirements of the Companies Act 2006, as described in "— Differences in Corporate Law — Annual General Meeting" and "— Differences in Corporate Law — Notice of General Meetings" in this prospectus.

Notice of General Meetings

The arrangements for the calling of general meetings are described in "— Differences in Corporate Law — Notice of General Meetings" in this prospectus.

Quorum of General Meetings

No business shall be transacted at any general meeting unless a quorum is present. At least two shareholders present in person or by proxy and entitled to vote shall be a quorum for all purposes.

Class Meetings

The provisions in the Articles relating to general meetings apply to every separate general meeting of the holders of a class of shares except that:

- the quorum for such class meeting shall be two holders in person or by proxy representing not less than one-third in nominal value of the issued shares of the class (excluding any shares held in treasury);
- at the class meeting, a holder of shares of the class present in person or by proxy may demand a poll and shall on a poll be entitled to one vote for every share of the class held by him; and
- if at any adjourned meeting of such holders a quorum is not present at the meeting, one holder of shares of the class present in person or by proxy at an adjourned meeting constitutes a quorum.

Directors

Number of Directors

We may not have less than two directors on the board of directors. We may, by ordinary resolution of the shareholders, vary the minimum and maximum number of directors from time to time.

Appointment of Directors

Subject to the provisions of the Articles, we may, by ordinary resolution of the shareholders, elect any person to be a director, either to fill a casual vacancy or as an addition to the existing board. However, any person that is not a director retiring from the existing board must be recommended by a shareholder not less than seven and not more than 21 days before the day of the appointment in order to be eligible for election.

Without prejudice to the power to appoint any person to be a director by shareholder resolution, the board has power to appoint any person to be a director, either to fill a casual vacancy or as an addition to the existing board but so that the total number of directors does not exceed the maximum number fixed by or in accordance with the Articles.

Any director appointed by the board will hold office only until the earlier to occur of the close of the next following annual general meeting and someone being appointed in his stead at that meeting. Such a director is eligible for re-election at that meeting but shall not be taken into account in determining the directors or the number of directors who are to retire by rotation at such meeting.

Rotation of Directors

At every annual general meeting, one-third of the directors or, if their number is not a multiple of three, then the number nearest to and not exceeding one-third, shall retire from office.

The directors to retire on each occasion shall be those subject to retirement by rotation who have been longest in office since their last election, but as between persons who became or were re-elected directors on the same day those to retire shall (unless they otherwise agree amongst themselves) be determined by lot.

A director who retires at the annual general meeting shall be eligible for re-election.

The shareholders may, at the meeting at which a director retires, fill the vacated office by electing a person and in default the retiring director shall, if willing to continue to act, be deemed to have been re-elected,

unless at such meeting it is expressly resolved not to fill such vacated office or unless a resolution for the re-election of such director shall have been put to the meeting and lost.

Directors' Interests

The directors may authorize, to the fullest extent permitted by law, any matter proposed to them which would otherwise result in a director infringing his duty to avoid a situation in which he has, or can have, a direct or indirect interest that conflicts, or possibly may conflict, with our interests. A director shall not, save as otherwise agreed by him, be accountable to us for any benefit which he derives from any matter authorized by the directors and any contract, transaction or arrangement relating thereto shall not be liable to be avoided on the grounds of any such benefit.

Subject to the requirements under sections 175, 177 and 182 of the Companies Act 2006, a director who is any way, whether directly or indirectly, interested in a proposed or existing transaction or arrangement with us shall declare the nature of his interest at a meeting of the directors.

In the case of interests arising where a director is in any way, directly or indirectly, interested in (a) a proposed transaction or arrangement with us or (b) a transaction or arrangement that has been entered into by us and save as otherwise provided by the Articles, such director shall not vote at a meeting of the board or of a committee of the board on any resolution concerning such matter in which he has a material interest (otherwise than by virtue of his interest in shares, debentures or other securities of, or otherwise in or through, us) unless his interest or duty arises only because the case falls within one or more of the following paragraphs:

- the resolution relates to the giving of any security, guarantee or indemnity to the director in respect of money lent or obligations incurred by the director at the request of or for the benefit of us or our subsidiaries;
- the resolution relates to the giving to a third party of a security or indemnity in respect of a debt or obligation of ours or any of our subsidiaries for which the director or a person connected with him has assumed responsibility in whole or part under a guarantee or indemnity or by the giving of security;
- his interest arises by virtue of any offer of shares or debentures or other securities by us or our subsidiaries for subscription or purchase in which offer the director is or may be entitled to participate as a holder of securities or in the director is interested as a participant in the underwriting or sub-underwriting thereof;
- the resolution relates in any way to any other company in which he is interested, directly or indirectly and whether as an officer or shareholder or otherwise howsoever, provided that he and any persons connected with him do not to his knowledge hold an interest in shares representing one per cent or more of any class of the equity share capital of such company or of the voting rights available to shareholder of such company;
- the resolution relates in any way to an arrangement in whole or in part for the benefit of our employees or any employees of our subsidiaries which does not award him as such any privilege or benefit not generally awarded to the employees to whom such arrangement relates;
- the resolution relates to the adoption, modification or operation of a superannuation fund or retirement, death or disability benefits scheme or employees' share scheme under which he may benefit and which has been approved by or is subject to and conditional upon approval by the U.K. tax authorities for taxation purposes and which does not award him any privilege or benefit not awarded to the employee to whom the scheme relates; or
- the resolution relates in any way to the purchase or maintenance for the directors of insurance against any liability which by virtue of any rule of law would otherwise attach to all or any of them in respect of any negligence, default, breach of duty or breach of trust in relation to us or any of our subsidiaries.

A director shall not be counted in the quorum present at a meeting in relation to a resolution on which he is not entitled to vote.

If a question arises at a meeting of the board or of a committee of the board as to the right of a director to vote or be counted in the quorum, and such question is not resolved by his voluntarily agreeing to abstain from voting or not to be counted in the quorum, the question shall be determined by a majority of votes of the remaining directors present at the meeting or if there is an equality of votes, the Chairman shall have a second or casting vote and his ruling in relation to any director other than himself shall be final and conclusive except in a case where the nature or extent of the interest of the director concerned has not been fairly disclosed.

Directors' Fees and Remuneration

Each of the directors shall be paid a fee at such rate as may from time to time be determined by the board (or for the avoidance of doubt any duly authorized committee of the board) provided that the aggregate of all such fees so paid to directors shall not exceed £500,000 per annum, or such higher amount as may from time to time be determined by ordinary resolution of shareholders.

Each director may be paid his traveling, hotel and incidental expenses of attending and returning from meetings of the board or committees of the board or general meetings or separate meetings of the holders class of shares or of debentures and shall be paid all expenses properly incurred by him in the conduct of the Company's business or in the discharge of his duties as a director. Any director who, by request, performs special or extra services which in the opinion of the board go beyond the ordinary duties of a director may be paid such extra remuneration as the board may determine.

An executive director shall receive such remuneration as the board may determine, and either in addition to or in lieu of his remuneration as a director as detailed above.

Borrowing Powers

The board may exercise all the powers to borrow money and to mortgage or charge our undertaking, property and assets (present or future) and uncalled capital or any part thereof and to issue debentures and other securities, whether outright or as collateral security for any debt, liability or obligation of us or of any third party.

Indemnity

Every director, alternate director, other officer or auditor of our group may be indemnified against all costs, charges, expenses, losses and liabilities incurred by him in connection with any negligence, default, breach of duty or breach of trust by him in relation to us or in relation to the actual or purported execution or discharge of his duties or the exercise or purported exercise of his powers or otherwise in relation to such members of our group.

Other U.K. Law Considerations

Notification of Voting Rights

A shareholder in a public company incorporated in the United Kingdom whose shares are admitted to trading on AIM is required pursuant to Rule 5 of the Disclosure and Transparency Rules of the U.K. Financial Conduct Authority to notify us of the percentage of his voting rights if the percentage of voting rights which he holds as a shareholder or through his direct or indirect holding of financial instruments (or a combination of such holdings) reaches, exceeds or falls below 3%, 4%, 5%, and each 1% threshold thereafter up to 100% as a result of an acquisition or disposal of shares or financial instruments.

Mandatory Purchases and Acquisitions

Pursuant to Sections 979 to 991 of the Companies Act 2006, where a takeover offer has been made for us and the offeror has acquired or unconditionally contracted to acquire not less than 90% in value of the shares to which the offer relates and not less than 90% of the voting rights carried by those shares, the offeror may give notice to the holder of any shares to which the offer relates which the offeror has not

acquired or unconditionally contracted to acquire that he wishes to acquire, and is entitled to so acquire, those shares on the same terms as the general offer. The offeror would do so by sending a notice to the outstanding minority shareholders telling them that it will compulsorily acquire their shares. Such notice must be sent within three months of the last day on which the offer can be accepted in the prescribed manner. The squeeze-out of the minority shareholders can be completed at the end of six weeks from the date the notice has been given, subject to the minority shareholders failing to successfully lodge an application to the court to prevent such squeeze-out any time prior to the end of those six weeks following which the offeror can execute a transfer of the outstanding shares in its favor and pay the consideration to us, which would hold the consideration on trust for the outstanding minority shareholders. The consideration offered to the outstanding minority shareholders whose shares are compulsorily acquired under the Companies Act 2006 must, in general, be the same as the consideration that was available under the takeover offer.

Sell Out

The Companies Act 2006 also gives our minority shareholders a right to be bought out in certain circumstances by an offeror who has made a takeover offer for all of our shares. The holder of shares to which the offer relates, and who has not otherwise accepted the offer, may require the offeror to acquire his shares if, prior to the expiry of the acceptance period for such offer, (i) the offeror has acquired or unconditionally agreed to acquire not less than 90% in value of the voting shares, and (ii) not less than 90% of the voting rights carried by those shares. The offeror may impose a time limit on the rights of minority shareholders to be bought out that is not less than three months after the end of the acceptance period. If a shareholder exercises his rights to be bought out, the offeror is required to acquire those shares on the terms of this offer or on such other terms as may be agreed.

Disclosure of Interest in Shares

Pursuant to Part 22 of the Companies Act 2006, we are empowered by notice in writing to any person whom we know or have reasonable cause to believe to be interested in our shares, or at any time during the three years immediately preceding the date on which the notice is issued has been so interested, within a reasonable time to disclose to us particulars of that person's interest and (so far as is within his knowledge) particulars of any other interest that subsists or subsisted in those shares.

Under the Articles, if a person defaults in supplying us with the required particulars in relation to the shares in question, or default shares within the prescribed period, the directors may by notice direct that:

- in respect of the default shares, the relevant member shall not be entitled to attend or vote (either in person or by proxy) at any general meeting or of a general meeting of the holders of a class of shares or upon any poll or to exercise any right conferred by the default shares;
- where the default shares represent at least 0.25% of their class, (a) any dividend or other money payable in respect of the default shares shall be retained by us without liability to pay interest, and/or (b) no transfers by the relevant member of any default shares may be registered (unless the member himself is not in default and the member proves to the satisfaction of the Board that no person in default as regards supplying such information is interested in any of the default shares); and/or
- any shares held by the relevant member in uncertificated form shall be converted into certificated form and that member shall not after that be entitled to convert all or any shares held by him into uncertificated form (unless the member himself is not in default as regards supplying the information required and the member proves to the satisfaction of the board that, after due and careful inquiry, the member is satisfied that none of the shares he is proposing to convert into uncertificated form is a default share).

Purchase of Own Shares

Under English law, a limited company may only purchase its own shares out of the distributable profits of the company or the proceeds of a fresh issue of shares made for the purpose of financing the purchase,

provided that they are not restricted from doing so by their articles. A limited company may not purchase its own shares if, as a result of the purchase, there would no longer be any issued shares of the company other than redeemable shares or shares held as treasury shares. Shares must be fully paid in order to be repurchased.

Subject to the above, we may purchase our own shares in the manner prescribed below. We may make a market purchase of our own fully paid shares pursuant to an ordinary resolution of shareholders. The resolution authorizing the purchase must:

- specify the maximum number of shares authorized to be acquired;
- determine the maximum and minimum prices that may be paid for the shares; and
- specify a date, not being later than five years after the passing of the resolution, on which the authority to purchase is to expire.

We may purchase our own fully paid shares otherwise than on a recognized investment exchange pursuant to a purchase contract authorized by resolution of shareholders before the purchase takes place. Any authority will not be effective if any shareholder from whom we propose to purchase shares votes on the resolution and the resolution would not have been passed if he had not done so. The resolution authorizing the purchase must specify a date, not being later than five years after the passing of the resolution, on which the authority to purchase is to expire.

Distributions and Dividends

Under the Companies Act 2006, before a company can lawfully make a distribution or dividend, it must ensure that it has sufficient distributable reserves (on a non-consolidated basis). The basic rule is that a company's profits available for the purpose of making a distribution are its accumulated, realized profits, so far as not previously utilized by distribution or capitalization, less its accumulated, realized losses, so far as not previously written off in a reduction or reorganization of capital duly made. The requirement to have sufficient distributable reserves before a distribution or dividend can be paid applies to us and to each of our subsidiaries that has been incorporated under English law.

It is not sufficient that we, as a public company, have made a distributable profit for the purpose of making a distribution. An additional capital maintenance requirement is imposed on us to ensure that the net worth of the company is at least equal to the amount of its capital. A public company can only make a distribution:

- if, at the time that the distribution is made, the amount of its net assets (that is, the total excess of assets over liabilities) is not less than the total of its called up share capital and undistributable reserves; and
- if, and to the extent that, the distribution itself, at the time that it is made, does not reduce the amount of the net assets to less than that total.

City Code on Takeovers and Mergers

As a public company incorporated in England and Wales with our registered office in England and Wales which has shares admitted to AIM, we are subject to the U.K. City Code on Takeovers and Mergers, or the City Code, which is issued and administered by the U.K. Panel on Takeovers and Mergers, or the Panel. The City Code provides a framework within which takeovers of companies subject to it are conducted. In particular, the City Code contains certain rules in respect of mandatory offers. Under Rule 9 of the City Code, if a person:

- acquires an interest in our shares which, when taken together with shares in which he or persons acting in concert with him are interested, carries 30% or more of the voting rights of our shares; or
- who, together with persons acting in concert with him, is interested in shares that in the aggregate carry not less than 30% and not more than 50% of the voting rights of our shares, and such persons, or any person acting in concert with him, acquires additional interests in shares that increase the percentage of shares carrying voting rights in which that person is interested,

the acquirer and depending on the circumstances, its concert parties, would be required (except with the consent of the Panel) to make a cash offer for our outstanding shares at a price not less than the highest price paid for any interests in the shares by the acquirer or its concert parties during the previous 12 months.

Exchange Controls

There are no governmental laws, decrees, regulations or other legislation in the United Kingdom that may affect the import or export of capital, including the availability of cash and cash equivalents for use by us, or that may affect the remittance of dividends, interest, or other payments by us to non-resident holders of our ordinary shares or ADSs, other than withholding tax requirements. There is no limitation imposed by English law or in the Articles on the right of non-residents to hold or vote shares.

Differences in Corporate Law

The applicable provisions of the Companies Act 2006 differ from laws applicable to U.S. corporations and their shareholders. Set forth below is a summary of certain differences between the provisions of the Companies Act 2006 applicable to us and the General Corporation Law of the State of Delaware relating to shareholders' rights and protections. This summary is not intended to be a complete discussion of the respective rights and it is qualified in its entirety by reference to Delaware law and English law.

	England and Wales	Delaware
Number of Directors	Under the Companies Act 2006, a public limited company must have at least two directors and the number of directors may be fixed by or in the manner provided in a company's articles of association.	Under Delaware law, a corporation must have at least one director and the number of directors shall be fixed by or in the manner provided in the bylaws.
Removal of Directors	Under the Companies Act 2006, shareholders may remove a director without cause by an ordinary resolution (which is passed by a simple majority of those voting in person or by proxy at a general meeting) irrespective of any provisions of any service contract the director has with the company, provided 28 clear days' notice of the resolution has been given to the company and its shareholders. On receipt of notice of an intended resolution to remove a director, the company must forthwith send a copy of the notice to the director concerned. Certain other procedural requirements under the Companies Act 2006 must also be followed such as allowing the director to make representations against his or her removal either at the meeting or in writing.	Under Delaware law, any director or the entire board of directors may be removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of directors, except (a) unless the certificate of incorporation provides otherwise, in the case of a corporation whose board of directors is classified, shareholders may effect such removal only for cause, or (b) in the case of a corporation having cumulative voting, if less than the entire board of directors is to be removed, no director may be removed without cause if the votes cast against his removal would be sufficient to elect him if then cumulatively voted at an election of the entire board of directors, or, if there are classes of directors, at an election of the class of directors of which he is a part.

	England and Wales	Delaware
Vacancies on the Board of Directors	Under English law, the procedure by which directors, other than a company's initial directors, are appointed is generally set out in a company's articles of association, provided that where two or more persons are appointed as directors of a public limited company by resolution of the shareholders, resolutions appointing each director must be voted on individually.	Under Delaware law, vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) or by a sole remaining director unless (a) otherwise provided in the certificate of incorporation or by-laws of the corporation or (b) the certificate of incorporation directs that a particular class of stock is to elect such director, in which case a majority of the other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.
Annual General Meeting	Under the Companies Act 2006, a public limited company must hold an annual general meeting in each six-month period following the company's annual accounting reference date.	Under Delaware law, the annual meeting of stockholders shall be held at such place, on such date and at such time as may be designated from time to time by the board of directors or as provided in the certificate of incorporation or by the bylaws.
General Meeting	Under the Companies Act 2006, a general meeting of the shareholders of a public limited company may be called by the directors. Shareholders holding at least 5% of the paid-up capital of the company carrying voting rights at general meetings (excluding nay paid up capital held as treasury shares) can require the directors to call a general meeting and, if the directors fail to do so within a certain period, may themselves convene a general meeting.	Under Delaware law, special meetings of the stockholders may be called by the board of directors or by such person or persons as may be authorized by the certificate of incorporation or by the bylaws.

	England and Wales	Delaware
Notice of General Meetings	Under the Companies Act 2006, 21 clear days' notice must be given for an annual general meeting and any resolutions to be proposed at the meeting. Subject to a company's articles of association providing for a longer period, at least 14 clear days' notice is required for any other general meeting. In addition, certain matters, such as the removal of directors or auditors, require special notice, which is 28 clear days' notice. The shareholders of a company may in all cases consent to a shorter notice period, the proportion of shareholders' consent required being 100% of those entitled to attend and vote in the case of an annual general meeting and, in the case of any other general meeting, a majority in number of the members having a right to attend and vote at the meeting, being a majority who together hold not less than 95% in nominal value of the shares giving a right to attend and vote at the meeting.	Under Delaware law, unless otherwise provided in the certificate of incorporation or bylaws, written notice of any meeting of the stockholders must be given to each stockholder entitled to vote at the meeting not less than ten nor more than 60 days before the date of the meeting and shall specify the place, date, hour, and purpose or purposes of the meeting.
Proxy	Under the Companies Act 2006, at any meeting of shareholders, a shareholder may designate another person to attend, speak and vote at the meeting on their behalf by proxy.	Under Delaware law, at any meeting of stockholders, a stockholder may designate another person to act for such stockholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period. A director of a Delaware corporation may not issue a proxy representing the director's voting rights as a director.

	England and Wales	Delaware
Pre-emptive Rights	Under the Companies Act 2006, "equity securities", being (i) shares in the company other than shares that, with respect to dividends and capital, carry a right to participate only up to a specified amount in a distribution ("ordinary shares") or (ii) rights to subscribe for, or to convert securities into, ordinary shares, proposed to be allotted for cash must be offered first to the existing equity shareholders in the company in proportion to the respective nominal value of their holdings, unless an exception applies or a special resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise in each case in accordance with the provisions of the Companies Act 2006.	Under Delaware law, shareholders have no preemptive rights to subscribe to additional issues of stock or to any security convertible into such stock unless, and except to the extent that, such rights are expressly provided for in the certificate of incorporation.
Authority to Allot	Under the Companies Act 2006, the directors of a company must not allot shares or grant of rights to subscribe for or to convert any security into shares unless an exception applies or an ordinary resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise in each case in accordance with the provisions of the Companies Act 2006.	Under Delaware law, if the corporation's charter or certificate of incorporation so provides, the board of directors has the power to authorize the issuance of stock. It may authorize capital stock to be issued for consideration consisting of cash, any tangible or intangible property or any benefit to the corporation or any combination thereof. It may determine the amount of such consideration by approving a formula. In the absence of actual fraud in the transaction, the judgment of the directors as to the value of such consideration is conclusive.
Liability of Directors and Officers	Under the Companies Act 2006, any provision, whether contained in a company's articles of association or any contract or otherwise, that purports to exempt a director of a company, to any extent, from any liability that would otherwise attach to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company is void.	Under Delaware law, a corporation's certificate of incorporation may include a provision eliminating or limiting the personal liability of a director to the corporation and its stockholders for damages arising from a breach of fiduciary duty as a director. However, no provision can limit the liability of a director for:

	England and Wales	Delaware
	Any provision by which a company directly or indirectly provides an indemnity, to any extent, for a director of the company or of an associated company against any liability attaching to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company of which he is a director is also void except as permitted by the Companies Act 2006, which provides exceptions for the company to (a) purchase and maintain insurance against such liability; (b) provide a "qualifying third party indemnity" (being an indemnity against liability incurred by the director to a person other than the company or an associated company or criminal proceedings in which he is convicted); and (c) provide a "qualifying pension scheme indemnity" (being an indemnity against liability incurred in connection with the company's activities as trustee of an occupational pension plan).	■ any breach of the director's duty of loyalty to the corporation or its stockholders; ■ acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law; ■ intentional or negligent payment of unlawful dividends or stock purchases or redemptions; or ■ any transaction from which the director derives an improper personal benefit.
Voting Rights	Under English law, unless a poll is demanded by the shareholders of a company or is required by the chairman of the meeting or the company's articles of association, shareholders shall vote on all resolutions on a show of hands. Under the Companies Act 2006, a poll may be demanded by (a) not fewer than five shareholders having the right to vote on the resolution; (b) any shareholder(s) representing not less than 10% of the total voting rights of all the shareholders having the right to vote on the resolution (excluding any voting rights attaching to treasury shares); or (c) any shareholder(s) holding shares in the company conferring a right to vote on the resolution (excluding any voting rights attaching to treasury shares) being shares on which an aggregate sum has been paid up equal to not less than 10% of the total sum paid up on all the shares conferring that right. A company's articles of association may provide more extensive rights for shareholders to call a poll.	Delaware law provides that, unless otherwise provided in the certificate of incorporation, each stockholder is entitled to one vote for each share of capital stock held by such stockholder.

	England and Wales	Delaware
	Under English law, an ordinary resolution is passed on a show of hands if it is approved by a simple majority (more than 50%) of the votes cast by shareholders present (in person or by proxy) and entitled to vote. If a poll is demanded, an ordinary resolution is passed if it is approved by holders representing a simple majority of the total voting rights of shareholders present, in person or by proxy, who, being entitled to vote, vote on the resolution. Special resolutions require the affirmative vote of not less than 75% of the votes cast by shareholders present, in person or by proxy, at the meeting.	
Shareholder Vote on Certain Transactions	The Companies Act 2006 provides for schemes of arrangement, which are arrangements or compromises between a company and any class of shareholders or creditors and used in certain types of reconstructions, amalgamations, capital reorganizations or takeovers. These arrangements require: ■ the approval at a shareholders' or creditors' meeting convened by order of the court, of a majority in number of shareholders or creditors representing 75% in value of the capital held by, or debt owed to, the class of shareholders or creditors, or class thereof present and voting, either in person or by proxy; and ■ the approval of the court.	Generally, under Delaware law, unless the certificate of incorporation provides for the vote of a larger portion of the stock, completion of a merger, consolidation, sale, lease or exchange of all or substantially all of a corporation's assets or dissolution requires: ■ the approval of the board of directors; and ■ approval by the vote of the holders of a majority of the outstanding stock or, if the certificate of incorporation provides for more or less than one vote per share, a majority of the votes of the outstanding stock of a corporation entitled to vote on the matter.

	England and Wales	Delaware
Standard of Conduct for Directors	Under English law, a director owes various statutory and fiduciary duties to the company, including: ■ to act in the way he considers, in good faith, would be most likely to promote the success of the company for the benefit of its members as a whole; ■ to avoid a situation in which he has, or can have, a direct or indirect interest that conflicts, or possibly conflicts, with the interests of the company; ■ to act in accordance with the company's constitution and only exercise his powers for the purposes for which they are conferred; ■ to exercise independent judgment; ■ to exercise reasonable care, skill and diligence; ■ not to accept benefits from a third party conferred by reason of his being a director or doing, or not doing, anything as a director; and ■ a duty to declare any interest that he has, whether directly or indirectly, in a proposed or existing transaction or arrangement with the company.	Delaware law does not contain specific provisions setting forth the standard of conduct of a director. The scope of the fiduciary duties of directors is generally determined by the courts of the State of Delaware. In general, directors have a duty to act without self-interest, on a well-informed basis and in a manner they reasonably believe to be in the best interest of the stockholders. Directors of a Delaware corporation owe fiduciary duties of care and loyalty to the corporation and to its shareholders. The duty of care generally requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself of all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he reasonably believes to be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. In general, but subject to certain exceptions, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. Delaware courts have also imposed a heightened standard of conduct upon directors of a Delaware corporation who take any action designed to defeat a threatened change in control of the corporation. In addition, under Delaware law, when the board of directors of a Delaware corporation approves the sale or break-up of a corporation, the board of directors may, in certain circumstances, have a duty to obtain the highest value reasonably available to the shareholders.

	England and Wales	Delaware
Stockholder Suits	Under English law, generally, the company, rather than its shareholders, is the proper claimant in an action in respect of a wrong done to the company or where there is an irregularity in the company's internal management. Notwithstanding this general position, the Companies Act 2006 provides that (i) a court may allow a shareholder to bring a derivative claim (that is, an action in respect of and on behalf of the company) in respect of a cause of action arising from a director's negligence, default, breach of duty or breach of trust and (ii) a shareholder may bring a claim for a court order where the company's affairs have been or are being conducted in a manner that is unfairly prejudicial to some of its shareholders.	Under Delaware law, a stockholder may initiate a derivative action to enforce a right of a corporation if the corporation fails to enforce the right itself. The complaint must: ■ state that the plaintiff was a stockholder at the time of the transaction of which the plaintiff complains or that the plaintiffs shares thereafter devolved on the plaintiff by operation of law; and ■ allege with particularity the efforts made by the plaintiff to obtain the action the plaintiff desires from the directors and the reasons for the plaintiff's failure to obtain the action; or ■ state the reasons for not making the effort. Additionally, the plaintiff must remain a stockholder through the duration of the derivative suit. The action will not be dismissed or compromised without the approval of the Delaware Court of Chancery.

DESCRIPTION OF AMERICAN DEPOSITARY SHARES

American Depositary Shares

Citibank, N.A., or Citibank, has agreed to act as the depositary for the ADSs. Citibank's depositary offices are located at 388 Greenwich Street, New York, New York 10013. ADSs represent ownership interests in securities that are on deposit with the depositary. ADSs may be represented by certificates that are commonly known as American Depositary Receipts, or ADRs. The depositary typically appoints a custodian to safekeep the securities on deposit. In this case, the custodian is Citibank, N.A., London Branch, located at 25 Canada Square, Canary Wharf, London, E14 5LB, United Kingdom.

We have appointed Citibank as depositary pursuant to a deposit agreement. A copy of the deposit agreement is on file with the SEC under cover of a registration statement on Form F-6. You may obtain a copy of the deposit agreement from the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549 and from the SEC's website (www.sec.gov). Please refer to registration number 333-217353 when retrieving such copy.

We are providing you with a summary description of the material terms of the ADSs and of your material rights as an owner of ADSs. Please remember that summaries by their nature lack the precision of the information summarized and that the rights and obligations of an owner of ADSs will be determined by reference to the terms of the deposit agreement and not by this summary. We urge you to review the deposit agreement in its entirety.

Each ADS represents the right to receive, and to exercise the beneficial ownership interests in, eight ordinary shares that are on deposit with the depositary and/or custodian. An ADS also represents the right to receive, and to exercise the beneficial interests in, any other property received by the depositary or the custodian on behalf of the owner of the ADS but that has not been distributed to the owners of ADSs because of legal restrictions or practical considerations. We and the depositary may agree to change the ADS-to-Share ratio by amending the deposit agreement. This amendment may give rise to, or change, the depositary fees payable by ADS owners. The custodian, the depositary and their respective nominees will hold all deposited property for the benefit of the holders and beneficial owners of ADSs. The deposited property does not constitute the proprietary assets of the depositary, the custodian or their nominees. Beneficial ownership in the deposited property will under the terms of the deposit agreement be vested in the beneficial owners of the ADSs. The depositary, the custodian and their respective nominees will be the record holders of the deposited property represented by the ADSs for the benefit of the holders and beneficial owners of the corresponding ADSs. A beneficial owner of ADSs may or may not be the holder of ADSs. Beneficial owners of ADSs will be able to receive, and to exercise beneficial ownership interests in, the deposited property only through the registered holders of the ADSs, the registered holders of the ADSs (on behalf of the applicable ADS owners) only through the depositary, and the depositary (on behalf of the owners of the corresponding ADSs) directly, or indirectly, through the custodian or their respective nominees, in each case upon the terms of the deposit agreement.

If you become an owner of ADSs, you will become a party to the deposit agreement and therefore will be bound to its terms and to the terms of any ADR that represents your ADSs. The deposit agreement and the ADR specify our rights and obligations as well as your rights and obligations as owner of ADSs and those of the depositary. As an ADS holder you appoint the depositary to act on your behalf in certain circumstances. The deposit agreement and the ADRs are governed by New York law. However, our obligations to the holders of ordinary shares will continue to be governed by the laws of England and Wales, which may be different from the laws in the United States.

In addition, applicable laws and regulations may require you to satisfy reporting requirements and obtain regulatory approvals in certain circumstances. You are solely responsible for complying with such reporting requirements and obtaining such approvals. Neither the depositary, the custodian, us or any of their or our

respective agents or affiliates shall be required to take any actions whatsoever on your behalf to satisfy such reporting requirements or obtain such regulatory approvals under applicable laws and regulations.

As an owner of ADSs, we will not treat you as one of our shareholders and you will not have direct shareholder rights. The depositary will hold on your behalf the shareholder rights attached to the ordinary shares underlying your ADSs. As an owner of ADSs you will be able to exercise the shareholders rights for the ordinary shares represented by your ADSs through the depositary only to the extent contemplated in the deposit agreement. To exercise any shareholder rights not contemplated in the deposit agreement you will, as an ADS owner, need to arrange for the cancellation of your ADSs and become a direct shareholder.

As an owner of ADSs, you may hold your ADSs either by means of an ADR registered in your name, through a brokerage or safekeeping account, or through an account established by the depositary in your name reflecting the registration of uncertificated ADSs directly on the books of the depositary (commonly referred to as the direct registration system or DRS). The direct registration system reflects the uncertificated (book-entry) registration of ownership of ADSs by the depositary. Under the direct registration system, ownership of ADSs is evidenced by periodic statements issued by the depositary to the holders of the ADSs. The direct registration system includes automated transfers between the depositary and The Depository Trust Company, or DTC, the central book-entry clearing and settlement system for equity securities in the United States. If you decide to hold your ADSs through your brokerage or safekeeping account, you must rely on the procedures of your broker or bank to assert your rights as ADS owner. Banks and brokers typically hold securities such as the ADSs through clearing and settlement systems such as DTC. The procedures of such clearing and settlement systems may limit your ability to exercise your rights as an owner of ADSs. Please consult with your broker or bank if you have any questions concerning these limitations and procedures. All ADSs held through DTC will be registered in the name of a nominee of DTC. This summary description assumes you have opted to own the ADSs directly by means of an ADS registered in your name and, as such, we will refer to you as the "holder." When we refer to "you," we assume the reader owns ADSs and will own ADSs at the relevant time.

The registration of the ordinary shares in the name of the depositary or the custodian shall, to the maximum extent permitted by applicable law, vest in the depositary or the custodian the record ownership in the applicable ordinary shares with the beneficial ownership rights and interests in such ordinary shares being at all times vested with the beneficial owners of the ADSs representing the ordinary shares. The depositary or the custodian shall at all times be entitled to exercise the beneficial ownership rights in all deposited property, in each case only on behalf of the holders and beneficial owners of the ADSs representing the deposited property.

Dividends and Other Distributions

As a holder of ADSs, you generally have the right to receive the distributions we make on the securities deposited with the custodian. Your receipt of these distributions may be limited, however, by practical considerations and legal limitations. Holders of ADSs will receive such distributions under the terms of the deposit agreement in proportion to the number of ADSs held as of the specified record date, after deduction the applicable fees, taxes and expenses.

Distributions of Cash

Whenever we make a cash distribution for the securities on deposit with the custodian, we will deposit the funds with the custodian. Upon receipt of confirmation of the deposit of the requisite funds, the depositary will arrange for the funds to be converted into U.S. dollars and for the distribution of the U.S. dollars to the holders, subject to the laws and regulations of England and Wales.

The conversion into U.S. dollars will take place only if practicable and if the U.S. dollars are transferable to the United States. The depositary will apply the same method for distributing the proceeds of the sale of any property (such as undistributed rights) held by the custodian in respect of securities on deposit.

The distribution of cash will be made net of the fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. The depositary will hold any cash amounts it is unable to distribute in a non-interest bearing account for the benefit of the applicable holders and beneficial owners of ADSs until the distribution can be effected or the funds that the depositary holds must be escheated as unclaimed property in accordance with the laws of the relevant states of the United States.

Distributions of Shares

Whenever we make a free distribution of ordinary shares for the securities on deposit with the custodian, we will deposit the applicable number of ordinary shares with the custodian. Upon receipt of confirmation of such deposit, the depositary will either distribute to holders new ADSs representing the ordinary shares deposited or modify the ADS-to-ordinary shares ratio, in which case each ADS you hold will represent rights and interests in the additional ordinary shares so deposited. Only whole new ADSs will be distributed. Fractional entitlements will be sold and the proceeds of such sale will be distributed as in the case of a cash distribution.

The distribution of new ADSs or the modification of the ADS-to-ordinary shares ratio upon a distribution of ordinary shares will be made net of the fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes or governmental charges, the depositary may sell all or a portion of the new ordinary shares so distributed.

No such distribution of new ADSs will be made if it would violate a law (*e.g.*, the U.S. securities laws) or if it is not operationally practicable. If the depositary does not distribute new ADSs as described above, it may sell the ordinary shares received upon the terms described in the deposit agreement and will distribute the proceeds of the sale as in the case of a distribution of cash.

Distributions of Rights

Whenever we intend to distribute rights to purchase additional ordinary shares, we will give prior notice to the depositary and we will assist the depositary in determining whether it is lawful and reasonably practicable to distribute rights to purchase additional ADSs to holders.

The depositary will establish procedures to distribute rights to purchase additional ADSs to holders and to enable such holders to exercise such rights if it is lawful and reasonably practicable to make the rights available to holders of ADSs, and if we provide all of the documentation contemplated in the deposit agreement (such as opinions to address the lawfulness of the transaction). You may have to pay fees, expenses, taxes and other governmental charges to subscribe for the new ADSs upon the exercise of your rights. The depositary is not obligated to establish procedures to facilitate the distribution and exercise by holders of rights to purchase new ordinary shares other than in the form of ADSs.

The depositary will *not* distribute the rights to you if:

- we do not timely request that the rights be distributed to you or we request that the rights not be distributed to you; or
- we fail to deliver satisfactory documents to the depositary; or
- it is not reasonably practicable to distribute the rights.

The depositary will sell the rights that are not exercised or not distributed if such sale is lawful and reasonably practicable. The proceeds of such sale will be distributed to holders as in the case of a cash distribution. If the depositary is unable to sell the rights, it will allow the rights to lapse.

Elective Distributions

Whenever we intend to distribute a dividend payable at the election of shareholders either in cash or in additional shares, we will give prior notice thereof to the depositary and will indicate whether we wish the elective distribution to be made available to you. In such case, we will assist the depositary in determining whether such distribution is lawful and reasonably practicable.

The depositary will make the election available to you only if it is reasonably practicable and if we have provided all of the documentation contemplated in the deposit agreement. In such case, the depositary will establish procedures to enable you to elect to receive either cash or additional ADSs, in each case as described in the deposit agreement.

If the election is not made available to you, you will receive either cash or additional ADSs, depending on what a shareholder in England and Wales would receive upon failing to make an election, as more fully described in the deposit agreement.

Other Distributions

Whenever we intend to distribute property other than cash, ordinary shares or rights to purchase additional ordinary shares, we will notify the depositary in advance and will indicate whether we wish such distribution to be made to you. If so, we will assist the depositary in determining whether such distribution to holders is lawful and reasonably practicable.

If it is reasonably practicable to distribute such property to you and if we provide all of the documentation contemplated in the deposit agreement, the depositary will distribute the property to the holders in a manner it deems practicable.

The distribution will be made net of fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes and governmental charges, the depositary may sell all or a portion of the property received.

The depositary will *not* distribute the property to you and will sell the property if:

- we do not request that the property be distributed to you or if we ask that the property not be distributed to you; or
- we do not deliver satisfactory documents to the depositary; or
- the depositary determines that all or a portion of the distribution to you is not reasonably practicable.

The proceeds of such a sale will be distributed to holders as in the case of a cash distribution.

Redemption

Whenever we decide to redeem any of the securities on deposit with the custodian, we will notify the depositary in advance. If it is practicable and if we provide all of the documentation contemplated in the deposit agreement, the depositary will provide notice of the redemption to the holders.

The custodian will be instructed to surrender the shares being redeemed against payment of the applicable redemption price. The depositary will convert the redemption funds received into U.S. dollars upon the terms of the deposit agreement and will establish procedures to enable holders to receive the net proceeds from the redemption upon surrender of their ADSs to the depositary. You may have to pay fees, expenses, taxes and other governmental charges upon the redemption of your ADSs. If less than all ADSs are being redeemed, the ADSs to be retired will be selected by lot or on a *pro rata* basis, as the depositary may determine.

Changes Affecting Ordinary Shares

The ordinary shares held on deposit for your ADSs may change from time to time. For example, there may be a change in nominal or par value, split-up, cancellation, consolidation or any other reclassification of such ordinary shares or a recapitalization, reorganization, merger, consolidation or sale of assets of the Company.

If any such change were to occur, your ADSs would, to the extent permitted by law, represent the right to receive the property received or exchanged in respect of the ordinary shares held on deposit. The depositary may in such circumstances deliver new ADSs to you, amend the deposit agreement, the ADRs and the applicable registration statement(s) on Form F-6, call for the exchange of your existing ADSs for new ADSs

and take any other actions that are appropriate to reflect as to the ADSs the change affecting the Shares. If the depositary may not lawfully distribute such property to you, the depositary may sell such property and distribute the net proceeds to you as in the case of a cash distribution.

Issuance of ADSs upon Deposit of Ordinary Shares

Upon completion of the U.S. offering, the ordinary shares being offered pursuant to this prospectus will be deposited by us with the custodian. Upon receipt of confirmation of such deposit, the depositary will issue ADSs to the underwriters named in this prospectus. After the completion of the U.S. offering, the ordinary shares that are being offered for sale pursuant to this prospectus will be deposited by us with the custodian. Upon receipt of confirmation of such deposit, the depositary will issue ADSs to the underwriters named in this prospectus.

After the closing of this offer, the depositary may create ADSs on your behalf if you or your broker deposit ordinary shares with the custodian. The depositary will deliver these ADSs to the person you indicate only after you pay any applicable issuance fees and any charges and taxes payable for the transfer of the ordinary shares to the custodian. Your ability to deposit ordinary shares and receive ADSs may be limited by U.S. and England and Wales legal considerations applicable at the time of deposit.

The issuance of ADSs may be delayed until the depositary or the custodian receives confirmation that all required approvals have been given and that the ordinary shares have been duly transferred to the custodian. The depositary will only issue ADSs in whole numbers.

When you make a deposit of ordinary shares, you will be responsible for transferring good and valid title to the depositary. As such, you will be deemed to represent and warrant that:

- the ordinary shares are duly authorized, validly issued, fully paid, non-assessable and legally obtained;
- all preemptive (and similar) rights, if any, with respect to such ordinary shares have been validly waived or exercised;
- you are duly authorized to deposit the ordinary shares;
- the ordinary shares presented for deposit are free and clear of any lien, encumbrance, security interest, charge, mortgage or adverse claim, and are not, and the ADSs issuable upon such deposit will not be, "restricted securities" (as defined in the deposit agreement); and
- the ordinary shares presented for deposit have not been stripped of any rights or entitlements.

If any of the representations or warranties are incorrect in any way, we and the depositary may, at your cost and expense, take any and all actions necessary to correct the consequences of the misrepresentations.

Transfer, Combination and Split Up of ADRs

As an ADR holder, you will be entitled to transfer, combine or split up your ADRs and the ADSs evidenced thereby. For transfers of ADRs, you will have to surrender the ADRs to be transferred to the depositary and also must:

- ensure that the surrendered ADR is properly endorsed or otherwise in proper form for transfer;
- provide such proof of identity and genuineness of signatures as the depositary deems appropriate;
- provide any transfer stamps required by the State of New York or the United States; and
- pay all applicable fees, charges, expenses, taxes and other government charges payable by ADR holders pursuant to the terms of the deposit agreement, upon the transfer of ADRs.

To have your ADRs either combined or split up, you must surrender the ADRs in question to the depositary with your request to have them combined or split up, and you must pay all applicable fees, charges and expenses payable by ADR holders, pursuant to the terms of the deposit agreement, upon a combination or split up of ADRs.

Withdrawal of Ordinary Shares Upon Cancellation of ADSs

As a holder, you will be entitled to present your ADSs to the depositary for cancellation and then receive the corresponding number of underlying ordinary shares at the custodian's offices. Your ability to withdraw the ordinary shares held in respect of the ADSs may be limited by U.S. and England and Wales considerations applicable at the time of withdrawal. In order to withdraw the ordinary shares represented by your ADSs, you will be required to pay to the depositary the fees for cancellation of ADSs and any charges and taxes payable upon the transfer of the ordinary shares. You assume the risk for delivery of all funds and securities upon withdrawal. Once canceled, the ADSs will not have any rights under the deposit agreement.

If you hold ADSs registered in your name, the depositary may ask you to provide proof of identity and genuineness of any signature and such other documents as the depositary may deem appropriate before it will cancel your ADSs. The withdrawal of the ordinary shares represented by your ADSs may be delayed until the depositary receives satisfactory evidence of compliance with all applicable laws and regulations. Please keep in mind that the depositary will only accept ADSs for cancellation that represent a whole number of securities on deposit.

You will have the right to withdraw the securities represented by your ADSs at any time except as a result of:

- temporary delays that may arise because (i) the transfer books for the ordinary shares or ADSs are closed, or (ii) ordinary shares are immobilized on account of a shareholders' meeting or a payment of dividends;
- obligations to pay fees, taxes and similar charges; and/or
- restrictions imposed because of laws or regulations applicable to ADSs or the withdrawal of securities on deposit.

The deposit agreement may not be modified to impair your right to withdraw the securities represented by your ADSs except to comply with mandatory provisions of law.

Voting Rights

As a holder, you generally have the right under the deposit agreement to instruct the depositary to exercise the voting rights for the ordinary shares represented by your ADSs. The voting rights of holders of ordinary shares are described in "Description of Share Capital and Articles of Association — Articles of Association" in this prospectus.

At our request, the depositary will distribute to you any notice of shareholders' meeting received from us together with information explaining how to instruct the depositary to exercise the voting rights of the securities represented by ADSs.

If the depositary timely receives voting instructions from a holder of ADSs, it will endeavor to vote the securities (in person or by proxy) represented by the holder's ADSs as follows:

- *In the event of voting by show of hands*, the depositary will vote (or cause the custodian to vote) all ordinary held on deposit at that time in accordance with the voting instructions received from a majority of holders of ADSs who provide timely voting instructions.
- *In the event of voting by poll*, the depositary will vote (or cause the custodian to vote) the ordinary shares held on deposit in accordance with the voting instructions received from the holders of ADSs.

Securities for which no voting instructions have been received will not be voted (except as otherwise contemplated herein). Please note that the ability of the depositary to carry out voting instructions may be limited by practical and legal limitations and the terms of the securities on deposit. We cannot assure you that you will receive voting materials in time to enable you to return voting instructions to the depositary in a timely manner.

Fees and Charges

As an ADS holder, you will be required to pay the following fees under the terms of the deposit agreement:

Service	Fee
Issuance of ADSs (e.g., an issuance of ADS upon a deposit of ordinary shares or upon a change in the ADS(s)-to-ordinary shares ratio), excluding ADS issuances as a result of distributions of ordinary shares	Up to $0.05 per ADS issued
Cancellation of ADSs (e.g., a cancellation of ADSs for delivery of deposited property or upon a change in the ADS(s)-to-ordinary shares ratio)	Up to $0.05 per ADS cancelled
Distribution of cash dividends or other cash distributions (e.g., upon a sale of rights and other entitlements)	Up to $0.05 per ADS held
Distribution of ADSs pursuant to (i) stock dividends or other free stock distributions, or (ii) exercise of rights to purchase additional ADSs	Up to $0.05 per ADS held
Distribution of securities other than ADSs or rights to purchase additional ADSs (e.g., upon a spin-off)	Up to $0.05 per ADS held
ADS Services	Up to $0.05 per ADS held on the applicable record date(s) established by the depositary

As an ADS holder you will also be responsible to pay certain charges such as:

- taxes (including applicable interest and penalties) and other governmental charges;
- the registration fees as may from time to time be in effect for the registration of ordinary shares on the share register and applicable to transfers of ordinary shares to or from the name of the custodian, the depositary or any nominees upon the making of deposits and withdrawals, respectively;
- certain cable, telex and facsimile transmission and delivery expenses;
- the expenses and charges incurred by the depositary in the conversion of foreign currency;
- the fees and expenses incurred by the depositary in connection with compliance with exchange control regulations and other regulatory requirements applicable to ordinary shares, ADSs and ADRs; and
- the fees and expenses incurred by the depositary, the custodian, or any nominee in connection with the servicing or delivery of deposited property.

ADS fees and charges payable upon (i) the issuance of ADSs, and (ii) the cancellation of ADSs are charged to the person to whom the ADSs are issued (in the case of ADS issuances) and to the person whose ADSs are cancelled (in the case of ADS cancellations). In the case of ADSs issued by the depositary into DTC, the ADS issuance and cancellation fees and charges may be deducted from distributions made through DTC, and may be charged to the DTC participant(s) receiving the ADSs being issued or the DTC participant(s) holding the ADSs being cancelled, as the case may be, on behalf of the beneficial owner(s) and will be charged by the DTC participant(s) to the account of the applicable beneficial owner(s) in accordance with the procedures and practices of the DTC participants as in effect at the time. ADS fees and charges in respect of distributions and the ADS service fee are charged to the holders as of the applicable ADS record date. In the case of distributions of cash, the amount of the applicable ADS fees and charges is deducted from the funds being distributed. In the case of (i) distributions other than cash and (ii) the ADS service

fee, holders as of the ADS record date will be invoiced for the amount of the ADS fees and charges and such ADS fees and charges may be deducted from distributions made to holders of ADSs. For ADSs held through DTC, the ADS fees and charges for distributions other than cash and the ADS service fee may be deducted from distributions made through DTC, and may be charged to the DTC participants in accordance with the procedures and practices prescribed by DTC and the DTC participants in turn charge the amount of such ADS fees and charges to the beneficial owners for whom they hold ADSs.

In the event of refusal to pay the depositary fees, the depositary may, under the terms of the deposit agreement, refuse the requested service until payment is received or may set off the amount of the depositary fees from any distribution to be made to the ADS holder. Certain of the depositary fees and charges (such as the ADS services fee) may become payable shortly after the closing of the ADS offering. Note that the fees and charges you may be required to pay may vary over time and may be changed by us and by the depositary. You will receive prior notice of such changes. The depositary may reimburse us for certain expenses incurred by us in respect of the ADR program, by making available a portion of the ADS fees charged in respect of the ADR program or otherwise, upon such terms and conditions as we and the depositary agree from time to time.

Amendments and Termination

We may agree with the depositary to modify the deposit agreement at any time without your consent. We undertake to give holders 30 days' prior notice of any modifications that would materially prejudice any of their substantial rights under the deposit agreement. We will not consider to be materially prejudicial to your substantial rights any modifications or supplements that are reasonably necessary for the ADSs to be registered under the Securities Act or to be eligible for book-entry settlement, in each case without imposing or increasing the fees and charges you are required to pay. In addition, we may not be able to provide you with prior notice of any modifications or supplements that are required to accommodate compliance with applicable provisions of law.

You will be bound by the modifications to the deposit agreement if you continue to hold your ADSs after the modifications to the deposit agreement become effective. The deposit agreement cannot be amended to prevent you from withdrawing the ordinary shares represented by your ADSs (except as permitted by law).

We have the right to direct the depositary to terminate the deposit agreement. Similarly, the depositary may in certain circumstances on its own initiative terminate the deposit agreement. In either case, the depositary must give notice to the holders at least 30 days before termination. Until termination, your rights under the deposit agreement will be unaffected.

Termination

After termination, the depositary will continue to collect distributions received (but will not distribute any such property until you request the cancellation of your ADSs) and may sell the securities held on deposit. After the sale, the depositary will hold the proceeds from such sale and any other funds then held for the holders of ADSs in a non-interest bearing account. At that point, the depositary will have no further obligations to holders other than to account for the funds then held for the holders of ADSs still outstanding (after deduction of applicable fees, taxes and expenses).

In connection with the termination of the deposit agreement, the depositary may, independently and without the need for any action by us, make available to holders a means to withdraw the ordinary shares and other deposited securities represented by their ADSs and to direct the deposit of such ordinary shares and other deposited securities into an unsponsored American depositary shares program established by the depositary, upon such terms and conditions as the depositary may deem reasonably appropriate, subject however, in each case, to satisfaction of the applicable registration requirements by the unsponsored American depositary shares program under the Securities Act, and to receipt by the depositary of payment of the applicable fees and charges of, and reimbursement of the applicable expenses incurred by, the depositary.

Books of Depositary

The depositary will maintain ADS holder records at its depositary office. You may inspect such records at such office during regular business hours but solely for the purpose of communicating with other holders in the interest of business matters relating to the ADSs and the deposit agreement.

The depositary will maintain in New York facilities to record and process the issuance, cancellation, combination, split-up and transfer of ADSs. These facilities may be closed from time to time, to the extent not prohibited by law.

Transmission of Notices, Reports and Proxy Soliciting Material

The depositary will make available for your inspection at its office all communications that it receives from us as a holder of deposited securities that we make generally available to holders of deposited securities. Subject to the terms of the deposit agreement, the depositary will send you copies of those communications or otherwise make those communications available to you if we ask it to.

Limitations on Obligations and Liabilities

The deposit agreement limits our obligations and the depositary's obligations to you. Please note the following:

- We and the depositary are obligated only to take the actions specifically stated in the deposit agreement without negligence or bad faith.
- The depositary disclaims any liability for any failure to carry out voting instructions, for any manner in which a vote is cast or for the effect of any vote, provided it acts in good faith and in accordance with the terms of the deposit agreement.
- The depositary disclaims any liability for any failure to determine the lawfulness or practicality of any action, for the content of any document forwarded to you on our behalf or for the accuracy of any translation of such a document, for the investment risks associated with investing in ordinary shares, for the validity or worth of the ordinary shares, for any tax consequences that result from the ownership of ADSs, for the credit-worthiness of any third party, for allowing any rights to lapse under the terms of the deposit agreement, for the timeliness of any of our notices or for our failure to give notice.
- We and the depositary will not be obligated to perform any act that is inconsistent with the terms of the deposit agreement.
- We and the depositary disclaim any liability if we or the depositary are prevented or forbidden from or subject to any civil or criminal penalty or restraint on account of, or delayed in, doing or performing any act or thing required by the terms of the deposit agreement, by reason of any provision, present or future of any law or regulation, or by reason of present or future provision of any provision of our Articles of Association, or any provision of or governing the securities on deposit, or by reason of any act of God or war or other circumstances beyond our control.
- We and the depositary disclaim any liability by reason of any exercise of, or failure to exercise, any discretion provided for in the deposit agreement or in our Articles of Association or in any provisions of or governing the securities on deposit.
- We and the depositary further disclaim any liability for any action or inaction in reliance on the advice or information received from legal counsel, accountants, any person presenting Shares for deposit, any holder of ADSs or authorized representatives thereof, or any other person believed by either of us in good faith to be competent to give such advice or information.
- We and the depositary also disclaim liability for the inability by a holder to benefit from any distribution, offering, right or other benefit that is made available to holders of ordinary shares but is not, under the terms of the deposit agreement, made available to you.
- We and the depositary may rely without any liability upon any written notice, request or other document believed to be genuine and to have been signed or presented by the proper parties.

- We and the depositary also disclaim liability for any consequential or punitive damages for any breach of the terms of the deposit agreement.
- No disclaimer of any Securities Act liability is intended by any provision of the deposit agreement.

Pre-Release Transactions

Subject to the terms and conditions of the deposit agreement, the depositary may issue to broker/dealers ADSs before receiving a deposit of ordinary shares or release ordinary shares to broker/dealers before receiving ADSs for cancellation. These transactions are commonly referred to as "pre-release transactions," and are entered into between the depositary and the applicable broker/dealer. The deposit agreement limits the aggregate size of pre-release transactions (not to exceed 30% of the ordinary shares on deposit in the aggregate) and imposes a number of conditions on such transactions (e.g., the need to receive collateral, the type of collateral required, the representations required from brokers, etc.). The depositary may retain the compensation received from the pre-release transactions.

Taxes

You will be responsible for the taxes and other governmental charges payable on the ADSs and the securities represented by the ADSs. We, the depositary and the custodian may deduct from any distribution the taxes and governmental charges payable by holders and may sell any and all property on deposit to pay the taxes and governmental charges payable by holders. You will be liable for any deficiency if the sale proceeds do not cover the taxes that are due.

The depositary may refuse to issue ADSs, to deliver, transfer, split and combine ADRs or to release securities on deposit until all taxes and charges are paid by the applicable holder. The depositary and the custodian may take reasonable administrative actions to obtain tax refunds and reduced tax withholding for any distributions on your behalf. However, you may be required to provide to the depositary and to the custodian proof of taxpayer status and residence and such other information as the depositary and the custodian may require to fulfill legal obligations. You are required to indemnify us, the depositary and the custodian for any claims with respect to taxes based on any tax benefit obtained for you.

Foreign Currency Conversion

The depositary will arrange for the conversion of all foreign currency received into U.S. dollars if such conversion is practical, and it will distribute the U.S. dollars in accordance with the terms of the deposit agreement. You may have to pay fees and expenses incurred in converting foreign currency, such as fees and expenses incurred in complying with currency exchange controls and other governmental requirements.

If the conversion of foreign currency is not practical or lawful, or if any required approvals are denied or not obtainable at a reasonable cost or within a reasonable period, the depositary may take the following actions in its discretion:

- Convert the foreign currency to the extent practical and lawful and distribute the U.S. dollars to the holders for whom the conversion and distribution is lawful and practical.
- Distribute the foreign currency to holders for whom the distribution is lawful and practical.
- Hold the foreign currency (without liability for interest) for the applicable holders.

Governing Law/Waiver of Jury Trial

The deposit agreement and the ADRs will be interpreted in accordance with the laws of the State of New York. The rights of holders of ordinary shares (including ordinary shares represented by ADSs) is governed by the laws of England and Wales.

AS A PARTY TO THE DEPOSIT AGREEMENT, YOU WAIVE YOUR RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF THE DEPOSIT AGREEMENT OR THE ADRs AGAINST US AND/OR THE DEPOSITARY.

ORDINARY SHARES AND ADSs ELIGIBLE FOR FUTURE SALE

Prior to the U.S. offering, there has been no market for our ADSs. Future sales of substantial amounts of our ADSs or ordinary shares in the public market, or the perception that such sales may occur, could adversely affect prevailing market prices of our ADSs or ordinary shares.

Upon the closing of the global offering and shareholder private placement, we will have 5,768,000 ADSs outstanding, representing 46,144,000 of our ordinary shares, and 99,014,164 ordinary shares outstanding (including ordinary shares in the form of ADSs), or 105,935,764 ordinary shares (including ordinary shares in the form of ADSs) if the underwriters exercise in full their option to purchase an additional 865,200 ADSs in the U.S. offering, based on our ordinary shares outstanding as of March 31, 2017. The ordinary shares and ADSs sold in the global offering will be freely tradable without restriction or further registration under the Securities Act, except for any ordinary shares or ADSs purchased by our "affiliates," as that term is defined in Rule 144 under the Securities Act, whose sale would be subject to Rule 144 resale restrictions described below, other than the holding period requirement. We expect 33,758,324 of our ordinary shares outstanding after the global offering and shareholder private placement will be subject to the contractual 180-day lock-up period described below.

Rule 144

In general, a person who has beneficially owned our ordinary shares or ADSs for at least six months would be entitled to sell such securities, provided that (i) such person is not deemed to have been one of our affiliates at the time of, or at any time during the 90 days preceding, a sale and (ii) we are subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale. Persons who have beneficially owned our ordinary shares or ADSs for at least six months but who are our affiliates at the time of, or any time during the 90 days preceding, a sale, would be subject to additional restrictions, by which such person would be entitled to sell within any three month period only a number of securities that does not exceed the greater of either of the following:

- 1% of the number of our ordinary shares then outstanding, which will equal approximately 990,142 ordinary shares immediately after the global offering and the shareholder private placement, assuming no exercise of the underwriters' option to purchase additional ADSs; or
- the average weekly trading volume of our ordinary shares in the form of ADSs on NASDAQ during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale;

provided, in each case, that we are subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale. Such sales both by affiliates and by non-affiliates must also comply with the manner of sale, current public information and notice provisions of Rule 144 to the extent applicable.

Rule 701

In general, under Rule 701, any of our employees, board members, executive officers, consultants or advisors who purchases ordinary shares from us in connection with a compensatory share or option plan or other written agreement before the effective date of the global offering is entitled to resell such shares 90 days after the effective date of the global offering in reliance on Rule 144, without having to comply with the holding period requirements or other restrictions contained in Rule 701.

The SEC has indicated that Rule 701 will apply to typical share options granted by an issuer before it becomes subject to the reporting requirements of the Exchange Act, along with the shares acquired upon exercise of such options, including exercises after the date of this prospectus. Securities issued in reliance on Rule 701 are restricted securities and, subject to the lock-up restrictions described below, beginning 90 days after the date of this prospectus, may be sold by persons other than "affiliates," as defined in Rule 144, subject only to the manner of sale provisions of Rule 144 and by "affiliates" under Rule 144 without compliance with its one-year minimum holding period requirement.

Regulation S

Regulation S provides generally that sales made in offshore transactions are not subject to the registration or prospectus-delivery requirements of the Securities Act.

Registration Rights

We have entered into a registration rights agreement in which we agreed under certain circumstances to file a registration statement to register the resale of the shares held by certain of our existing shareholders, as well as to cooperate in certain public offerings of such shares. Registration of these shares under the Securities Act would result in these shares becoming freely tradable without restriction under the Securities Act immediately upon the effectiveness of the registration, except for shares purchased by affiliates. See "Related Party Transactions — Registration Rights Agreement."

Lock-up Agreements

All of our board members and executive officers and certain other holders of our ordinary shares and other securities have agreed, subject to limited exceptions, not to offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise dispose of, directly or indirectly, or enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of our ADSs or ordinary shares or such other securities for a period of 180 days after the date of this prospectus, without the prior written consent of Jefferies LLC and Stifel, Nicolaus & Company, Incorporated. See "Underwriting."

MATERIAL TAX CONSIDERATIONS

Material U.S. Federal Income Tax Considerations for U.S. Holders

The following is a description of the material U.S. federal income tax consequences to the U.S. Holders described below of owning and disposing of our ordinary shares or ADSs. It is not a comprehensive description of all tax considerations that may be relevant to a particular person's decision to acquire securities. This discussion applies only to a U.S. Holder that holds our ordinary shares or ADSs as a capital asset for tax purposes (generally, property held for investment). In addition, it does not describe all of the tax consequences that may be relevant in light of a U.S. Holder's particular circumstances, including state and local tax consequences, estate tax consequences, alternative minimum tax consequences, the potential application of the Medicare contribution tax, and tax consequences applicable to U.S. Holders subject to special rules, such as:

- banks, insurance companies, and certain other financial institutions;
- U.S. expatriates and certain former citizens or long-term residents of the United States;
- dealers or traders in securities who use a mark-to-market method of tax accounting;
- persons holding ordinary shares or ADSs as part of a hedging transaction, "straddle," wash sale, conversion transaction or integrated transaction or persons entering into a constructive sale with respect to ordinary shares or ADSs;
- persons whose "functional currency" for U.S. federal income tax purposes is not the U.S. dollar;
- brokers, dealers or traders in securities, commodities or currencies;
- tax-exempt entities or government organizations;
- S corporations, partnerships, or other entities or arrangements classified as partnerships for U.S. federal income tax purposes;
- regulated investment companies or real estate investment trusts;
- persons who acquired our ordinary shares or ADSs pursuant to the exercise of any employee stock option or otherwise as compensation;
- persons that own or are deemed to own ten percent or more of our voting shares; and
- persons holding our ordinary shares or ADSs in connection with a trade or business, permanent establishment, or fixed base outside the United States.

If an entity that is classified as a partnership for U.S. federal income tax purposes holds ordinary shares or ADSs, the U.S. federal income tax treatment of a partner will generally depend on the status of the partner and the activities of the partnership. Partnerships holding ordinary shares or ADSs and partners in such partnerships are encouraged to consult their tax advisers as to the particular U.S. federal income tax consequences of holding and disposing of ordinary shares or ADSs.

The discussion is based on the Internal Revenue Code of 1986, as amended, or the Code, administrative pronouncements, judicial decisions, final, temporary and proposed Treasury Regulations, and the income tax treaty between the United Kingdom and the United States (the "Treaty") all as of the date hereof, changes to any of which may affect the tax consequences described herein — possibly with retroactive effect.

A "U.S. Holder" is a holder who, for U.S. federal income tax purposes, is a beneficial owner of ordinary shares or ADSs who is eligible for the benefits of the Treaty and is:

(1) a citizen or individual resident of the United States;

(2) 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

(3) an estate or trust the income of which is subject to U.S. federal income taxation regardless of its source.

U.S. Holders are encouraged to consult their tax advisers concerning the U.S. federal, state, local and foreign tax consequences of owning and disposing of ordinary shares or ADSs in their particular circumstances.

The discussion below assumes that the representations contained in the deposit agreement are true and that the obligations in the deposit agreement and any related agreement will be complied with in accordance with their terms. Generally, a holder of an ADS should be treated for U.S. federal income tax purposes as holding the ordinary shares represented by the ADS. Accordingly, no gain or loss will be recognized upon an exchange of ADSs for ordinary shares. The U.S. Treasury has expressed concerns that intermediaries in the chain of ownership between the holder of an ADS and the issuer of the security underlying the ADS may be taking actions that are inconsistent with the beneficial ownership of the underlying security. Accordingly the creditability of foreign taxes, if any, as described below, could be affected by actions taken by intermediaries in the chain of ownership between the holders of ADSs and our Company if as a result of such actions the holders of ADSs are not properly treated as beneficial owners of the underlying ordinary shares.

Passive Foreign Investment Company Rules

Because we do not expect to earn revenue from our business operations during the current taxable year, and because our sole source of income currently is interest on bank accounts held by us, we believe we will likely be a PFIC for the current taxable year. A non-U.S. corporation will be classified as a PFIC for any taxable year in which, after applying certain look-through rules, either:

- at least 75% of its gross income is passive income (such as interest income); or
- at least 50% of its gross assets (determined on the basis of a quarterly average) is attributable to assets that produce passive income or are held for the production of passive income.

We will be treated as owning our proportionate share of the assets and earning our proportionate share of the income of any other corporation, the equity of which we own, directly or indirectly, 25% or more (by value).

A separate determination must be made after the close of each taxable year as to whether we are a PFIC for that year. As a result, our PFIC status may change. While it is possible we may not meet the PFIC test described above once we start generating substantial revenue from our business operations, the analysis is factual and it is possible we may continue to be a PFIC for future years. In particular, the total value of our assets for purposes of the asset test generally will be calculated using the market price of the ordinary shares or ADSs, which may fluctuate considerably. Fluctuations in the market price of the ordinary shares or ADSs may result in our being a PFIC for any taxable year.

If we are classified as a PFIC in any year with respect to which a U.S. Holder owns the 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 the ordinary shares or ADSs, regardless of whether we continue to meet the tests described above unless (1) we cease to be a PFIC and the U.S. Holder has made a "deemed sale" election under the PFIC rules, or (2) the U.S. Holder makes a QEF Election (defined below) with respect to taxable years in which we are a PFIC. If such election is made, you will be deemed to have sold the ordinary shares or ADSs you hold at their fair market value and any gain from such deemed sale would be subject to the rules described below. After the deemed sale election, so long as we do not become a PFIC in a subsequent taxable year, your ordinary shares or ADSs with respect to which such election was made will not be treated as shares in a PFIC and you will not be subject to the rules described below with respect to any "excess distribution" you receive from us or any gain from an actual sale or other disposition of the ordinary shares or ADSs. U.S. Holders should consult their tax advisors as to the possibility and consequences of making a deemed sale election if we cease to be a PFIC and such election becomes available.

For each taxable year we are treated as a PFIC with respect to you, you will be subject to special tax rules with respect to any "excess distribution" you receive and any gain you recognize from a sale or other disposition (including a pledge) of ordinary shares or ADSs, unless you make a QEF Election or a mark-to-market election as discussed below. Distributions you receive in a taxable year that are greater than 125% of the average annual distributions you received during the shorter of the three preceding taxable years or your holding period for the ordinary shares or ADSs will be treated as an excess distribution. Under these special tax rules:

- the excess distribution or gain will be allocated ratably over your holding period for the ordinary shares or ADSs;
- the amount allocated to the current taxable year, and any taxable year prior to the first taxable year in which we became a PFIC, will be treated as ordinary income; and
- the amount allocated to each other year will be subject to the highest tax rate in effect for that year and the interest charge generally applicable to underpayments of tax will be imposed on the resulting tax attributable to each such year.

The tax liability for amounts allocated to years prior to the year of disposition or "excess distribution" cannot be offset by any net operating losses for such years, and gains (but not losses) realized on the sale of the ordinary shares or ADSs cannot be treated as capital, even if you hold the ordinary shares or ADSs as capital assets.

If we are a PFIC, a U.S. Holder will generally be subject to similar rules with respect to distributions we receive from, and our dispositions of the stock of, any of our direct or indirect subsidiaries that also are PFICs, as if such distributions were indirectly received by, and/or dispositions were indirectly carried out by, such U.S. Holder. U.S. Holders should consult their tax advisors regarding the application of the PFIC rules to our subsidiaries.

U.S. Holders can avoid the interest charge on excess distributions or gain relating to the ordinary shares or ADSs by making a mark-to-market election with respect to the ordinary shares or ADSs, provided that the ordinary shares or ADSs are "marketable." Ordinary shares or ADSs will be marketable if they are "regularly traded" on certain U.S. stock exchanges or on a foreign stock exchange that meets certain conditions. For these purposes, the ordinary shares or ADSs will be considered regularly traded during any calendar year during which they are traded, other than in de minimis quantities, on at least 15 days during each calendar quarter Any trades that have as their principal purpose meeting this requirement will be disregarded. Our ADSs will be listed on the NASDAQ, which is a qualified exchange for these purposes. Consequently, if our ADSs remain listed on the NASDAQ and are regularly traded, and you are a holder of ADSs, we expect the mark-to-market election would be available to you if we are a PFIC (which we believe likely for the current year). Each U.S. Holder should consult its tax advisor as to the whether a mark-to-market election is available or advisable with respect to the ordinary shares or ADSs.

A U.S. Holder that makes a mark-to-market election must include in ordinary income for each year an amount equal to the excess, if any, of the fair market value of the ordinary shares or ADSs at the close of the taxable year over the U.S. Holder's adjusted tax basis in the ordinary shares or ADSs. An electing holder may also claim an ordinary loss deduction for the excess, if any, of the U.S. Holder's adjusted basis in the ordinary shares or ADSs over the fair market value of the ordinary shares or ADSs at the close of the taxable year, but this deduction is allowable only to the extent of any net mark-to-market gains for prior years. Gains from an actual sale or other disposition of the ordinary shares or ADSs will be treated as ordinary income, and any losses incurred on a sale or other disposition of the shares will be treated as an ordinary loss to the extent of any net mark-to-market gains for prior years. Once made, the election cannot be revoked without the consent of the IRS unless the ordinary shares or ADSs cease to be marketable.

However, a mark-to-market election generally cannot be made for equity interests in any lower-tier PFICs that we own, unless shares of such lower-tier PFIC are themselves "marketable." We believe that

Rhinopharma Limited will likely be treated as a lower-tier PFIC. As a result, even if a U.S. Holder validly makes a mark-to-market election with respect to our ordinary shares or ADSs, the U.S. Holder may continue to be subject to the PFIC rules (described above) with respect to its indirect interest in any of our investments that are treated as an equity interest in a PFIC for U.S. federal income tax purposes. U.S. Holders should consult their tax advisors as to the availability and desirability of a mark-to-market election, as well as the impact of such election on interests in any lower-tier PFICs.

Alternatively, a U.S. Holder can make an election, if we provide the necessary information, to treat us and each lower-tier PFIC as a qualified electing fund (a "QEF Election") in the first taxable year we (and our relevant subsidiaries) are treated as a PFIC with respect to the holder. If such election remains in place while we and any lower-tier PFIC subsidiaries are PFICs, we and our subsidiaries will not be treated as PFICs with respect to such U.S. Holder when we cease to be a PFIC. A U.S. Holder must make the QEF Election for each PFIC by attaching a separate properly completed IRS Form 8621 for each PFIC to the holder's timely filed U.S. federal income tax return. We will provide the information necessary for a U.S. Holder to make a QEF Election with respect to us and will cause each lower-tier PFIC which we control to provide such information with respect to such lower-tier PFIC.

If a U.S. Holder makes a QEF Election with respect to a PFIC, the holder will be currently taxable on its pro rata share of the PFIC's ordinary earnings and net capital gain (at ordinary income and capital gain rates, respectively) for each taxable year that the entity is classified as a PFIC. If a U.S. Holder makes a QEF Election with respect to us, any distributions paid by us out of our earnings and profits that were previously included in the holder's income under the QEF Election would not be taxable to the holder. A U.S. Holder will increase its tax basis in its ordinary shares or ADSs by an amount equal to any income included under the QEF Election and will decrease its tax basis by any amount distributed on the ordinary shares or ADSs that is not included in the holder's income. In addition, a U.S. Holder will recognize capital gain or loss on the disposition of ordinary shares or ADSs in an amount equal to the difference between the amount realized and the holder's adjusted tax basis in the ordinary shares or ADSs. U.S. Holders should note that if they make QEF Elections with respect to us and lower-tier PFICs, they may be required to pay U.S. federal income tax with respect to their ordinary shares or ADSs for any taxable year significantly in excess of any cash distributions received on the ordinary shares or ADSs for such taxable year. U.S. Holders should consult their tax advisors regarding making QEF Elections in their particular circumstances.

Unless otherwise provided by the U.S. Treasury, each U.S. shareholder of a PFIC is required to file an annual report containing such information as the U.S. Treasury may require. A U.S. Holder's failure to file the annual report will cause the statute of limitations for such U.S. Holder's U.S. federal income tax return to remain open with regard to the items required to be included in such report until three years after the U.S. Holder files the annual report, and, unless such failure is due to reasonable cause and not willful neglect, the statute of limitations for the U.S. Holder's entire U.S. federal income tax return will remain open during such period. U.S. Holders should consult their tax advisors regarding the requirements of filing such information returns under these rules.

Taxation of Distributions

Subject to the discussion above under "Passive Foreign Investment Company Rules," distributions paid on ordinary shares or ADSs, other than certain *pro rata* distributions of ordinary shares or ADSs, will generally be treated as dividends to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Because we do not calculate our earnings and profits under U.S. federal income tax principles, we expect that distributions generally will be reported to U.S. Holders as dividends. Subject to applicable limitations, dividends paid to certain non-corporate U.S. Holders may be taxable at preferential rates applicable to "qualified dividend income." However, the qualified dividend income treatment may not apply if we are treated as a PFIC with respect to the U.S. Holder. The amount of a dividend will include any amounts withheld by us in respect of United Kingdom income taxes. The amount of the dividend will be treated as foreign-source dividend income to U.S. Holders and will not be eligible for the dividends-received deduction generally available to U.S. corporations under

the Code. Dividends will generally be included in a U.S. Holder's income on the date of the U.S. Holder's receipt of the dividend. The amount of any dividend income paid in foreign currency will be the U.S. dollar amount calculated by reference to the exchange rate in effect on the date of actual or constructive receipt, regardless of whether the payment is in fact converted into U.S. dollars. If the dividend is converted into U.S. dollars on the date of receipt, a U.S. Holder should not be required to recognize foreign currency gain or loss in respect of the dividend income. A U.S. Holder may have foreign currency gain or loss if the dividend is converted into U.S. dollars after the date of receipt. Such gain or loss would generally be treated as U.S.-source ordinary income or loss. The amount of any distribution of property other than cash (and other than certain pro rata distributions of ordinary shares or ADSs or rights to acquire ordinary shares or ADSs) will be the fair market value of such property on the date of distribution.

For foreign tax credit purposes, our dividends will generally be treated as passive category income. Subject to applicable limitations, some of which vary depending upon the U.S. Holder's particular circumstances, any United Kingdom income taxes withheld from dividends on ordinary shares or ADSs at a rate not exceeding the rate provided by the Treaty will be creditable against the U.S. Holder's U.S. federal income tax liability. The rules governing foreign tax credits are complex and U.S. Holders should consult their tax advisers regarding the creditability of foreign taxes in their particular circumstances. In lieu of claiming a foreign tax credit, U.S. Holders may, at their election, deduct foreign taxes, including any United Kingdom income tax, in computing their taxable income, subject to generally applicable limitations under U.S. law. An election to deduct foreign taxes instead of claiming foreign tax credits applies to all foreign taxes paid or accrued in the taxable year.

Sale or Other Taxable Disposition of Ordinary Shares and ADSs

Subject to the discussion above under "Passive Foreign Investment Company Rules," gain or loss realized on the sale or other taxable disposition of ordinary shares or ADSs will be capital gain or loss, and will be long-term capital gain or loss if the U.S. Holder held the ordinary shares or ADSs for more than one year. The amount of the gain or loss will equal the difference between the U.S. Holder's tax basis in the ordinary shares or ADSs disposed of and the amount realized on the disposition, in each case as determined in U.S. dollars. This gain or loss will generally be U.S.-source gain or loss for foreign tax credit purposes. The deductibility of capital losses is subject to limitations.

If the consideration received by a U.S. Holder is not paid in U.S. dollars, the amount realized will be the U.S. dollar value of the payment received determined by reference to the spot rate of exchange on the date of the sale or other disposition. However, if the ordinary shares or ADSs are treated as traded on an "established securities market" and you are either a cash basis taxpayer or an accrual basis taxpayer that has made a special election (which must be applied consistently from year to year and cannot be changed without the consent of the IRS), you will determine the U.S. dollar value of the amount realized in a non-U.S. dollar currency by translating the amount received at the spot rate of exchange on the settlement date of the sale. If you are an accrual basis taxpayer that is not eligible to or does not elect to determine the amount realized using the spot rate on the settlement date, you will recognize foreign currency gain or loss to the extent of any difference between the U.S. dollar amount realized on the date of sale or disposition and the U.S. dollar value of the currency received at the spot rate on the settlement date.

WE STRONGLY URGE YOU TO CONSULT YOUR TAX ADVISOR REGARDING THE IMPACT OF OUR PFIC STATUS ON YOUR INVESTMENT IN THE ORDINARY SHARES OR ADSs AS WELL AS THE APPLICATION OF THE PFIC RULES TO YOUR INVESTMENT IN THE ORDINARY SHARES OR ADSs.

Information Reporting and Backup Withholding

Payments of dividends and sales proceeds that are made within the United States or through certain U.S.-related financial intermediaries generally are subject to information reporting, and may be subject to backup withholding, unless (i) the U.S. Holder is a corporation or other exempt recipient or (ii) in the case of backup withholding, the U.S. Holder provides a correct taxpayer identification number and certifies that it is not subject to backup withholding.

Backup withholding is not an additional tax. The amount of any backup withholding from a payment to a U.S. Holder will be allowed as a credit against the holder's U.S. federal income tax liability and may entitle it to a refund, provided that the required information is timely furnished to the IRS.

Information with Respect to Foreign Financial Assets

Certain U.S. Holders who are individuals (and, under proposed regulations, certain entities) may be required to report information relating to the ordinary shares or ADSs, subject to certain exceptions (including an exception for ordinary shares or ADSs held in accounts maintained by certain U.S. financial institutions). U.S. Holders should consult their tax advisers regarding their reporting obligations with respect to their ownership and disposition of the ordinary shares or ADSs.

United Kingdom Taxation

The following paragraphs are intended as a general guide to current U.K. tax law and HM Revenue & Customs published practice applying as at the date of this prospectus (both of which are subject to change at any time, possibly with retrospective effect) relating to the holding of ordinary shares or ADSs. They do not constitute legal or tax advice and do not purport to be a complete analysis of all U.K. tax considerations relating to the holding of ordinary shares or ADSs. They relate only to persons who are absolute beneficial owners of ordinary shares or ADSs (and where the ordinary shares or ADSs are not held through an Individual Savings Account or a Self-Invested Personal Pension) and who are resident for tax purposes in (and only in) the U.K. ("U.K. Holders") (except to the extent that the position of non-U.K. resident persons is expressly referred to).

These paragraphs may not relate to certain classes of U.K. Holders, such as (but not limited to):

- persons who are connected with the Company;
- insurance companies;
- charities;
- collective investment schemes;
- pension schemes;
- brokers or dealers in securities or persons who hold ordinary shares or ADSs otherwise than as an investment;
- persons who have (or are deemed to have) acquired their ordinary shares or ADSs by virtue of an office or employment or who are or have been officers or employees of the Company or any of its affiliates; and
- individuals who are subject to U.K. taxation on a remittance basis.

These paragraphs do not describe all of the circumstances in which holders of ordinary shares or ADSs may benefit from an exemption or relief from U.K. taxation. It is recommended that all holders of ordinary shares or ADSs obtain their own tax advice. In particular, non-U.K. resident or domiciled persons are advised to consider the potential impact of any relevant double tax agreements.

These paragraphs assume that a holder of ADSs is the beneficial owner of the underlying ordinary shares and any dividends paid in respect of the underlying ordinary shares (where the dividends are regarded for U.K. purposes as that person's own income) for U.K. direct tax purposes.

Dividends

Withholding Tax

Dividends paid by the Company will not be subject to any withholding or deduction for or on account of U.K. tax, irrespective of the residence or particular circumstances of the holders of ordinary shares or ADSs.

Income Tax

An individual U.K. Holder may, depending on his or her particular circumstances, be subject to U.K. tax on dividends received from the Company. An individual holder of ordinary shares or ADSs who is not resident

for tax purposes in the U.K. should not be chargeable to U.K. income tax on dividends received from the Company unless he or she carries on (whether solely or in partnership) any trade, profession or vocation in the U.K. through a branch or agency to which the ordinary shares or ADSs are attributable (subject to certain exceptions for trading through independent agents, such as some brokers and investment managers).

All individual U.K. Holders will receive a tax-free allowance of £5,000 per annum (announced to reduce to £2,000 from April 2018). Dividend income in excess of this tax-free allowance will be charged at 7.5% for basic rate taxpayers, 32.5% for higher rate taxpayers, and 38.1% for additional rate taxpayers. Dividend income is treated as the top slice of the total income chargeable to U.K. income tax.

Corporation Tax

Corporate U.K. Holders should not be subject to U.K. corporation tax on any dividend received from the Company so long as the dividends qualify for exemption, which should be the case, although certain conditions are met (including anti-avoidance conditions).

Chargeable Gains

A disposal of ordinary shares or ADSs by a U.K. Holder may, depending on the U.K. Holder's circumstances and subject to any available exemptions or reliefs, give rise to a chargeable gain or an allowable loss for the purposes of U.K. capital gains tax and corporation tax on chargeable gains.

If an individual U.K. Holder who is subject to U.K. income tax at either the higher or the additional rate becomes liable to U.K. capital gains tax on the disposal of ordinary shares or ADSs, the current applicable rate would be 20%. For an individual U.K. Holder who is subject to U.K. income tax at the basic rate and liable to U.K. capital gains tax on such disposal, the current applicable rate would be 10%, save to the extent that any capital gains exceed the unused basic rate tax band. In that case, the current rate applicable to the excess would be 20%.

If a corporate U.K. Holder becomes liable to U.K. corporation tax on the disposal of ordinary shares or ADSs, the main rate of U.K. corporation tax (20% in 2016/17 and 19% in 2017/18) would apply. An indexation allowance may be available to such a holder to give an additional deduction based on the indexation of its base cost in the shares by reference to U.K. retail price inflation over its holding period. An indexation allowance can only reduce a gain on a future disposal, and cannot create a loss.

A holder of ordinary shares or ADSs which is not resident for tax purposes in the U.K. should not normally be liable to U.K. capital gains tax or corporation tax on chargeable gains on a disposal of ordinary shares or ADSs. However, an individual holder of ordinary shares or ADSs who has ceased to be resident for tax purposes in the U.K. for a period of less than five years and who disposes of ordinary shares or ADSs during that period may be liable on his or her return to the U.K. to U.K. tax on any capital gain realized (subject to any available exemption or relief).

Any gains or losses in respect of currency fluctuations relating to the ordinary shares or ADSs would be brought into account on the disposal.

Stamp Duty and Stamp Duty Reserve Tax ("SDRT")

The discussion below relates to holders of ordinary shares or ADSs wherever resident.

Transfer of Ordinary Shares

Neither U.K. stamp duty nor SDRT should arise on transfers of ordinary shares on AIM (including instruments transferring ordinary shares or agreement to transfer ordinary shares) based on the following assumptions:

- that the ordinary shares are admitted to trading on AIM but are not listed on any market (with the term "listed" being construed in accordance with section 99A of the U.K. Finance Act 1986); and
- that AIM continues to be accepted as a "recognised growth market" (as construed in accordance with section 99A of the U.K. Finance Act 1986).

In the event that either of the above assumptions does not apply, transfers of, or agreements to transfer, ordinary shares may give rise to U.K. stamp duty or SDRT in certain circumstances.

Transfers of ADSs

No U.K. stamp duty will in practice be payable on a written instrument transferring an ADS or on a written agreement to transfer an ADS, provided that the instrument of transfer or the agreement to transfer is executed and remains at all times outside the U.K. Where these conditions are not met, the transfer of, or agreement to transfer, an ADS could, depending on the circumstances, attract a charge to U.K. stamp duty at the rate of 0.5% of the value of the consideration.

No SDRT will be payable in respect of agreement to transfer an ADS.

UNDERWRITING

Subject to the terms and conditions set forth in the underwriting agreement, dated April 26, 2017, among us and Jefferies LLC and Stifel, Nicolaus & Company, Incorporated, as the representatives of the underwriters named below and the joint book-running managers of the global offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of ADSs and ordinary shares shown opposite its name below:

UNDERWRITER	NUMBER OF ADSs	NUMBER OF ORDINARY SHARES
Jefferies LLC	2,624,440	571,026
Stifel, Nicolaus & Company, Incorporated	1,874,600	407,875
Wedbush Securities Inc.	634,480	138,050
SunTrust Robinson Humphrey, Inc.	634,480	138,050
Total	5,768,000	1,255,001

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the ADSs and ordinary shares offered by this prospectus if any of them are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of the U.S. offering and the European private placement, they currently intend to make a market in our ADSs and ordinary shares as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading markets for our ADSs or ordinary shares that you will be able to sell any of the ADSs or ordinary shares held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering our ADSs and ordinary shares subject to their acceptance of our ADSs and ordinary shares from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part. In addition, the underwriters have advised us that they do not intend to confirm sales to any account over which they exercise discretionary authority.

Commission and Expenses

The underwriters have advised us that they propose to offer our ADSs and ordinary shares to the public at the initial public offering price per ADS and offering price per ordinary share set forth on the cover page of this prospectus and to certain dealers, which may include the underwriters, at that price less a concession not in excess of $0.567 per ADS and £0.055 per ordinary share. After the global offering, the offering price, concession and reallowance to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus.

The following table shows the offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with the global offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional ADSs.

			TOTAL	
	PER ADS	PER ORDINARY SHARE	No exercise	Full exercise
Offering price	$ 13.50	£ 1.32	$79,985,633	$91,665,833
Underwriting discounts and commissions paid by us	$ 0.9450	£0.0924	$ 5,598,994	$ 6,416,608
Proceeds to us, before expenses	$12.5550	£1.2276	$74,386,639	$85,249,225

We estimate expenses payable by us in connection with the global offering, other than the underwriting discounts and commissions referred to above, will be approximately $3,500,000. We have also agreed to reimburse the underwriters for certain expenses, including up to an aggregate of $35,000 in connection with the clearance of the global offering with the Financial Industry Regulatory Authority, or FINRA, as set forth in the underwriting agreement.

Sales of our ordinary shares made outside of the United States may be made by affiliates of the underwriters.

Our existing institutional investors affiliated with certain of our directors have indicated an interest in purchasing up to an aggregate of approximately $23 million (or the pounds sterling equivalent) in the global offering on the same terms as the other purchasers in the global offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no securities offered in the global offering to any of these investors, or any of these investors may determine to purchase more, less or no securities offered in the global offering. The underwriters will receive the same underwriting discount on any securities purchased by these investors as they will on any other securities sold to the public in the global offering.

Our chairman of the board of directors and an existing shareholder have agreed to purchase an aggregate of approximately £335,400 (or the U.S. dollar equivalent) of our ordinary shares in a private placement separate from the global offering, contingent on and concurrent with the completion of the global offering at a price per share equal to the offering price per ordinary share in the European private placement. The underwriters will serve as placement agents for such shareholder private placement and receive a placement agent fee equal to a percentage of the total purchase price of the private placement shares, which percentage will be equal to the percentage discount the underwriters will receive on shares sold in this global offering.

Determination of Offering Price

Prior to the U.S. offering, there has not been a public market for our ADSs. Consequently, the initial public offering price for our ADSs has been determined by negotiations between us and the representatives. Among the factors considered in these negotiations were prevailing market conditions, the trading price of our ordinary shares on AIM, our financial information, market valuations of other companies that we and the underwriters believe to be comparable to us, estimates of our business potential, the present state of our development and other factors deemed relevant.

We offer no assurances that the initial public offering price will correspond to the price at which our ADSs will trade in the public market subsequent to the global offering or that an active trading market for our ADSs will develop and continue after the U.S. offering.

Listing

Our ordinary shares trade on AIM, a market of the London Stock Exchange, under the symbol "VRP." Our ADSs have been approved for listing on The NASDAQ Global Market under the trading symbol "VRNA."

Stamp Taxes

If you purchase ADSs or ordinary shares offered in this prospectus, you may be required to pay stamp taxes and other charges under the laws and practices of the country of purchase, in addition to the offering price listed on the cover page of this prospectus.

Option to Purchase Additional ADSs

We have granted to the underwriters options, exercisable for 30 days from the date of this prospectus, to purchase, from time to time, in whole or in part, up to an aggregate of 865,200 additional ADSs from us at the public offering price set forth on the cover page of this prospectus, less underwriting discounts and commissions. If the underwriters exercise their option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional ADSs proportionate to that underwriter's initial purchase commitment as indicated in the table above. This option may be exercised only if the underwriters sell more ADSs than the total number set forth on the cover page of this prospectus.

No Sales of Similar Securities

We, our board members and executive officers and certain other holders of our ordinary shares and other securities have agreed, subject to specified exceptions, not to directly or indirectly:

- sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open "put equivalent position" within the meaning of Rule 16a-l(h) under the Securities Exchange Act of 1934, as amended; or
- otherwise dispose of any ordinary shares or ADSs, options or warrants to acquire ordinary shares or ADSs, or securities exchangeable or exercisable for or convertible into ordinary shares or ADSs currently or hereafter owned either of record or beneficially; or
- publicly announce an intention to do any of the foregoing for a period of 180 days after the date of this prospectus without the prior written consent of the representatives.

This restriction terminates after the close of trading of our ADSs and ordinary shares on AIM and including the 180th day after the date of this prospectus.

The representatives may, in their sole discretion and at any time or from time to time before the termination of the 180-day period release all or any portion of the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any of our shareholders who will execute a lock-up agreement, providing consent to the sale of ADSs or ordinary shares prior to the expiration of the lock-up period.

Stabilization

The underwriters have advised us that, pursuant to Regulation M under the Securities Exchange Act of 1934, as amended, they may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with the global offering. These activities may have the effect of stabilizing or maintaining the market price of our ADSs and ordinary shares at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either "covered" short sales or "naked" short sales.

"Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional ADSs in the global offering. The underwriters may close out any covered short position by either exercising their option to purchase additional ADSs or purchasing our ADSs in the open market. In

determining the source of ADSs to close out the covered short position, the underwriters will consider, among other things, the price of ADSs available for purchase in the open market as compared to the price at which they may purchase ADSs through the option to purchase additional ADSs.

Naked short sales are sales in excess of the option to purchase additional ADSs. The underwriters must close out any naked short position by purchasing ADSs in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our ADSs and ordinary shares in the open market after pricing that could adversely affect investors who purchase in the global offering.

A stabilizing bid is a bid for the purchase of ADSs and ordinary shares on behalf of the underwriters for the purpose of fixing or maintaining the price of our ADSs and ordinary shares. A syndicate covering transaction is the bid for or the purchase of ADSs and ordinary shares on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the global offering. Similar to other purchase transactions, the underwriter's purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our ADSs and ordinary shares or preventing or retarding a decline in the market price of our ADSs and ordinary shares. As a result, the price of our ADSs and ordinary shares may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the global offering if our ADSs and ordinary shares originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our ADSs and ordinary shares. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our ADSs on The NASDAQ Global Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of ADSs in the U.S. offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Distribution

A prospectus in electronic format may be made available by e-mail or on the websites or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of ADSs or ordinary shares for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' websites and any information contained in any other website maintained by any of the underwriters is not part of this prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their affiliates have, from time to time, performed, and may in

the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and certain of their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially our ADSs and ordinary shares offered hereby. Any such short positions could adversely affect future trading prices of the ADSs and ordinary shares offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Disclaimers About Non-U.S. Jurisdictions

Canada

(A) Resale Restrictions

The distribution of our ADSs in Canada is being made only in the provinces of Ontario, Quebec, Alberta and British Columbia on a private placement basis exempt from the requirement that we prepare and file a prospectus with the securities regulatory authorities in each province where trades of these securities are made. Any resale of our ADSs in Canada must be made under applicable securities laws which may vary depending on the relevant jurisdiction, and which may require resales to be made under available statutory exemptions or under a discretionary exemption granted by the applicable Canadian securities regulatory authority. Purchasers are advised to seek legal advice prior to any resale of the securities.

(B) Representations of Canadian Purchasers

- By purchasing our ADSs in Canada and accepting delivery of a purchase confirmation, a purchaser is representing to us and the dealer from whom the purchase confirmation is received that:
- the purchaser is entitled under applicable provincial securities laws to purchase our ADSs without the benefit of a prospectus qualified under those securities laws as it is an "accredited investor" as defined under National Instrument 45-106 — Prospectus Exemptions,
- the purchaser is a "permitted client" as defined in National Instrument 31-103 — Registration Requirements, Exemptions and Ongoing Registrant Obligations,
- where required by law, the purchaser is purchasing as principal and not as agent, and
- the purchaser has reviewed the text above under Resale Restrictions.

(C) Conflicts of Interest

Canadian purchasers are hereby notified that each of the underwriters is relying on the exemption set out in section 3A.3 or 3A.4, if applicable, of National Instrument 33-105 — Underwriting Conflicts from having to provide certain conflict of interest disclosure in this document.

(D) Statutory Rights of Action

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if the prospectus (including any amendment thereto) such as this document contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser of these securities in Canada should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

(E) Enforcement of Legal Rights

All of our directors and officers as well as the experts named herein may be located outside of Canada and, as a result, it may not be possible for Canadian purchasers to effect service of process within Canada upon us or those persons. All or a substantial portion of our assets and the assets of those persons may be located outside of Canada and, as a result, it may not be possible to satisfy a judgment against us or those persons in Canada or to enforce a judgment obtained in Canadian courts against us or those persons outside of Canada.

(F) Taxation and Eligibility for Investment

Canadian purchasers of our ADSs should consult their own legal and tax advisors with respect to the tax consequences of an investment in our ADSs in their particular circumstances and about the eligibility of our ADSs for investment by the purchaser under relevant Canadian legislation.

Australia

This prospectus is not a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, has not been lodged with the Australian Securities & Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus in Australia:

A. You confirm and warrant that you are either:

   a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;

   a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the Company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;

   a person associated with the Company under Section 708(12) of the Corporations Act; or

   a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act.

   To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act any offer made to you under this prospectus is void and incapable of acceptance.

B. You warrant and agree that you will not offer any of the securities issued to you pursuant to this prospectus for resale in Australia within 12 months of those securities being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

European Economic Area

In relation to each member state of the European Economic Area which has implemented the Prospectus Directive, or each referred as a "Relevant Member State", an offer to the public of any ADSs or ordinary

shares which are the subject of the global offering contemplated by this prospectus may not be made in that Relevant Member State except that an offer to the public in that Relevant Member State of any ADSs or ordinary shares may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

(a) to any legal entity which is a "qualified investor" as defined in the Prospectus Directive;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the underwriters or the underwriters nominated by us for any such offer; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive;

Provided that no such offer of ADSs or ordinary shares shall require us or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this provision, the expressions "offer ADSs to the public" in relation to our ADSs and "offer ordinary shares to the public" in relation to our ordinary shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and our ADSs or ordinary shares to be offered so as to enable an investor to decide to purchase or subscribe to our ADSs or ordinary shares, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

People's Republic of China

This prospectus may not be circulated or distributed in the PRC and our ADSs may not be offered or sold, and will not offer or sell to any person for re-offering or resale directly or indirectly to any resident of the PRC except pursuant to applicable laws and regulations of the PRC. For the purpose of this paragraph, PRC does not include Taiwan and the special administrative regions of Hong Kong and Macau.

Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong, or the SFO, and any rules made under that Ordinance; or in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong, or the CO, or which do not constitute an offer or invitation to the public for the purpose of the CO or the SFO. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the SFO and any rules made under that Ordinance.

This prospectus has not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus and the relevant offering documents and that he is

not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Israel

This document does not constitute a prospectus under the Israeli Securities Law, 5728-1968, or the Securities Law, and has not been filed with or approved by the Israel Securities Authority. In Israel, this prospectus is being distributed only to, and is directed only at, and any offer of our ADSs is directed only at, (i) a limited number of persons in accordance with the Israeli Securities Law and (ii) investors listed in the first addendum, or the Addendum, to the Israeli Securities Law, consisting primarily of joint investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange, underwriters, venture capital funds, entities with equity in excess of NIS 50 million and "qualified individuals," each as defined in the Addendum (as it may be amended from time to time), collectively referred to as qualified investors (in each case, purchasing for their own account or, where permitted under the Addendum, for the accounts of their clients who are investors listed in the Addendum). Qualified investors are required to submit written confirmation that they fall within the scope of the Addendum, are aware of the meaning of same and agree to it.

Japan

The global offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the underwriters will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus has not been and will not be lodged or registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the securities may not be circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

(a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

(b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation

or that trust has acquired the securities pursuant to an offer made under Section 275 of the SFA except:

(i) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

(ii) where no consideration is or will be given for the transfer;

(iii) where the transfer is by operation of law;

(iv) as specified in Section 276(7) of the SFA; or

(v) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or the SIX, or on any other stock exchange or regulated trading facility in Switzerland. This prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus nor any other offering or marketing material relating to the offering, the Company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or the CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that also are (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, or the Order, and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated (each such person being referred to as a "relevant person").

This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents. Any investment or investment activity to which this prospectus relates is available only to relevant persons and will be engaged in only with relevant persons.

EXPENSES OF THE GLOBAL OFFERING

We estimate that our expenses in connection with the global offering, other than underwriting discounts and commissions, will be as follows:

Expenses	Amount
Securities and Exchange Commission registration fee	$ 10,628
FINRA filing fee	12,789
The NASDAQ Global Market listing fee	125,000
AIM listing fee	40,327
Printing and engraving expenses	195,000
Legal fees and expenses	2,250,000
Accounting fees and expenses	750,000
Miscellaneous costs	116,256
Total	$3,500,000

All amounts in the table are estimates except the SEC registration fee, the NASDAQ Global Market listing fee and the FINRA filing fee. We will pay all of the expenses of the global offering.

LEGAL MATTERS

The validity of our ADSs and ordinary shares and certain other matters of English law and U.S. federal law will be passed upon for us by Latham & Watkins LLP. Legal counsel to the underwriters in connection with the global offering are White & Case LLP with respect to English law and Cooley LLP, New York, New York, with respect to U.S. federal law.

AUDITORS

At the annual general meeting on June 11, 2015, UHY Hacker Young, our auditor for the financial year ended December 31, 2014, did not offer themselves for re-election, and our shareholders appointed PricewaterhouseCoopers LLP as our auditor for the year ending December 31, 2015 as proposed by our board of directors. Accordingly UHY Hacker Young was not re-elected for another term as our independent registered public accounting firm.

The report of UHY Hacker Young for the financial year ended December 31, 2014 did not contain any adverse opinion or disclaimer of opinion and was not qualified or modified as to uncertainty, audit scope or accounting principles. There was no disagreement whatsoever relating to the year ended December 31, 2014 with UHY Hacker Young on any matter of accounting principles or practices, financial statement disclosure, or auditing scope or procedure, which disagreement, if not resolved to the satisfaction of the former auditor, would have caused them to make reference to the subject matter of the disagreement in connection with their report, or any "reportable event" as described in Item 16F(a)(1)(v) of Form 20-F. The report of UHY Hacker Young for the financial year ended December 31, 2014 is not included in this prospectus.

We have provided a copy of the above statements to UHY Hacker Young and requested that UHY Hacker Young furnish us with a letter addressed to the SEC stating whether or not they agree with the above disclosure. A copy of that letter, dated December 20, 2016, is filed as an exhibit to the registration statement of which this prospectus forms a part.

EXPERTS

The financial statements as of December 31, 2015 and 2016 and for the years ended December 31, 2015 and 2016 included in this prospectus have been so included in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in accounting and auditing.

The registered business address of PricewaterhouseCoopers LLP is 1 Embankment Place, London, WC2N 6RH, United Kingdom.

SERVICE OF PROCESS AND ENFORCEMENT OF LIABILITIES

We are incorporated and currently existing under the laws of England and Wales. In addition, certain of our directors and officers reside outside of the United States and most of the assets of our non-U.S. subsidiaries are located outside of the United States. As a result, it may be difficult for investors to effect service of process on us or those persons in the United States or to enforce in the United States judgments obtained in United States courts against us or those persons based on the civil liability or other provisions of the United States securities laws or other laws.

In addition, uncertainty exists as to whether the courts of England and Wales would:

- recognize or enforce judgments of United States courts obtained against us or our directors or officers predicated upon the civil liabilities provisions of the securities laws of the United States or any state in the United States; or
- entertain original actions brought in England and Wales against us or our directors or officers predicated upon the securities laws of the United States or any state in the United States.

We have been advised by Latham & Watkins LLP that there is currently no treaty between (i) the United States and (ii) England and Wales providing for reciprocal recognition and enforcement of judgments of United States courts in civil and commercial matters (although the United States and the United Kingdom are both parties to the New York Convention on the Recognition and Enforcement of Foreign Arbitral Awards) and that a final judgment for the payment of money rendered by any general or state court in the United States based on civil liability, whether or not predicated solely upon the United States securities laws, would not be automatically enforceable in England and Wales. We have also been advised by Latham & Watkins LLP that any final and conclusive monetary judgment for a definite sum obtained against us in United States courts would be treated by the courts of England and Wales 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:

- the relevant U.S. court had jurisdiction over the original proceedings according to English conflicts of laws principles at the time when proceedings were initiated;
- England and Wales courts had jurisdiction over the matter on enforcement and we either submitted to such jurisdiction or were resident or carrying on business within such jurisdiction and were duly served with process;
- the U.S. judgment was final and conclusive on the merits in the sense of being final and unalterable in the court that pronounced it and being for a definite sum of money;
- the judgment given by the courts was not in respect of penalties, taxes, fines or similar fiscal or revenue obligations (or otherwise based on a U.S. law that an English court considers to relate to a penal, revenue or other public law);
- the judgment was not procured by fraud;
- recognition or enforcement of the judgment in England and Wales would not be contrary to public policy or the Human Rights Act 1998;
- the proceedings pursuant to which judgment was obtained were not contrary to natural justice;
- the U.S. judgment was not arrived at by doubling, trebling or otherwise multiplying a sum assessed as compensation for the loss or damages sustained and not being otherwise in breach of Section 5 of the UK Protection of Trading Interests Act 1980, or is a judgment based on measures designated by the Secretary of State under Section 1 of that Act;
- there is not a prior decision of an English court or the court of another jurisdiction on the issues in question between the same parties; and
- the English enforcement proceedings were commenced within the limitation period.

Whether these requirements are met in respect of a judgment based upon the civil liability provisions of the United States 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.

Subject to the foregoing, investors may be able to enforce in England and Wales judgments in civil and commercial matters that have been obtained from U.S. federal or state courts. Nevertheless, we cannot assure you that those judgments will be recognized or enforceable in England and Wales.

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. In addition, it may not be possible to obtain an English judgment or to enforce that judgment if the judgment debtor is or becomes subject to any insolvency or similar proceedings, or if the judgment debtor has any set-off or counterclaim against the judgment creditor. Also note that, in any enforcement proceedings, the judgment debtor may raise any counterclaim that could have been brought if the action had been originally brought in England unless the subject of the counterclaim was in issue and denied in the U.S. proceedings.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement (including amendments and exhibits to the registration statement) on Form F-1 under the Securities Act. This prospectus, which is part of the registration statement, does not contain all of the information set forth in the registration statement and the exhibits and schedules to the registration statement. For further information, we refer you to the registration statement and the exhibits and schedules filed as part of the registration statement. If a document has been filed as an exhibit to the registration statement, we refer you to the copy of the document that has been filed. Each statement in this prospectus relating to a document filed as an exhibit is qualified in all respects by the filed exhibit.

Upon completion of the U.S. offering, we will become subject to the informational requirements of the Exchange Act. Accordingly, we will be required to file reports and other information with the SEC, including annual reports on Form 20-F and reports on Form 6-K. You may inspect and copy reports and other information filed with the SEC at the Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Information on the operation of the Public Reference Room may be obtained by calling the SEC at 1-800-SEC-0330. In addition, the SEC maintains an Internet website that contains reports and other information about issuers, like us, that file electronically with the SEC. The address of that website is www.sec.gov.

As a foreign private issuer, we are exempt under the Exchange Act from, among other things, the rules prescribing the furnishing and content of proxy statements, and our board members, executive officers, and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we will not be required under the Exchange Act to file periodic reports and financial statements with the SEC as frequently or as promptly as U.S. companies whose securities are registered under the Exchange Act.

We will send our transfer agent a copy of all notices of our general meetings of shareholders and other reports, communications and information that are made generally available to shareholders. The transfer agent has agreed to mail to all shareholders a notice containing the information (or a summary of the information) contained in any notice of a meeting of our shareholders received by the transfer agent and will make available to all shareholders such notices and all such other reports and communications received by the transfer agent.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Consolidated financial statements
as of and for the years ended December 31, 2015 and 2016

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders of Verona Pharma Plc:

In our opinion, the accompanying consolidated statement of financial position and the related consolidated statements of comprehensive income (loss), of changes in equity and of cash flows, present fairly, in all material respects, the financial position of Verona Pharma Plc and its subsidiaries as at December 31, 2016 and December 31, 2015, and the results of their operations and their cash flows for each of the two years in the period ended December 31, 2016 in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

We draw attention to note 23 of the consolidated financial statements which describes the share consolidation the Company effected on February 8, 2017. Management have reflected this share consolidation in the accompanying financial statements to give retroactive effect to the loss per share amounts.

As discussed in Note 2.2 to the consolidated financial statements, the company restated its comparative financial statements to correct an error in 2015.

/s/ PricewaterhouseCoopers LLP
Reading, United Kingdom
March 2, 2017

VERONA PHARMA PLC
CONSOLIDATED STATEMENT OF COMPREHENSIVE INCOME
FOR THE YEARS ENDED DECEMBER 31, 2015 AND 2016

	Notes	Restated Year ended December 31, 2015	Year ended December 31, 2016
		£	£
Research and development costs		(7,268,847)	(4,521,820)
General and administrative costs		(1,705,944)	(2,498,349)
Operating loss	7	(8,974,791)	(7,020,169)
Finance income	9	44,791	1,841,282
Finance expense	9	(72,291)	(793,690)
Loss before taxation		(9,002,291)	(5,972,577)
Taxation — credit	10	1,509,448	954,184
Loss for the year		(7,492,843)	(5,018,393)
Other comprehensive income:			
Exchange differences on translating foreign operations		3,784	42,559
Total comprehensive loss attributable to owners of the Company		(7,489,059)	(4,975,834)
Loss per ordinary share — basic and diluted (pence)	5	(37.1)	(15.0)

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

VERONA PHARMA PLC
CONSOLIDATED STATEMENT OF FINANCIAL POSITION
AS OF DECEMBER 31, 2015 AND 2016

	Notes	Restated As of December 31, 2015	As of December 31, 2016
		£	£
ASSETS			
Non-current assets:			
Property, plant and equipment	14	13,163	13,838
Intangible assets	15	1,813,756	1,876,684
Goodwill	16	441,000	441,000
		2,267,919	2,331,522
Current assets:			
Prepayments and other receivables	11	513,300	2,958,587
Current tax receivable		1,534,788	1,067,460
Cash and cash equivalents	12	3,524,387	39,785,098
		5,572,475	43,811,145
Total assets		7,840,394	46,142,667
EQUITY AND LIABILITIES			
Capital and reserves attributable to equity holders:			
Share capital	17	1,009,923	2,568,053
Share premium		26,650,098	58,526,502
Share-based payment reserve		1,525,897	2,101,790
Accumulated loss		(23,752,204)	(28,728,038)
Total equity		5,433,714	34,468,307
Current liabilities:			
Trade and other payables	13	1,798,682	2,823,489
Tax payable—U.S. Operations		14,057	126,063
Derivative financial instrument	21	—	7,922,603
Total current liabilities		1,812,739	10,872,155
Non-current liabilities:			
Assumed contingent obligation	20	593,941	802,205
Total non-current liabilities		593,941	802,205
Total equity and liabilities		7,840,394	46,142,667

The financial statements on pages F-3 to F-37 were approved by the Company's board of directors on February 27, 2017 and signed on its behalf by Dr. Jan-Anders Karlsson, Chief Executive Officer of the Company.

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

VERONA PHARMA PLC
CONSOLIDATED STATEMENT OF CASH FLOWS
FOR THE YEARS ENDED DECEMBER 31, 2015 AND 2016

	Restated Year ended December 31, 2015	Year ended December 31, 2016
	£	£
Cash used in operating activities:		
Loss before taxation	(9,002,291)	(5,972,577)
Finance income	(44,791)	(1,841,282)
Finance expense	72,291	793,690
Share-based payment charge	398,943	575,893
Decrease / (increase) in prepayments and other receivables	57,633	(1,808,832)
Increase in trade and other payables	1,274,370	1,067,595
Depreciation of property, plant and equipment	9,689	10,051
Loss on disposal of property, plant and equipment	—	2,625
Loss on disposal of intangible assets	134,532	8
Amortization of intangible assets	43,428	51,571
Cash used in operating activities	(7,056,196)	(7,121,258)
Cash inflow from taxation	699,519	1,533,287
Net cash used in operating activities	(6,356,677)	(5,587,971)
Cash flow from investing activities:		
Interest received	50,592	86,542
Purchase of plant and equipment	(1,193)	(13,351)
Payment for patents and computer software	(141,878)	(114,506)
Net cash used in investing activities	(92,479)	(41,315)
Cash flow from financing activities:		
Gross proceeds from issue of shares and warrants	—	44,750,364
Transaction costs on issue of shares and warrants	—	(2,910,461)
Transaction costs on upcoming Global Offering	—	(636,455)
Net cash generated from financing activities	—	41,203,448
Net (decrease) / increase in cash and cash equivalents	(6,449,156)	35,574,162
Cash and cash equivalents at the beginning of the year	9,969,759	3,524,387
Effect of exchange rates on cash and cash equivalents	3,784	686,549
Cash and cash equivalents at the end of the period	3,524,387	39,785,098

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

VERONA PHARMA PLC
CONSOLIDATED STATEMENT OF CHANGES IN EQUITY
FOR THE YEARS ENDED DECEMBER 31, 2015 AND 2016

	Share Capital	Share Premium	Share-based Expenses	Total Accumulated Losses	Total Equity
	£	£	£	£	£
Balance at January 1, 2015 (Restated)	1,009,923	26,650,098	1,126,954	(16,263,145)	12,523,830
Loss for the year	—	—	—	(7,492,843)	(7,492,843)
Other comprehensive income for the year:					
Exchange differences on translating foreign operations	—	—	—	3,784	3,784
Total comprehensive loss for the period	—	—	—	(7,489,059)	(7,489,059)
Share-based payments	—	—	398,943	—	398,943
Balance at December 31, 2015 (Restated)	1,009,923	26,650,098	1,525,897	(23,752,204)	5,433,714
Balance at January 1, 2016	1,009,923	26,650,098	1,525,897	(23,752,204)	5,433,714
Loss for the year	—	—	—	(5,018,393)	(5,018,393)
Other comprehensive income for the year:					
Exchange differences on translating foreign operations	—	—	—	42,559	42,559
Total comprehensive loss for the period	—	—	—	(4,975,834)	(4,975,834)
New share capital issued	1,555,796	34,151,439	—	—	35,707,235
Transaction costs on share capital issued	—	(2,325,035)	—	—	(2,325,035)
Share options exercised during the period	2,334	50,000	—	—	52,334
Share-based payments	—	—	575,893	—	575,893
Balance at December 31, 2016	2,568,053	58,526,502	2,101,790	(28,728,038)	34,468,307

The currency translation reserve for 2015 and 2016 was not considered material and as such was not presented in a separate reserve but was included in the total accumulated losses reserve.

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

1. General information

Verona Pharma plc (the "Company") and its subsidiaries (together, the "Group") are 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 is a public limited company, which is listed on the Alternative Investment Market of the London Stock Exchange and incorporated and domiciled in the United Kingdom.

The Company has two subsidiaries, Verona Pharma, Inc. and Rhinopharma Limited ("Rhinopharma"), both of which are wholly owned.

On February 8, 2017, our shareholders approved a 50-for-1 consolidation of its shares. Earnings per share information in these consolidated financial statements has been retrospectively adjusted, to reflect the consolidation as if it had occurred at the beginning of the earliest period presented. Prior to the consolidation the total number of issued shares as at December 31, 2016 would read as 2,568,053,160 shares and after the consolidation this number would read as 51,361,063 shares.

2. Accounting policies

A summary of the principal accounting policies, all of which have been applied consistently throughout the year, is set out below.

2.1 Basis of preparation

The consolidated financial statements of the Group have been prepared in accordance with International Financial Reporting Standards ("IFRS") as issued by the International Accounting Standards Board. The consolidated financial statements have been prepared under the historical cost convention, with the exception of derivative financial instruments which have been measured at fair value.

The preparation of financial statements in conformity with IFRS requires the use of certain critical accounting estimates. It also requires management to exercise its judgement in the process of applying the Group's accounting policies. The areas involving a higher degree of judgement or complexity, or areas where assumptions and estimates are significant to the consolidated financial statements are disclosed in note 4.

Going concern

During the year ended December 31, 2016, the Group had a loss of £5,018 thousand (2015: £7,493 thousand). As of December 31, 2016, the Group had net assets of £34,468 thousand (2015: £5,434 thousand) of which £39,785 thousand (2015: £3,524 thousand) was cash and cash equivalents.

The operation of the Group is currently being financed from funds that the Company raised from share placings. On July 29, 2016, the Company raised gross proceeds of £44.7 million from a placing, subscription and open offer (the "July Placement"). These funds are expected to be used primarily to support the development of RPL554 in chronic obstructive pulmonary disease ("COPD") as well as corporate and general administrative expenditures.

The Directors believe that the Group has sufficient funds to complete the current clinical trials, to cover corporate and general administration costs and for it to comply with all commitments for at least 12 months

2. Accounting policies (Continued)

from the end of the reporting period and, accordingly, are satisfied that the going concern basis remains appropriate for the preparation of these consolidated financial statements.

Business combination

The Group applies the acquisition method to account for business combinations regardless of whether equity instruments or other assets are acquired. 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 Group. The consideration transferred includes the fair value of any asset or liability resulting from a contingent consideration arrangement and the fair value of any pre-existing equity interest in the subsidiary. The excess of the cost of acquisition over the fair value of the Group's share of the identifiable net assets acquired is recorded as goodwill. Goodwill arising on acquisitions is capitalized and is subject to an impairment review, both annually and when there are indications that the carrying value may not be recoverable.

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.

Basis of consolidation

These consolidated financial statements include the accounts of Verona Pharma plc and its wholly owned subsidiaries Verona Pharma, Inc. and Rhinopharma. The acquisition method of accounting was used to account for the acquisition of Rhinopharma.

Inter-company transactions, balances and unrealized gains on transactions between Group companies are eliminated.

Verona Pharma Inc. and Rhinopharma adopt the same accounting policies as the Company.

2.2 Correction of errors in 2015 comparative figures

Acquisition of Rhinopharma Limited

On September 19, 2006, the Group acquired Rhinopharma for a total consideration of £1,520 thousand payable in ordinary shares. Net assets of £51 thousand were recorded as part of the acquisition, resulting in excess consideration of £1,469 thousand, which was classified in its entirety as goodwill in the statement of financial position.

During 2016, the Company identified an error relating to the accounting for this acquisition. After further due diligence it has been identified that the excess consideration should have been recorded as an in-process research and development intangible ("IP R&D") and a corresponding deferred tax liability should have been recorded in relation to this intangible. In addition, there was a financial liability in relation to an assumed contingent obligation that Rhinopharma held with Vernalis plc ("Vernalis") that was not identified and fair valued at the date of the acquisition. The intangible asset and the financial liability should have been recognized at fair value on the acquisition date. The impact of these as of the time of the acquisition was as follows:

- Reclassification from goodwill to IP R&D of £1,469 thousand;

2. Accounting policies (Continued)

- Recognition of a deferred tax liability of £441 thousand; and
- Recognition of goodwill of £441 thousand.

The assumed contingent obligation was deemed to be insignificant at the acquisition date and therefore not recognized.

Subsequent to the business combination the following should have been applied:

Goodwill and IP R&D are not amortized as explained in the accounting policy in note 2.8 and should be annually tested for impairment. The cash generating unit ("CGU") has been tested for impairment annually and no impairment has been recorded.

The assumed contingent obligation is subsequently carried at amortized cost using the effective interest method. Further, since 2006, a corresponding deferred tax asset has been recognized in relation to Verona Pharma plc losses which offset the deferred tax liability.

The financial statements have been restated retrospectively for these errors. The entries to the 2015 opening Consolidated Statement of Financial Position as of January 1, 2015 are:

- an IP R&D asset of £1,469 thousand;
- an assumed contingent obligation of £522 thousand;
- a decrease in goodwill of £1,028 thousand; and
- a reduction in accumulated loss of £81 thousand.

The entries to the Consolidated Statement of Financial Position on December 31, 2015 as a result of the errors identified, are:

- an IP R&D asset of £1,469 thousand;
- an assumed contingent obligation of £594 thousand;
- a decrease in goodwill of £1,028 thousand; and
- a reduction in accumulated loss of £81 thousand.

As a consequence the net impact on the Consolidated Statement of Comprehensive Income for 2015 is:

- a £72 thousand finance expense in respect of the movement in the value of the assumed contingent obligation. Further details are set out in note 20 to these consolidated financial statements.

The following tables set forth a summary of the restatements performed:

January 1, 2015

Financial statement element	Pre restatement £'000	Correction amount	Post restatement £'000
Intangibles — IP R&D	—	1,469	1,469
Assumed contingent obligation	—	(522)	(522)
Goodwill	1,469	(1,028)	441
Accumulated loss	15,733	81	15,814

2. Accounting policies (Continued)

December 31, 2015

Financial statement element	Pre restatement £'000	Correction amount	Post restatement £'000
Intangibles — IP R&D	—	1,469	1,469
Assumed contingent obligation	—	(594)	(594)
Goodwill	1,469	(1,028)	441
Accumulated loss	23,096	81	23,177
Finance expense	—	72	72

Reclassifications

During the period, five reclassifications have been made to the December 31, 2015 primary statements as follows:

- Taxation recoverable amounting to £1,535 thousand has been reclassified from prepayments and other receivables to current tax receivable.
- Computer software with a net book value of £1 thousand has been reclassified from property, plant and equipment to intangible assets
- Exchange differences arising on translating foreign operations have been reclassified from research and development to other comprehensive gains due to an error in the prior period amounting to £4 thousand.
- Transfers of previously expensed share-based payment charges upon lapse of options between the share-based payment reserve and the total accumulated losses have been reclassified amounting to £503 thousand.
- U.S. taxation payable amounting to £14 thousand has been reclassified from trade and other payables to tax payable — U.S. operations.

The following table sets forth a reconciliation of accumulated loss before restatements and reclassifications to the accumulated loss following the restatements and reclassifications.

January 1, 2015

	£'000
Accumulated loss before restatements/reclassification	15,733
Impact of business combination restatement	81
Accumulated loss following restatement above	15,814
Impact of reclassification from the share based payment reserve	449
Accumulated losses per the statement of changes in equity	16,263

2. Accounting policies (Continued)

December 31, 2015

	£'000
Accumulated loss before restatements/reclassification	23,096
Impact of business combination restatement	81
Accumulated loss following restatement above	23,177
Assumed contingent obligation income statement charge	72
Impact of reclassification from the share based payment reserve	503
Accumulated losses per the statement of changes in equity	23,752

IAS 8 requires the disclosure of an opening balance sheet when an error has occurred before the earliest period presented. Management has judged that this disclosure gives sufficient information for a user to understand the impact on the opening balance sheet. Management has also judged, due to the nature of this adjustment, which is mainly a balance sheet gross up, that not including the full opening balance sheet would not be misleading to the user.

2.3 Foreign currency translation

Items included in the Group's consolidated financial statements are measured using the currency of the primary economic environment in which the Group operates ("the functional currency"). The consolidated financial statements are presented in pounds sterling ("£"), which is the functional and presentational currency of the Company and the presentational currency of the Group.

Transactions in foreign currencies are recorded using the rate of exchange ruling at the date of the transaction. Monetary assets and liabilities denominated in foreign currencies are translated using the rate of exchange ruling at the balance sheet date and the gains or losses on translation are included in the Consolidated Statement of Comprehensive Income. Non-monetary items that are measured in terms of historical cost in a foreign currency are translated using the exchange rates at the dates of the original transactions. Non-monetary items measured at fair value in a foreign currency are translated using the exchange rates at the date when the fair value was determined.

The assets and liabilities of foreign operations are translated into pounds sterling at the rate of exchange ruling at the balance sheet date. Income and expenses are translated at weighted average exchange rates for the period. The exchange differences arising on translation for consolidation are recognized in Other Comprehensive Income.

2.4 Cash and cash equivalents

Cash and cash equivalents includes cash in hand, deposits held at call with banks, and other short-term highly liquid investments with original maturities of three months or less.

2.5 Deferred taxation

Deferred tax is provided in full, using the liability method, on temporary differences arising between the tax bases of assets and liabilities and their carrying amounts in the consolidated financial statements. Deferred

2. Accounting policies (Continued)

tax is determined using tax rates (and laws) that have been enacted or substantially enacted by the balance sheet date and expected to apply when the related deferred tax is realized or the deferred liability is settled.

Deferred tax assets are recognized to the extent that it is probable that the future taxable profit will be available against which the temporary differences can be utilized.

2.6 Research and development costs

Capitalization of expenditure on product development commences from the point at which technical feasibility and commercial viability of the product can be demonstrated and the Group is satisfied that it is probable that future economic benefits will result from the product once completed. No such costs have been capitalized to date, given the early stage of the Group's product candidate development.

Expenditure on research and development activities that do not meet the above criteria is charged to the Consolidated Statement of Comprehensive Income as incurred.

2.7 Property, plant and equipment

Property, plant and equipment are stated at cost, net of depreciation and any provision for impairment. Cost includes the original purchase price of the asset and the costs attributable to bringing the asset to its working condition for its intended use. Depreciation is calculated so as to write off the cost less their estimated residual values, on a straight-line basis over the expected useful economic lives of the assets concerned. The principal annual periods used for this purpose are:

Computer hardware	3 years
Office equipment	5 years

2.8 Intangible assets and goodwill

(a) Goodwill

Goodwill arises on the acquisition of subsidiaries and represents the excess of the consideration transferred over the fair value of the identifiable net assets acquired.

(b) Patents

Patent costs associated with the preparation, filing, and obtaining of patents are capitalized and amortized on a straight-line basis over the estimated useful lives of the patents of ten years.

(c) Computer software

Amortization is calculated so as to write off the cost less estimated residual values, on a straight-line basis over the expected useful economic life of two years.

(d) In-process research & development

IP R&D assets acquired through business combinations which, at the time of acquisition, have not reached technical feasibility are recognized at fair value. The amounts are capitalized and are not amortized but are

2. Accounting policies (Continued)

subject to impairment testing until completion, abandonment of the projects or when the research findings are commercialized through a revenue generating project. The Group determines whether intangible assets (including goodwill) are impaired on an annual basis and this requires the estimation of the higher of fair value less costs of disposal and value in use. Upon successful completion or commercialization of the relevant project, IP R&D will be reclassified to developed technology. The Group will make a determination as to the then useful life of the developed technology, generally determined by the period in which the substantial majority of the cash flows are expected to be generated, and begin amortization. In case of abandonment the asset will be impaired.

2.9 Impairment of intangible assets, goodwill and non-financial assets

Goodwill and intangible assets that have an indefinite useful life and intangible assets not ready to use are not subject to amortization. These assets are tested annually for impairment or more frequently if impairment indicators exist. Non-financial assets that are subject to amortization are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount may not be recoverable. An impairment loss is recognized for the amount by which the asset's carrying amount exceeds its recoverable amount. The recoverable amount is the higher of an asset's fair value (less costs of disposal) and value in use.

For the purpose of assessing impairment, assets are grouped at the lowest levels for which there are separately identifiable cash flows, which are largely independent of the cash flows from other assets or group of assets (i.e. CGU).

Goodwill is allocated to CGUs for the purpose of impairment testing. The allocation is made to those CGUs or groups of CGUs that are expected to benefit from the business combination in which the goodwill arose. The units or group of units are identified at the lowest level at which goodwill is monitored for internal management purposes, being the operating segments.

The Group is a single cash generating unit. Goodwill that arose on the acquisition of Rhinopharma has been thus allocated to this single CGU. IP R&D is tested for impairment at this level as well, since it is the lowest level at which independent cash flows can be identified.

Non-financial assets, other than goodwill, that have been previously impaired are reviewed for possible reversal of the impairment at each subsequent reporting date.

2.10 Employee Benefits

(a) Pension

The Group operates a defined contribution pension scheme for UK employees. Contributions payable for the year are charged to the Consolidated Statement of Comprehensive Income. The contributions are recognized as employee benefit expense when they are due. Differences between contributions payable in the year and contributions actually paid are shown as either accruals or prepayments in the Consolidated Statement of Financial Position. The Group has no further payment obligation once the contributions have been paid.

2. Accounting policies (Continued)

(b) Bonus plans

The Company recognizes a liability and an expense for bonus plans if contractually obligated or if there is a past practice that has created a constructive obligation.

2.11 Share-based payments

The Group operates a number of equity-settled, share-based compensation schemes. The fair value of share-based payments under such schemes is expensed on a straight-line basis over the vesting period, based on the Group's estimate of shares that will eventually vest.

Where equity settled transactions are entered into with third party service providers, fair value is determined by reference to the value of the services provided in lieu of payment. The expense is measured based on the services received at the date of receipt of those services and is charged to the Consolidated Statement of Comprehensive Income over the period for which the services are received and a corresponding credit is made to reserves. For other equity-settled transactions fair value is determined using the Black-Scholes model and requires several assumptions and estimates as disclosed in note 20.

2.12 Provisions

Provisions are recognized when the Group has a present legal or constructive obligation as a result of past events, it is probable that an outflow of resources will be required to settle the obligation, and the amount can be reliably estimated. Provisions are measured at the present value of the expenditures expected to be required to settle the obligation using a pre-tax rate that reflects current market assessments of the time value of money and the risks specific to the obligation.

2.13 Assumed contingent obligation related to the business combinations

On September 19, 2006, the Group acquired Rhinopharma for a total consideration of £1,520 thousand payable in ordinary shares. In addition, the Group assumed certain contingent obligations owed by Rhinopharma to Vernalis under an assignment and license agreement (the "assumed contingent consideration") following the sale of IP by Vernalis to Rhinopharma. Pursuant to the agreement, Vernalis (i) assigned to the Company all of its rights to certain patents and patent applications relating to RPL554 and related compounds (the "Vernalis Patents") and (ii) granted to the Company an exclusive, worldwide, royalty-bearing license under certain Vernalis know-how to develop, manufacture and commercialize products (the "Licensed Products") developed using Vernalis Patents, Vernalis know-how and the physical stock of certain compounds.

The assumed contingent obligation comprises (a) a milestone payment on obtaining the first approval of any regulatory authority for the commercialization of a Licensed Product; (b) low-to-mid single digit royalties based on the future sales performance of all Licensed Products; and (c) a portion equal to a mid-twenty percent of any consideration received from any sub-licensees for the Vernalis Patents and for Vernalis know-how.

On the date of acquisition the fair value of the assumed contingent obligation was estimated as the expected value of the milestone payment, royalty payments and sub-license payments, based on management's estimate of the likely probability of success. The risk-weighted value of the assumed contingent arrangement was then discounted back to its net present value applying an effective interest rate

2. Accounting policies (Continued)

of 12%. The initial fair value of the assumed contingent obligation as of December 31, 2006 was deemed to be insignificant at the date of the acquisition, so it was not recorded.

The amount of royalties payable under the agreement is based on the future sales performance of certain products, and so the total amount payable is unlimited. The level of sales that may be achieved under the agreement is inherently uncertain and difficult to predict and the range of outcomes cannot be reliably estimated.

The value of this assumed contingent obligation is measured at amortized cost using the effective interest rate method, and is re-measured for changes in estimated cash flows, which may include charges based upon management's assessment as to the timing or the probability of achieving the various outcomes which trigger payment, or due to the time value of money, or due to changes in exchange rates, which affect the expected value of future net sales made in foreign currencies. The assumed contingent obligation is accounted for as a liability, and any adjustments made to the value of the liability will be recognized in the Consolidated Statement of Comprehensive Income for the period.

2.14 Government and other grants

The Group may receive government, regional or charitable grants to support its research efforts in defined projects where these grants provide for reimbursement of approved costs incurred as defined in the respective grants. Income in respect of such grants would include contributions towards the costs of research and development. Income would be recognized when costs under each grant are incurred in accordance with the terms and conditions of the grant and the collectability of the receivable is reasonably assured. Government, regional and charitable grants relating to costs would be deferred and recognized in the Consolidated Statement of Comprehensive Income over the period necessary to match them with the costs they are intended to compensate. When the cash in relation to recognized government, regional or charitable grants is not yet received the amount is included as a receivable on the Consolidated Statement of Financial Position.

Where the grant income is directly related to the specific items of expenditure incurred, the income would be netted against such expenditure. Where the grant income is not a specific reimbursement of expenditure incurred, the Group would include such income under "Other income" in the Consolidated Statement of Comprehensive Income. Grants or investment credits may be repayable if the Group successfully commercializes a relevant program that was funded in whole or in part by the grant or investment credit within a particular timeframe. Prior to successful commercialization, the Group would not make any provision for repayment.

2.15 Financial instruments — initial recognition and subsequent measurement

Initial Recognition

The Company classifies a financial instrument, or its component parts as a financial liability, a financial asset or an equity instrument in accordance with the substance of the contractual arrangement and the definitions of a financial liability, a financial asset and an equity instrument.

The Company evaluates the terms of the financial instrument to determine whether it contains an asset, a liability or an equity component. Such components shall be classified separately as financial assets, financial liabilities or equity instruments.

2. Accounting policies (Continued)

A financial instrument is any contract that gives rise to a financial asset of one entity and a financial liability or equity instrument of another entity.

(a) Financial assets, initial recognition and measurement

All financial assets, such as receivables and deposits, are recognized initially at fair value plus transaction costs, for all financial assets not recorded at fair value through profit or loss. Financial assets carried at fair value through profit or loss are initially recognized at fair value, and transaction costs are expensed in the income statement.

(b) Financial liabilities, initial recognition and measurement

Financial liabilities are classified, at initial recognition, as financial liabilities at fair value through profit or loss, loans and borrowings, or payables, as appropriate. All financial liabilities are recognized initially at fair value and, in the case of loans and borrowings and payables, net of directly attributable transaction costs.

The Company's financial liabilities include trade and other payables and derivative financial instruments.

(c) Subsequent measurement

The measurement of financial assets and financial liabilities depends on their classification.

Financial liabilities at fair value through profit or loss include financial liabilities held for trading and financial liabilities designated upon initial recognition as at fair value through profit or loss. These are subsequently measured at fair value with any gains or losses recognized in profit or loss. All other financial liabilities are measured at amortized cost using the effective interest method

Financial assets such as receivables and deposits are subsequently measured at amortized cost. The Company does not hold any financial assets at fair value through profit or loss or available for sale financial assets.

(d) Derivative financial instruments

Derivatives are initially recognized at fair value on the date a derivative contract is entered into and are subsequently re-measured at fair value at the end of each reporting date. The Company holds only one type of derivative financial instrument, the warrants, as explained in Note 2.16.

The full fair value of the derivative is classified as a non-current asset or liability when the item is more than 12 months and as a current asset or liability when the remaining maturity of the item is less than 12 months.

Changes in fair value of a derivative financial liability when related to a financing arrangement are recognized in the Consolidated Statement of Comprehensive Income within Finance income or Finance expense. Fair value gains or losses on derivatives used for non-financing arrangements are recognized in other operating income or expense.

2. Accounting policies (Continued)

2.16 Warrants

Warrants issued by the Company to investors as part of a share subscription are compound financial instruments where the warrant meets the definition of a financial liability.

The financial liability component is initially measured at fair value in the Consolidated Statement of Financial Position. Equity is measured at the residual between the subscription price for the entire instrument and the liability component. Subsequently the financial liability component is subsequently remeasured depending on its classification. Equity is not subsequently remeasured.

2.17 Transaction costs

Qualifying transaction costs are often incurred in anticipation of an issuance of equity instruments and may cross reporting periods. The entity defers these costs on the balance sheet until the equity instrument is recognised. Deferred costs are subsequently reclassified as a deduction from equity when the equity instruments are recognised, to the extent that the costs are directly attributable to the equity transaction. If the equity instruments are not subsequently issued, the transaction costs are expensed. Any costs not directly attributable to the equity transaction are expensed.

Transaction costs that relate to the issue of a compound financial instrument are allocated to the liability and equity components of the instrument in proportion to the allocation of proceeds. Where the liability component is held at fair value through profit or loss, the transaction costs are expensed to the Consolidated Statement of Comprehensive Income. For liabilities held at amortized cost, transaction costs are deducted from the liability and subsequently amortized. The amount of transaction costs accounted for as a deduction from equity in the period is disclosed separately in accordance with IAS 1.

2.18 New standards, amendments and interpretations adopted by the Group

The following amendment has been adopted by the Group for the first time for the financial year beginning on or after January 1, 2016. It did not materially impact the Group's results:

- Annual Improvements 2014 (2012-2014 cycle)

2.19 New standards, amendments and interpretations issued but not effective for the financial year beginning January 1, 2016 and not early adopted

A number of new standards and amendments to standards and interpretations have been issued but are not yet effective for annual periods beginning after January 1, 2017 (noted below), and have not been adopted in preparing these consolidated financial statements.

- IFRS 9) "Financial instruments" (effective for annual periods beginning on or after January 1, 2018)
- IFRS 15 "Revenue from contracts with customers" (effective for annual periods beginning on or after January 1, 2018
- IFRS 16 "Leases" (effective for annual periods beginning on or after January 1, 2019)

IFRS 9 is not expected to have a material impact on the accounting for the assumed contingent obligation or the derivative financial instrument. IFRS 15 and 16 will have an immaterial impact on the financial statements of the Company as the Company is not currently revenue generating and does not have any leases of over one year.

3. Financial Instruments

3.1 Financial Risk Factors

The Company's activities have exposed it to a variety of financial risks: market risk (including currency risk and interest rate risk), credit risk, and liquidity risk. The Company's overall risk management program is focused on preservation of capital and the unpredictability of financial markets and has sought to minimize potential adverse effects on the Company's financial performance and position.

(a) Currency risk

Foreign currency risk reflects the risk that the Group's net assets will be negatively impacted due to fluctuations in exchange rates. The Group has not entered into foreign exchange contracts to hedge against gains or losses from foreign exchange fluctuations. As of December 31, 2016, cash and cash equivalents included £282 thousand, US$13,110 thousand, and SEK 20 thousand, and accounts payable and accrued liabilities included balances of £211 thousand and US$80 thousand.

Foreign currency denominated trade payables are short term in nature (generally 30 to 45 days). The Group has a U.S.-operation, whose net assets are exposed to foreign currency translation risk.

(b) Credit risk

Credit risk reflects the risk that the Group may be unable to recover contractual receivables. The Group is still in the development stage; therefore, no policies are required at this time to mitigate this risk.

For banks and financial institutions, only independently rated parties with a minimum rating of "B+" are accepted. The Directors recognize that this is an area in which they may need to develop specific policies should the Group become exposed to further financial risks as the business develops.

As of December 31, 2016 and December 31, 2015, the majority of cash and cash equivalents were placed at the following banks:

	Year ended December 31, 2015	Credit rating	Year ended December 31, 2016	Credit rating
	£'000		£'000	
Banks				
Royal Bank of Scotland	63	A3	11,287	A3
Lloyds Bank	3,460	A1	28,447	A1
Wells Fargo[1]	1	Aa1	51	Aa2
Total	3,524		39,785	

(1) The Wells Fargo account holds the operating account for the Verona Pharma Inc. U.S. operations.

(c) Management of capital

The Group considers capital to be its equity reserves. At the current stage of the Group's life cycle, the Group's objective in managing its capital is to ensure funds raised meet the research and operating requirements until the next development stage of the Group's suite of projects.

3. Financial Instruments (Continued)

The Group ensures it is meeting its objectives by reviewing its Key Performance Indicators ("KPIs") to ensure the research activities are progressing in line with expectations, costs are controlled and unused funds are placed on deposit to conserve resources and increase returns on surplus cash held.

(d) Interest rate risk

As of December 31, 2016, the Group had cash deposits of £39,785 thousand (2015: £3,524 thousand). The rates of interest received during 2016 ranged between 0.0% and 0.5%. The Group's exposure to interest rate risk, which is the risk that the interest received will fluctuate as a result of changes in market interest rates on classes of financial assets and financial liabilities, was as follows:

	December 31, 2016	
	Floating interest rate	Fixed Interest rate
	£	£
Financial asset		
Cash deposits	11,338,225	28,446,873

(e) Liquidity risk

The Group prepares periodic working capital forecasts for the foreseeable future, allowing an assessment of the cash requirements of the Group, to manage liquidity risk. The following table provides an analysis of the remaining contractually agreed cash flows for the Group's non-derivative financial liabilities on an undiscounted basis, which therefore differs from both the carrying value and fair value. Balances due within 12 months equal their carrying value balances as the impact of discounting is not significant.

	LESS THAN 1 YEAR	BETWEEN 1 AND 2 YEARS	BETWEEN 2 AND 5 YEARS	OVER 5 YEARS[1]
	£	£	£	£
At December 31, 2015				
Trade payables	1,108,991	—	—	—
Corporation tax payable — US operation	14,057	—	—	—
Trade payables due to related parties	172,955	—	—	—
Other payables	40,907	—	—	—
Total	1,336,910	—	—	—

(1) This table excludes a milestone payment, which may fall due under the assumed contingent obligation, of £5 million and sales based royalties.

3. Financial Instruments (Continued)

	LESS THAN 1 YEAR	BETWEEN 1 AND 2 YEARS	BETWEEN 2 AND 5 YEARS	OVER 5 YEARS[1]
	£	£	£	£
At December 31, 2016				
Trade payables	592,931	—	—	—
Corporation tax payable — US operation	126,063	—	—	—
Trade payables due to related parties	—	—	—	—
Other payables	180,567	—	—	—
Total	899,561	—	—	—

(1) This table excludes a milestone payment which may fall due under the assumed contingent obligation, of £5 million and sales based royalties.

3.2 Fair value estimation

The carrying amounts of cash and cash equivalents, receivables, accounts payable, accrued liabilities and the assumed contingent obligation, approximate to fair value due to their short-term nature.

For financial instruments that are measured in the Consolidated Statement of Financial Position at fair value, IFRS 7 requires disclosure of fair value measurements by level of the following fair value measurement hierarchy:

- Quoted prices (unadjusted) in active markets for identical assets or liabilities (level 1);
- Inputs other than quoted prices included within level 1 that are observable for the asset or liability, either directly or indirectly (level 2); and
- Inputs for the asset or liability that are not based on observable market data (level 3).

For the year ended December 31, 2016 and 2015 fair value adjustments to financial instruments through profit and loss resulted in the recognition of finance income of £1,068 thousand and £nil respectively.

The fair value of financial instruments that are not traded in an active market is determined by using valuation techniques. These valuation techniques maximize the use of observable market data where it is available and rely as little as possible on entity specific estimates. If all significant inputs required to ascertain the fair value of an instrument are observable, the instrument is included in level 2. If one or more of the significant inputs are not based on observable market data, the instrument is included in level 3. The carrying amount of a financial asset or financial liability is a reasonable approximation of the fair value and therefore information about the fair values of each class has not been disclosed.

	Level 1	Level 2	Level 3	Total
	£	£	£	£
At December 31, 2016				
Derivative financial instrument	—	—	7,922,603	7,922,603
Total	—	—	7,922,603	7,922,603

3. Financial Instruments (Continued)

Movements in Level 3 items during the year ended December 31, 2016 are as follows:

	Derivative financial instrument	Total
	£	£
At January 1, 2016	—	—
Initial recognition of derivative financial instrument	8,990,794	8,990,794
Fair value adjustments recognized in profit or loss	(1,068,191)	(1,068,191)
At December 31, 2016	7,922,603	7,922,603

Further details relating to the derivative financial instrument are set out in notes 4 and 21 of these financial statements.

In determining the fair value of the derivative financial instrument the Company applied the Black Scholes model; key inputs include the share price at reporting date, estimations on timelines, volatility and risk-free rates. These assumptions and the impact of changes in these assumptions, where material, are disclosed in note 21.

4. Critical accounting estimates

The preparation of financial statements in conformity with IFRS requires the use of accounting estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the financial statements and the reported amounts of income and expenses during the reporting period. Although these estimates are based on management's best knowledge of current events and actions, actual results ultimately may differ from those estimates. IFRS also requires management to exercise its judgement in the process of applying the Group's accounting policies.

The areas involving a higher degree of judgement or complexity, or areas where assumptions and estimates are significant to the consolidated financial statements are as follows:

(a) Impairment of intangible assets

The Group is required to test goodwill and the IP R&D annually for impairment in accordance with the accounting policy in note 2.9. Goodwill and the IP R&D are tested for impairment at the Group level, which is viewed as a single CGU in accordance with the accounting policy in note 2.9.

The Group determines the recoverable amount of the single CGU and compares it to its carrying amount. Impairment is recognized when the carrying amount exceeds the recoverable amount of the CGU.

Determining the recoverable amount of the CGU, containing goodwill and IP R&D for impairment purposes requires estimation.

Since the Group is a single CGU, the entity measures its recoverable amount with reference to the market capitalization of the Group, as an indication of the fair value less costs of disposal. Details of the Group's impairment assessment for the CGU containing goodwill and IP R&D are disclosed in notes 15 and 16.

4. Critical accounting estimates (Continued)

(b) Share-based payments

The Group records charges for share-based payments. For option based share-based payments management estimates certain factors used in the option pricing model, including volatility, vesting date of options and number of options likely to vest. If these estimates vary from actual occurrence, this will impact the value of the equity carried in reserves. Further details of the Group's estimation of share-based payments are disclosed in note 19.

(c) Assumed contingent obligation

The Group has a material obligation for the future payment of royalties and milestones associated with contractual obligations on RPL554, a development product acquired as part of the acquisition of Rhinopharma. The estimation of the fair value of the assumed contingent obligation requires the selection of an appropriate valuation model at the date of acquisition, consideration as to the inputs necessary for the valuation model chosen, the estimation of the likelihood that the regulatory milestone will be achieved and fair value of the future cash flows (for further detail see note 20). The estimates for the assumed contingent obligation are based on a discounted cash flow model. Key assessments and judgements included in the calculation of deferred consideration are:

- development, regulatory and marketing risks associated with progressing the product to market approval in key target territories;
- market size and product acceptance by clinicians, patients and reimbursement bodies;
- gross and net selling price;
- costs of manufacturing, product distribution and marketing support;
- launch of competitive products; and
- discount rate and time to crystallization of contingent consideration.

In accordance with IAS 39 ("Financial Instruments Recognition and Measurement" (para AG8)), when there is a change in the projected cash flows, the assumed contingent obligation will be remeasured with the change in value going through the Consolidated Statement of Comprehensive Income. The assumed contingent obligation is measured at amortized cost with the discount unwinding in the Consolidated Statement of Comprehensive Income throughout the year. Actual outcomes could differ significantly from the estimates made.

The value of the assumed contingent obligation as of December 31, 2016 amounts to £802 thousand. (2015: £594 thousand. The increase in value of the assumed contingent obligation during 2016 amounted to £208 thousand (2015: 72 thousand) and was recorded as finance expense. Periodic remeasurement is triggered by changes in updated timelines of achieving commercialization and updated probabilities of success resulting from clinical programs. The discount percentage applied is 12%.

(d) Valuation of the July 2016 warrants

The fair value is determined by applying the Black-Scholes valuation model and requires several assumptions and estimates as disclosed in note 4(d) and 12.

4. Critical accounting estimates (Continued)

Pursuant to the July Placement, the Company issued 31,115,926 units to new and existing investors at the placing price of £1.4365 per unit. Each unit comprises one ordinary share and one warrant. The warrants entitle the investors to subscribe for in aggregate a maximum of 12,446,370 ordinary shares.

In accordance with IAS 32 and Company accounting policy as disclosed in note 2.17, the Company classified the warrants as a derivative financial liability to be presented on the Company's Consolidated Statement of Financial Position.

The fair value of these warrants is determined by applying the Black-Scholes model. Assumptions are made on inputs such as time to maturity, the share price, volatility and risk free rate, in order to determine the fair value per warrant. For further details please see note 21.

Transaction costs arising on the issues of these shares and warrants are allocated to the equity and warrant liability components in proportion to the allocation of proceeds.

5. Earnings per share

Basic loss per ordinary share of 15.0p (2015: 37.1p) for the Group is calculated by dividing the loss for the year ended December 31, 2016 by the weighted average number of ordinary shares in issue of 33,499,413 as of December 31, 2016 (2015: 20,198,469). Potential ordinary shares are not treated as dilutive as the entity is loss making and such shares would be anti-dilutive.

Prior to the 50-for-1 consolidation of shares (as described in Note 1) the above numbers would read as follows: Basic loss per share of 0.30p (2015: 0.74p) for the Group is calculated by dividing the loss for the year ended December 31, 2016 by the weighted average number of ordinary shares in issue of 1,674,970,686 as of December 31, 2016 (2015: 1,009,923,481).

6. Segmental reporting

During 2016, there has been a change to management's assessment of the operating and reporting segments of the Group and how the Chief Operating Decision Maker reviews management information. Management has concluded that the Group's activities now consist of one operating and reportable segment: Drug development. Previously management had two reporting segments: Clinical research for RPL554 and Basic research, which contained VRP700 and NAIP. During the year ended December 31, 2015, the Group abandoned the development of the product candidates VRP700 and NAIP. As a consequence, management information is only prepared and reviewed for RPL554, resulting in a single operating and reportable segment.

All non-current assets are based in the United Kingdom.

7. Operating loss

	Year ended December 31, 2015	Year ended December 31, 2016
	£	£
Operating Loss is stated after charging:		
Research and development costs:		
Employee benefits (note 8)	1,322,109	2,036,505
Amortization of patents (note 15)	43,262	50,972
Loss on disposal of patents (note 15)	134,532	8
Other research and development expenses	5,768,944	2,434,335
Total research and development costs	7,268,847	4,521,820
General and administrative costs:		
Employee benefits (note 8)	624,821	865,250
Legal and professional fees	608,447	884,040
Amortization of computer software (note 15)	166	599
Loss on disposal of property, plant and equipment (note 14)	—	2,625
Depreciation of property, plant and equipment (note 14)	9,689	10,051
Operating lease charge — land and buildings	156,632	168,763
Loss / (gain) on variations in foreign exchange rate	20,732	139,091
Other general and administrative expenses	285,457	427,930
Total general and administrative costs	1,705,944	2,498,349
Operating loss	8,974,791	7,020,169

During the periods indicated, the Group obtained the services from and paid the fees of the Group's auditors and their associates as detailed below:

	Year ended December 31, 2015	Year ended December 31, 2016
	£	£
Audit of Verona Pharma plc and consolidated financial statements	25,000	80,000
Audit related services	—	525,000
IT services review	9,972	—
Total	34,972	605,000

For the year ended December 31, 2016, audit related services include assurance reporting on historical financial information included in the Company's U.S. initial public offering registration statement that was confidentially filed with the U.S. Securities and Exchange Commission on November 23, 2016. As per December 31, 2016 an amount of £466 thousand in relation to these services was booked in deferred IPO costs as they will be offset against share premium on completion of the plans to conduct a registered initial public offering in the United States (the "Global Offering") (see note 11).

8. Directors' emoluments and staff costs

	Year ended December 31, 2015	Year ended December 31, 2016
The average number of employees of the Group during the year:	8	7

	Year ended December 31, 2015	Year ended December 31, 2016
	£	£
Aggregate emoluments of directors:		
Salaries and other short-term employee benefits	854,012	1,068,529
Incremental payment for additional services	89,051	44,000
Pension costs	37,989	18,882
Total directors' emoluments	981,052	1,131,411
Share-based payment charge	231,790	256,615
Directors' emoluments including share-based payment charge	1,212,842	1,388,026

	Year ended December 31, 2015	Year ended December 31, 2016
	£	£
Aggregate other staff costs:		
Wages and salaries	539,802	1,027,339
Social security costs	41,966	97,827
Incremental payment for additional services	—	57,917
Share-based payment charge	137,393	319,278
Pension costs	14,927	11,368
Total other staff costs	734,088	1,513,729

The Group operates a defined contribution pension scheme for U.K. employees and executive directors. The total pension cost during the year ended December 31, 2016 was £30 thousand (2015: £53 thousand). There were no prepaid or accrued contributions to the scheme at December 31, 2016.

9. Finance income and expense

	Year ended December 31, 2015	Year ended December 31, 2016
	£	£
Finance income:		
Interest received on cash balances	44,791	86,542
Foreign exchange gain on translating foreign currency denominated bank balances	—	686,549
Fair value adjustment on derivative financial instruments (note 21)	—	1,068,191
Total finance income	44,791	1,841,282

9. Finance income and expense (Continued)

	Year ended December 31, 2015	Year ended December 31, 2016
	£	£
Finance expense:		
Transaction costs allocated to the issue of warrants (note 21)	—	585,425
Remeasurement of assumed contingent arrangement (note 20)	9,239	123,554
Unwinding of discount factor related to the assumed contingent arrangement (note 20)	63,052	84,711
Total finance expense	72,291	793,690

10. Taxation

	Year ended December 31, 2015	Year ended December 31, 2016
	£	£
Analysis of tax credit for the year		
Current tax:		
UK and US tax	(1,520,732)	(937,772)
Adjustment in respect of prior periods	11,284	(16,412)
Total tax credit	(1,509,448)	(954,184)
Factors affecting the tax charge for the year		
Loss on ordinary activities	(9,002,291)	(5,972,577)
Multiplied by standard rate of corporation tax of 20% (2015: 20.25%)	(1,822,964)	(1,194,515)
Effects of:		
Non-deductible expenses	113,529	78,489
Research and development incentive	(599,368)	(427,304)
Timing differences not recognized	(1,880)	(4,131)
Difference in overseas tax rates	—	55,581
Tax losses carried forward not recognized	789,951	554,108
	(1,520,732)	(937,772)
Adjustment in respect of prior periods	11,284	(16,412)
Total tax credit	(1,509,448)	(954,184)

UK corporation tax is charged at 20% (2015: 20.25%) and U.S. federal tax at 35% (2015: 35%).

10. Taxation (Continued)

Deferred tax

The following tables represent deferred tax balances recognized in the Consolidated Statement of Financial Position, and the movements in both the deferred tax asset and the deferred tax liability.

	Year ended December 31, 2015	Year ended December 31, 2016
	£	£
Deferred tax assets	265,000	249,749
Deferred tax liabilities	(265,000)	(249,749)
Net balances	—	—

	Year ended December 31, 2015	Year ended December 31, 2016
	£	£
Movements on the deferred tax asset		
January 1	294,000	265,000
Impact of rate changes	(29,000)	(15,251)
December 31	265,000	249,749

	Year ended December 31, 2015	Year ended December 31, 2016
	£	£
Movements on the deferred tax liability		
January 1	(294,000)	(265,000)
Impact of rate changes	29,000	15,251
December 31	(265,000)	(249,749)

Factors that may affect future tax charges

The Group has UK tax losses available for offset against future profits in the UK. However an additional deferred tax asset has not been recognized in respect of such items due to uncertainty of future profit streams. As of December 31, 2016, the unrecognized deferred tax asset at 17% is estimated to be £3,149 thousand (2015: £2,819 thousand at 18%).

11. Prepayments and other receivables

	As of December 31, 2015	As of December 31, 2016
	£	£
Prepayments and accrued income	196,313	1,360,812
Deferred IPO costs	—	1,526,829
Other receivables	316,987	70,946
Total prepayments and other receivables	513,300	2,958,587

Deferred IPO costs relate to the Global Offering. These costs will be offset against share premium in the period in which the Global Offering is completed.

11. Prepayments and other receivables (Continued)

The prepayments balance includes prepayments for insurance and clinical activities.

There are no impaired assets within prepayments and other receivables.

12. Cash and cash equivalents

	As of December 31, 2015	As of December 31, 2016
	£	£
Cash at bank and in hand	3,524,387	39,785,098

The increase in cash during 2016 resulted from the July Placement.

13. Trade and other payables

	As of December 31, 2015	As of December 31, 2016
	£	£
Trade payables	1,108,991	718,994
Trade payables due to related parties	172,955	—
Other payables	40,907	54,504
Accruals	475,829	2,049,991
Total trade and other payables	1,798,682	2,823,489

As of December 31, 2016 accruals include £890 thousand related to expenses associated with the Global Offering.

14. Property, plant and equipment

	Computer hardware	Office equipment	Total
	£	£	£
Cost			
At January 1, 2015	41,302	36,461	77,763
Additions	1,193	—	1,193
At December 31, 2015	42,495	36,461	78,956
Accumulated depreciation			
At January 1, 2015	35,890	20,214	56,104
Charge for the year	2,664	7,025	9,689
At December 31, 2015	38,554	27,239	65,793
Net book value			
At December 31, 2015	3,941	9,222	13,163

14. Property, plant and equipment (Continued)

	Computer hardware	Office equipment	Total
	£	£	£
Cost			
At January 1, 2016	42,495	36,461	78,956
Additions	13,351	—	13,351
Disposals	(38,845)	(36,461)	(75,306)
At December 31, 2016	17,001	—	17,001
Accumulated depreciation			
At January 1, 2016	38,554	27,239	65,793
Charge for the year	3,027	7,024	10,051
Disposals	(38,418)	(34,263)	(72,681)
At December 31, 2016	3,163	—	3,163
Net book value			
At December 31, 2016	13,838	—	13,838

15. Intangible assets

	IP R&D	Computer software	Patents	Total
	£	£	£	£
Cost				
At January 1, 2015	1,469,112	23,934	515,569	2,008,615
Additions	—	637	141,239	141,876
Disposal	—	—	(174,944)	(174,944)
At December 31, 2015	1,469,112	24,571	481,864	1,975,547
Accumulated amortization				
At January 1, 2015	—	23,746	135,029	158,775
Charge for year	—	166	43,262	43,428
Disposal	—	—	(40,412)	(40,412)
At December 31, 2015	—	23,912	137,879	161,791
Net book value				
At December 31, 2015	1,469,112	659	343,985	1,813,756

15. Intangible assets (Continued)

	IP R&D	Computer software	Patents	Total
	£	£	£	£
Cost				
At January 1, 2016	1,469,112	24,571	481,864	1,975,547
Additions	—	4,750	109,757	114,507
Disposal	—	(23,982)	—	(23,982)
At December 31, 2016	1,469,112	5,339	591,621	2,066,072
Accumulated amortization				
At January 1, 2016	—	23,912	137,879	161,791
Charge for year	—	599	50,972	51,571
Disposal	—	(23,974)	—	(23,974)
At December 31, 2016	—	537	188,851	189,388
Net book value				
At December 31, 2016	1,469,112	4,802	402,770	1,876,684

Intangible assets comprise patents, computer software and an IP R&D asset that arose on the acquisition of Rhinopharma and investment in patents to protect RPL554.

IP R&D is currently not amortized and is reviewed for impairment on an annual basis or where there is an indication that the assets might be impaired until the asset is brought into use.

Patents are amortized over a period of ten years and are regularly reviewed for impairment to ensure the carrying amount exceeds the recoverable amount in accordance with note 2.9.

Recognizing that the Company is still in pre-revenue phase and that the research projects are not yet ready for commercial use, the Company assesses the recoverable amount of the CGU containing the IP R&D with reference to the Company's market capitalization as of December 31, 2016, the date of testing of goodwill impairment. The market capitalization of the Company was approximately £80 million as of December 31, 2016, compared to the Company's net assets of £34.5 million. Therefore, no impairment was recognized.

16. Goodwill

	As of December 31, 2015	As of December 31, 2016
	£	£
Goodwill at January 1 and December 31	441,000	441,000

Goodwill represents the excess of the purchase price over the fair value of the net assets acquired in connection with the acquisition of Rhinopharma in September 2006. Goodwill is not amortized, but is tested annually for impairment. Annual impairment testing is performed by comparing the expected recoverable amount of the CGU to the carrying amount of the CGU to which goodwill has been allocated to the carrying amount of the CGU. See notes 2.9, 4 and 15 to these consolidated financial statements.

17. Share Capital

The movements in the Company's share capital are summarized below:

Date	Description	Number of shares	Share Capital amounts in £
January 1, 2015	Brought forward	1,009,923,481	1,009,923
December 31, 2015		**1,009,923,481**	**1,009,923**
July 29, 2016	Issuance of shares	1,555,796,345	1,555,796
September 12, 2016	Exercise of options	166,667	167
October 24, 2016	Exercise of options	166,667	167
December 28, 2016	Exercise of options	2,000,000	2,000
December 31, 2016		**2,568,053,160**	**2,568,053**

As disclosed in note 23, on February 8, 2017 the board of the Company approved a share consolidation where every 50 existing ordinary shares of £0.001 were consolidated into one ordinary share of £0.05. The retrospective effect of this share consolidation on the Company's share capital movements during the year is summarized below:

Date	Description	Number of shares	Share Capital amounts in £
January 1, 2015	Brought forward	20,198,469	1,009,923
December 31, 2015		**20,198,469**	**1,009,923**
July 29, 2016	Issuance of shares	31,115,926	1,555,796
September 12, 2016	Exercise of options	3,334	167
October 24, 2016	Exercise of options	3,334	167
December 28, 2016	Exercise of options	40,000	2,000
December 31, 2016		**51,361,063**	**2,568,053**

The total number of authorized ordinary shares, with a nominal value of £0.05 each, is 200,000,000 (share capital of £10,000,000). All 51,361,063 ordinary shares at December 31, 2016 are allotted, unrestricted, called up and fully paid.

On July 29, 2016, the Company issued 31,115,926 units to new and existing investors at the placing price of £1.4365 per unit. Each unit comprises one ordinary share and one warrant (with an entitlement to subscribe for 0.4 of an ordinary share at a per share exercise price of 120% of the placing price or £1.7238). The warrants entitle the investors to subscribe for in aggregate a maximum of 12,446,370 shares. The gross proceeds received of £44.7 million were in exchange for both ordinary shares and the warrants. During 2016, the Company issued 46,666 ordinary shares (2015: nil) upon exercise of employee share options.

18. Related parties transactions

The Company entered into relationship agreements with Vivo Capital Fund VIII ("Vivo Capital"), Orbimed Private Investments VI L.P. ("Orbimed"), Abingworth Bioventures VI L.P. ("Abingworth") and Arix Bioscience plc ("Arix"), Arthurian Life Sciences SPV GP Limited, ("Arthurian"). As agreed in these relationship agreements, the above parties invested in the Company as part of the July Placement, and the Company agreed to appoint representatives designated by Vivo Capital, OrbiMed, Arix and Arthurian, and Abingworth to the board of directors, who are Dr. Mahendra Shah, Mr. Rishi Gupta, Dr. Ken Cunningham and Dr. Andrew Sinclair, respectively.

These agreements will continue in effect after the consummation of the Global Offering, except that the appointment rights within the relationship agreement with Arix and Arthurian have been terminated. The respective appointment rights under the remaining relationship agreements will automatically terminate upon (i) Vivo Capital, OrbiMed or Abingworth (or any of their associates), as applicable, ceasing to beneficially hold 6.5% of the issued ordinary shares, or (ii) the ordinary shares ceasing to be admitted to AIM.

The Company also has a management rights agreement with Novo A/S under which Novo A/S is entitled to appoint an observer to the Board until the earlier to occur of the Company's intended NASDAQ listing or a sale by Novo A/S of 50% of its shares in the Company.

The Company entered into a shareholder agreement with the Wales Life Sciences Investment Fund ("WLSIF") in connection with the March 2014 financing under which the Company has certain obligations to the WLSIF, including the obligation to maintain the registered office in Wales and to carry out certain other activities in Wales.

For the year ended December 31, 2015, the Company was charged £2,376 thousand by Simbec-Orion in respect of clinical and pre-clinical support and research services, a group of which Prof. Trevor Jones is a Director. As of December 31, 2015, the Company owed £173 thousand to this related party. Prof. Trevor Jones was a Director of the Company until September 2015. During 2016, there were no transactions with Simbec-Orion or any other related parties. As of December 31, 2016, there were no outstanding balances to related parties.

The Directors have authority and responsibility for planning, directing and controlling the activities of the Group and they therefore comprise key management personnel as defined by IAS 24, ("Related Party Disclosures"). Remuneration of Directors and senior management is disclosed in the Directors' emoluments report in note 8.

19. Share-based payments charge

In accordance with IFRS 2 "Share Based Payments," the cost of equity-settled transactions is measured by reference to their fair value at the date at which they are granted. Where equity-settled transactions were entered into with third party service providers, fair value is determined by reference to the value of the services provided. For other equity-settled transactions fair value is determined using the Black-Scholes model. The cost of equity-settled transactions is recognized over the period until the award vests. No expense is recognized for awards that do not ultimately vest. At each reporting date, the cumulative expense

19. Share-based payments charge (Continued)

recognized for equity-based transactions reflects the extent to which the vesting period has expired and the number of awards that, in the opinion of the Directors at that date, will ultimately vest.

The costs of equity-settled share-based payments to employees are recognized in the Statement of Comprehensive Loss, together with a corresponding increase in equity during the vesting period. During the twelve months ended December 31, 2016, the Company recognized a share-based payment expense of £576 thousand (2015: £399 thousand). The charge is included within both general and administrative costs as well as in research and development costs and represents the current year's allocation of the expense for relevant share options.

The Company grants share options under an Unapproved Share Option Scheme (the "Unapproved Scheme") and under its tax efficient EMI Option Scheme (the "EMI Scheme"). Under the Unapproved Scheme, options are granted to employees, directors and consultants to acquire shares at a price to be determined by the Directors which is typically set at a price that is above the share price at the date of the grant. In general, options are granted at a premium to the share price at the date of grant and vest over a period of three years from the date of the grant in two different methods. The first method is with one half vesting over 24 months and the other half vesting over 36 months. The second method is one third vesting over one year, the second third vesting over two years and the final third vesting over three years. The vesting period is defined as the period between the date of grant and the date when the options become exercisable. The options are exercisable during a period ending ten years after the date of grant. Options also are issued to advisors under the Unapproved Scheme. Such options generally vest immediately and are exercisable between one and two years after grant. Under the EMI Scheme, options are granted to employees and directors who are contracted to work at least 25 hours a week for the Company or for at least 75% of their working time. The options granted under the EMI Scheme are exercisable at a price that is above the share price at the date of the grant and in accordance with a vesting schedule determined by the Directors at the time of grant and have an exercise period of ten years from the date of grant.

In the year ended December 31, 2016, the Company granted 32,000 (2015: 102,000) share options under the EMI Scheme and 1,670,000 (2015: 550,000) share options under the Unapproved Scheme. The total fair values were estimated either by reference to the fair value of the services provided in respect of equity-settled transactions that were entered into with third-party service providers, or using the Black-Scholes option-pricing model for other equity-settled transactions and amounted to £1,927 thousand (2015: £371 thousand). The cost is amortized over the vesting period of the options on a straight-line basis.

Prior to the July Placement, management determined to take an option's contractual maximum life as an input into the Black-Scholes option-pricing model. Starting from the July Placement and in line with the continued development of the Company's clinical trials, the Company determined the time to maturity to be used in the valuation model to be better represented by the weighted-average life of the options granted.

19. Share-based payments charge (Continued)

The following assumptions were used for the Black-Scholes valuation of share options granted in 2015 and 2016. For the options granted under the Unapproved Scheme the table indicates the ranges used in determining the fair-market values, aligning with the various dates of the underlying grants. The volatility is calculated using historic weekly averages of the Company's share price over a period that is in line with the expected life of the options.

	EMI Scheme Employees	Unapproved Scheme Employees
Issued in 2015		
Options granted	102,000	550,000
Risk-free interest rate	1.42%	1.42%
Expected life of options	10 years	10 years
Annualized volatility	76.5%	76.5%
Dividend rate	0.00%	0.00%
Issued in 2016		
Options granted	32,000	1,670,000
Risk-free interest rate	1.42%	0.23% - 1.42%
Expected life of options	10 years	5.5 - 10 years
Annualized volatility	88.0%	74.3% - 88.0%
Dividend rate	0.00%	0.00%

The Company had the following share options movements in the year ended December 31, 2016:

Year of issue	Exercise price (£)	At January 1, 2016	Options granted	Options exercised	Options forfeited	Options expired	At December 31, 2016	Expiry date
2006	2.50	160,000	—	—	—	(160,000)	—	September 18, 2016*
2012	2.50 - 7.50	100,000	—	—	—	—	100,000	June 1, 2022
2013	2.40	100,000	—	—	—	(100,000)	—	January 31, 2016**
2013	2.00	100,000	—	—	—	—	100,000	April 15, 2023
2013	2.00	20,000	—	—	—	—	20,000	June 1, 2023***
2013	2.00	160,000	—	—	—	—	160,000	July 29, 2023
2014	1.75	110,000	—	—	—	—	110,000	May 15, 2024
2014	1.75	70,000	—	—	(6,667)	—	63,333	May 15, 2024***
2014	1.10	120,000	—	(40,000)	(80,000)	—	—	September 26, 2024***
2014	1.10 - 1.75	200,000	—	—	—	—	200,000	August 6, 2018****
2015	1.25	102,000	—	(6,666)	(13,334)	—	82,000	January 29, 2025***
2015	1.25	550,000	—	—	(40,000)	—	510,000	January 29, 2025
2016	2.00	—	260,000	—	—	—	260,000	February 2, 2026
2016	2.00	—	32,000	—	(10,000)	—	22,000	February 2, 2026***
2016	1.80	—	810,000	—	—	—	810,000	August 3, 2026
2016	1.89	—	300,000	—	—	—	300,000	September 13, 2026
2016	2.04	—	300,000	—	—	—	300,000	September 16, 2026
Total		1,792,000	1,702,000	(46,666)	(150,001)	(260,000)	3,037,333	

* 200,000 directors' options with an expiry date on September 18, 2011 were extended for five years to September 18, 2016 (40,000 of these options expired during 2015)

19. Share-based payments charge (Continued)

** Options granted to agents upon closing of a placing or financing facility.

***Options granted under the EMI Scheme.

****Valued based on fair value of services received.

The average fair value at grant date, by year of grant and plan, of the exercisable options as per December 31, 2016 is presented in the below table.

Year of issue	EMI Scheme	Unapproved Scheme
2012	0.63 - 1.20	—
2013	0.83	0.79 - 0.95
2014	0.76	0.23 - 0.76
2015	0.57	0.57
2016	1.35	0.93 - 1.35

Outstanding and exercisable share options by scheme as of December 31, 2016:

Plan	Outstanding	Exercisable	Weighted average exercise price in £ for Outstanding	Weighted average exercise price in £ for Exercisable
Unapproved	2,790,000	616,667	1,78	1.65
EMI	247,333	180,666	2.90	3.37
Total	3,037,333	797,333	1.87	2.04

The options outstanding at December 31, 2016 had a weighted average remaining contractual life of 8.2 years (2015: 6.6 years). For 2015 and 2016, the number of options granted and expired and the weighted average exercise price of options were as follows:

	Number of options	Weighted average exercise price (£)
At January 1, 2015	1,203,114	2.12
Options granted in 2015:		
Employees	312,000	1.25
Directors	340,000	1.25
Options expired in the year	(63,114)	2.71
At December 31, 2015	1,792,000	1.78
Exercisable at December 31, 2015	846,666	2.24

19. Share-based payments charge (Continued)

	Number of options	Weighted average exercise price (£)
At January 1, 2016	1,792,000	1.78
Options granted in 2016:		
Employees	1,002,000	1.92
Directors	700,000	2.05
Options exercised in the year	(46,666)	1.12
Options forfeited in the year	(150,001)	1.24
Options expired in the year	(260,000)	2.46
At December 31, 2016	3,037,333	1.87
Exercisable at December 31, 2016	797,333	2.04

20. Assumed contingent obligation related to the business combination

The value of the assumed contingent obligation as of December 31, 2016 amounts to £802 thousand. (2015: £594 thousand). The increase in value of the assumed contingent obligation during 2016 amounted to £208 thousand (2015: £72 thousand) and was recorded as finance expense. Periodic remeasurement is triggered by changes in updated timelines of achieving commercialization and updated probabilities of success resulting from clinical programs. In 2016 remeasurement was triggered by the success of the results of the Company's Phase 2a clinical trials which were presented in March 2016. The discount percentage applied is 12%.

	2015 £	2016 £
January 1, 2016	521,650	593,941
Re-measurement of assumed contingent obligation	9,239	123,554
Unwinding of discount factor	63,052	84,710
December 31, 2016	593,941	802,205

The table below describes the reported change to the value of the liability during 2016 of £208 thousand (2015: £72 thousand) compared to what this number would be following the presented variations to the underlying assumptions:

	2015	2016
Change in value of the assumed contingent obligation, in £ thousand	£72	£208
1% lower discount rate %	£73	£216
1% higher discount rate %	£71	£201
10% lower revenue assumption	£69	£202
10% higher revenue assumption	£75	£215
1% lower risk assumption	£70	£216
1% higher risk assumption	£75	£201

21. Warrants

Pursuant to the July Placement the Company issued 31,115,926 units to new and existing investors at the placing price of £1.4365 per unit. Each unit comprises 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 120% of the placing price or £1.7238. The warrant holders can opt for a cashless exercise of their warrants. The warrant holders can choose to exchange the warrants held for 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 shares. The warrants were therefore classified as a derivative financial liability, since their exercise might result into a variable number of shares to be issued.

The warrants entitle the investors to subscribe for in aggregate a maximum of 12,446,370 shares. The warrants can be exercised on the earlier of the consummation of the Global Offering or the first anniversary of the grant, and the exercise period shall end on the fifth anniversary of such date.

The ordinary share and warrant were accounted for as a compound financial instrument. The warrants component of the instrument issued at the July Placement were classified as a derivative financial liability and were initially measured at fair value of £8,991 thousand. The residual amount of proceeds totaling £35,707,235 has been recognized within equity. Subsequently the financial liability was re-measured at the reporting date at fair value through profit or loss. A change in fair value of £1,068 thousand is recognized in the Consolidated Statement of Comprehensive Income within finance income.

The residual value of the proceeds less the fair value of the financial instrument of £8,991 thousand was attributed to the equity component of the instrument.

The total of transaction costs the Company incurred for the above transactions amounted to £2,910 thousand of which £585 thousand was allocated to the warrants and the remaining £2,325 thousand has been presented as a reduction to share premium, by reference to the proceeds allocated to each component. The amount assigned to the financial liability of the warrants was subsequently presented as finance expense in the Consolidated Statement of Comprehensive Income.

The table below presents the assumptions in applying the Black-Scholes model to determine the fair value of the warrants at date of recognition and the reporting date of December 31, 2016. For valuation purposes at recognition the Company used the closing share price on July 29, 2016.

Issued in 2016	At recognition on July 29, 2016	At December 31, 2016
Warrants	12,446,370	12,446,370
Exercise price	£1.7238	£1.7238
Risk-free interest rate	0.039%	0.088%
Expected life of options	2.86 years	2.43 years
Annualized volatility	82.61%	73.53%
Dividend rate	0.00%	0.00%

The figures disclosed above relating to the issue of the shares and warrants have been retrospectively adjusted to reflect the 50-for-1 share consolidation as described in note 23. The original number of units issued to new and existing investors was 1,555,796,345 units at a placing price of 2.873 pence per unit

21. Warrants (Continued)

and an exercise price of 3.4476 pence per share. This entitled the investors to subscribe for in aggregate a maximum of 622,318,538 shares.

As per the reporting date the Company updated the underlying assumptions and calculated a fair value of these warrants amounting to £7,923 thousand. The variance of £1,068 thousand is recorded as finance income in the Consolidated Statement of Comprehensive Income.

	Derivative financial instrument	Total
	£	£
At January 1, 2016	—	—
Derivative Financial instrument issued following the July Placement	8,990,794	8,990,794
Fair value adjustments recognized in profit or loss	(1,068,191)	(1,068,191)
At December 31, 2016	7,922,603	7,922,603

For the amount recognized at December 31, 2016, the effect, when some of these underlying parameters would deviate up or down, is presented in the below table.

	Volatility (up / down 10% pts)	Time to maturity (up / down 6 months)
	£	£
Variable up	8,972,313	8,686,827
Base case, reported fair value	**7,922,603**	**7,922,603**
Variable down	6,825,999	7,046,248

22. Financial commitments

As of December 31, 2016, the Group was committed to making the following payments under non-cancellable operating leases related to its facilities.

	Land and Buildings	Land and Buildings
	2015	2016
	£	£
Operating leases which expire:		
Within one year	151,240	270,350
Beyond one year	—	—
Total	151,240	270,350

23. Events after the reporting date

On February 8, 2017 the board of the Company approved a share consolidation where every 50 existing ordinary shares of £0.001 each shall be consolidated into one ordinary share of £0.05. Prior to the consolidation the total number of issued shares as at December 31, 2016 would read as a total of 2,568,053,160 shares and after the consolidation this number would read as a total of 51,361,063 shares. Earnings per share information in these consolidated financial statements has been retrospectively adjusted, to reflect the consolidation as if it had occurred at the beginning of the earliest period presented.

47,399,001 Ordinary Shares

(including Ordinary Shares in the form of American Depositary Shares)

PROSPECTUS

Jefferies **Stifel**

Wedbush PacGrow

SunTrust Robinson Humphrey

April 26, 2017

Through and including May 21, 2017 (25 days after the date of this prospectus), all dealers that buy, sell or trade ADSs or ordinary shares, whether or not participating in the global offering, may be required to deliver a prospectus. This delivery requirement is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.